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Hypoxia parameters, physical variables, and severity of obstructive sleep apnea

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Abstract

Objective: To determine the relation between hypoxia and physical parameters in patients who had different levels of severity of obstructive sleep apnea (OSA).

Methods: This was a retrospective, cross-sectional study of 259 men who were evaluated with overnight polysomnography. Severity of OSA was graded based on the apnea-hypopnea index (AHI): normal/simple snoring (n=31); mild OSA (n=70); moderate OSA (n=63); severe OSA (n=95). Patients with different severity were divided into subgroups, based on having the lowest or highest values of the total sleep time with oxygen saturation <90% (ST_{90}) or minimum oxygen saturation (min SaO_2).

Results: Median AHI was 20.4 events/hour. Univariate analysis showed that ST_{90} was correlated with AHI (r=0.772; p≤0.001) and Epworth sleepiness scale (ESS) (r=0.344; p≤0.001), and min SaO_2 was inversely correlated with AHI (r=-0.748; p≤0.001) and ESS (r=-0.319; p≤0.001). Multivariate linear regression showed that ST_{90} was independently associated with AHI, ESS, and neck circumference, and min SaO_2 was independently inversely associated with AHI, ESS, and body mass index (BMI). In patients who had severe OSA, the subgroups which had lowest and highest min SaO_2 differed significantly in BMI, modified Mallampati score, neck and waist circumferences, and retroglossal Müller grade. In patients with percentage of sleep time with oxygen saturation below 90% (CT_{90}) <10%, the upper limit of ST_{90} was 36 minutes and corresponded to 70% lower limit of min SaO_2.

Conclusion: Hypoxia parameters show significant variation in OSA severity categories. None of the physical parameters had clinically useful relations with hypoxia parameters in OSA patients except patients who had severe OSA.

Keywords: Apnea-hypopnea index, oxygen saturation, physical parameters.

Özet: Hipoksi parametreleri, fiziksel değişkenler ve obstrüktif uyku apnesinin şiddet derecesi

Amaç: Farklı şiddet derecesinde obstrüktif uyku apnesi (OUA) olan hastalarda hipoksiyle fiziksel parametreler arasındaki ilişkinin belirlenmesi.

Yöntem: Bu çalışma bir gecelik polisomnografik incelemeyle değerlendirilmiş 259 erkekte uygulanan retrospektif çapraz kesitsel bir çalışmadır. OUA'nın şiddet derecesi apne/hipopne indeksine (AHİ) göre derecelendirildi: normal/basit horlama (n=31); hafif derecede OUA (n=70); orta derecede OUA (n=63); şiddetli derecede OUA (n=95). Farklı şiddet derecesinde OUA'sı olan hastalar, oksijen satürasyonu <%90 (ST_{90}) veya minimal oksijen satürasyonu (min SaO_2) olan en uzun veya en kısa toplam uyku süresine göre altgruplara ayrıldı.

Bulgular: Ortalama AHİ 20.4 olay/saat idi. Tek değişkenli analize göre ST_{90}, AHİ (r=0.772; p≤0.001) ve Epworth uykululuk ölçeği (ESS) (r=0.344; p≤0.001) ile korelasyon gösterirken min SaO_2, AHI (r=-0.748; p≤0.001) ve ESS (r=-0.319; p≤0.001) ile tersine korelasyon gösterdi. Çok değişkenli doğrusal regresyon modelinde ST_{90} bağımsız olarak AHİ, ESS ve boyun çevresiyle korele idi, min SaO_2 ise bağımsız olarak AHİ, ESS ve vücut kitle indeksi (VKİ) ile ilişkiliydi. Ağır derecede OUA geçiren hastalarda en düşük ve en yüksek min SaO_2'si olan altgruplarda VKİ, modifiye Mallampati skoru, boyun ve bel çevresi ve retroglossal Müller derecesi anlamlı derecede farklıydı. Oksijen satürasyonu <%90 ile karakterize uyku zamanı yüzdesi (CT_{90}) <%10 hastalarda, ST_{90}'ın üst sınırı 36 dakika olup min SaO_2'nin alt sınırının %70'ine tekabül etmekteydi.

Sonuç: Hipoksi parametreleri OUA şiddet derecesi kategorilerine göre anlamlı değişiklikler göstermektedir. Fiziksel parametrelerin hiçbiri şiddetli OUA geçiren hastalar dışında OUA hastalarında hipoksi parametreleriyle klinik açıdan yararlı ilişkiler içinde değildir.

Anahtar sözcükler: Apne hipopne indeksi, oksijen satürasyonu, fiziksel parametreler.

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Pharyngeal airway closure in obstructive sleep apnea (OSA) may involve multiple sites including the retropalatal or retroglossal airways.[1–3] There is a fine balance between the neurophysiologic feedback mechanisms and the absolute anatomic patency of the airway during sleep.[4] However, no medical history and/or anatomic parameters may distinguish patients with OSA from patients with snoring. Therefore, patients with snoring should be evaluated at a minimum by a nocturnal screening test for OSA.[5]

The apnea-hypopnea index (AHI) is the frequency of apnea and hypopnea episodes per hour of sleep, regardless of duration and morphology of the episodes. Patients who have similar AHI may have different duration of breathing cessation and depth of oxygen desaturation. These differences may affect the degree of OSA.[6] Therefore, the pathology of OSA is complex, with contributions from a structurally small airway and inadequate neuromuscular compensation during sleep.[7] Regardless of the cause, upper airway collapse may cause chronic intermittent hypoxia, oxidative stress, chronic inflammation, and detrimental effects on cardiovascular, neurocognitive, and metabolic function.[8,9] However, there is no widely accepted quantitative clinical test to measure the severity of hypoxia.[6]

In the present study, we divided the patients who had different severity of OSA into subgroups based on the values of total sleep time with oxygen saturation <90% (ST_{90}), and minimum oxygen saturation (min SaO_2). We hypothesized that there may be differences in the severity of hypoxia parameters and physical abnormalities in patients who have similar AHI. The purpose of this study was to determine the relation between hypoxia and physical parameters on the severity of OSA, and the clinical importance of this relation for treatment.

Materials and Methods

Subjects

In this retrospective, cross-sectional study, consecutive patients were included who had OSA syndrome and simple snoring, who were evaluated in the Department of Otolaryngology-Head and Neck Surgery, Faculty of Medicine, Başkent University Hospital from 2012 to 2015. Patients who were evaluated with overnight polysomnography met the inclusion criteria (259 men, 0 women; age: mean, 46±11 years; range, 20–79 years). Other patients were excluded due to severe chronic hepatic, cardiac, or renal failure, abnormal lung function, or other sleep disorders. The study was classified as exempt from review by the local institutional review board because the study was designed to collect data during standard treatment of OSA.

Evaluation

All patients had a clinical history and physical and otolaryngology examination including (1) determination of body mass index (BMI), (2) measurement of neck and waist circumference, (3) oropharyngeal examination including determination of modified Mallampati (MMP) grade, (4) Müller maneuver (forced inspiratory suction with mouth and nose closed) with fiberoptic endoscopy to determine retropalatal and retroglossal grade, (5) determination of Epworth sleepiness scale (ESS), and (6) polysomnography. Patients were evaluated for hypertension, other cardiovascular diseases, diabetes mellitus, hypothyroidism, nasal obstruction, and allergic rhinitis. Nasal and pharyngeal configurations were assessed semiquantitatively. Each patient performed the Müller maneuver in the seated position to estimate the degree of obstruction at the base of the tongue and soft palate. All otolaryngology examinations were performed and graded by one examiner [SA] (Table 1).

The BMI was calculated as body weight (kg) divided by the square of body height (m) and graded (Table 1). Neck circumference was measured at the level of the cricothyroid membrane. Waist circumference was measured at the level of the umbilicus. Tonsil size was classified (Table 1). The oral cavity was inspected for the relative position of the palate and base of the tongue; patients were asked to open the mouth with the tongue relaxed, and examination findings were assessed and graded with MMP score (Table 1). Nasal examination was performed with anterior rhinoscopy using a speculum, with the patient seated and the head tilted slightly backward, and findings were graded according to septal deviation, inferior turbinate hypertrophy, or other nasal obstructive pathology (Table 1).

The upper airway was evaluated with fiberoptic endoscopy through the nose with the subject seated erect and the head and neck placed in neutral position by aligning the Frankfurt plane between the infraorbital rim of the tragus of the external ear parallel to the floor. Topical nasal anesthesia was achieved with 10% lidocaine spray. The fiberoptic endoscope was passed through a nostril and advanced until the epiglottis was well visualized. The Müller maneuver was performed, and the endoscope was used to inspect the oropharynx (at the level of the uvula tip and nasopharynx) and hypopharynx (at the level of the supraglottis). The Müller maneuver was repeated ≥3 times until the patient had strong inspiratory suction. Upper airway collapse was graded at the retropalatal space (oropharynx) and retroglossal space (hypopharynx) with Müller grade (Table 1).

Table 1. Characteristics of patients who were included in the study of obstructive sleep apnea.*

Variables	Grade and definition	Value	
Age (y)		46±11	45 (20–79)
ST_{90} (min)		32±63	4.3 (0–337.4)
CT_{90} (%)		8±15	1.0 (0–75.6)
Min SaO_2 (%)		81±10	84.0 (41–96)
AHI (events/h)		28±23	20.4 (0.3–97.2)
BMI (kg/m^2)		32±5	31.1 (21.9–48.4)
Neck circumference (cm)		42±3	41.5 (35–51)
Waist circumference (cm)		107±11	106 (77–140)
ESS		10±6	10 (0–24)
OSA severity	(1) Normal / simple snoring: AHI <5	31	(12)
	(2) Mild OSA: 5 ≤ AHI < 15	70	(27)
	(3) Moderate OSA: 15 ≤ AHI < 30	63	(24)
	(4) Severe OSA: AHI ≥30	95	(37)
BMI (kg/m^2)	(1) Normal: BMI <25	19	(7)
	(2) Overweight: 25 ≤ BMI < 30	79	(31)
	(3) Obese: 30 ≤ BMI < 40	145	(56)
	(4) Morbidly obese: BMI ≥40	16	(6)
Tonsil size†	(0) Previous tonsillectomy	9	(4)
	(1) Inside tonsillar fossa lateral to posterior pillars	93	(36)
	(2) Occupying 25% to 50% of oropharynx	139	(54)
	(3) Occupying >50% to 75% of oropharynx	18	(7)
MMP	(1) Soft palate, pillars, and tonsils clearly visible	20	(8)
	(2) Uvula, pillars, and upper poles of tonsils visible	144	(56)
	(3) Only part of soft palate visible	87	(34)
	(4) Only hard palate visible	8	(3)
Nasal obstruction	Septal deviation and/or turbinate hypertrophy		
	(1) <25%	56	(22)
	(2) >25% to 50%	181	(70)
	(3) >50% to 75%	20	(8)
	(4) >75% to 100%	2	(0.8)
Retropalatal Müller grade	Collapse of pharyngeal walls		
	(1) <25%	40	(15)
	(2) >25% to 50%	83	(32)
	(3) >50% to 75%	74	(29)
	(4) >75% to 100%	62	(24)
Retroglossal Müller grade	(1) Vallecula completely visible	91	(35)
	(2) Vallecula partly visible	126	(49)
	(3) Tongue base touching epiglottis	38	(15)
	(4) Tongue base pushing epiglottis	4	(2)
ESS	(1) <11	147	(57)
	(2) 11 ≤ ESS ≤ 14	46	(18)
	(3) 14 < ESS ≤ 18	44	(17)
	(4) >18	22	(9)

*N=259 patients. Data reported as mean ± standard deviation, median (range: minimum to maximum), or number (%). †There were no patients who had grade 4 tonsil size. **AHI:** apnea-hypopnea index; **BMI:** body mass index; **CT_{90}:** percentage of cumulative sleep time with oxygen saturation <90%; **ESS:** Epworth sleepiness scale; **min SaO_2:** minimum oxygen saturation; **MMP:** modified Mallampati; **OSA:** obstructive sleep apnea; **ST_{90}:** total sleep time with oxygen saturation <90%.

Polysomnography

All study participants underwent polysomnography at the Başkent University Alanya Hospital Chest Disease Sleep Laboratory, using a computerized polysomnography device (Compumedics, E series, 44 channels, Victoria, Australia). The polysomnography study (16 channels) documented the following parameters: 4-channel electroencephalogram, electro-oculogram, submental and leg electromyogram, electrocardiogram, nasal airflow using nasal pressure cannula, airflow at the nose and mouth (thermistors), chest and abdominal respiratory movement, oxygen saturation (pulse oximetry), snoring microphone, and body position. All studies were interpreted by a sleep specialist who was blinded to participant characteristics. Apnea was defined as cessation of airflow for ≥10 seconds with continued effort (obstructive) or lack of effort (central) to breathe. Hypopnea was defined as >50% decrease in a valid measure of airflow without a requirement for associated oxygen desaturation or arousal, and with a lesser airflow reduction in association with oxygen desaturation >3%, or an arousal for ≥10 seconds. Sleep staging was performed according to American Academy of Sleep Medicine criteria (Table 1).[10]

Statistical analysis

Data analysis was performed with statistical software (IBM SPSS for Windows, Version 22.0, IBM Corp., Armonk, NY, USA). Continuous variables were reported as mean ± standard deviation or median (range, minimum to maximum). Categorical variables were reported as frequencies and percentages. Normality of the continuous variables was evaluated with Shapiro-Wilk test. Differences between the 2 groups according to continuous variables were determined with Mann-Whitney U test. Comparisons of >2 independent groups were performed with Kruskal-Wallis test. Pairwise comparisons were performed with Siegel-Castellan test. Relations between the continuous variables were determined with Spearman correlation coefficient. Multiple stepwise linear regression analysis was used to determine the factors affecting ST_{90} and min SaO_2. Statistical significance was defined by $p \leq 0.05$.

Results

Patients were middle aged men, and most patients had mild, moderate, or severe OSA (Table 1). Most patients were overweight or obese and had tonsils that occupied 25% to 50% of oropharynx (Table 1). The median AHI was 20.4 events/hour, ESS was 10, ST_{90} was 4.3 min; percentage of sleep time with oxygen saturation below 90% (CT_{90}) was 1.0%, and min SaO_2 was 84% (Table 1)

Univariate analysis showed significant correlations between ST_{90} and age, AHI, BMI, neck and waist circumferences, ESS, OSA severity, BMI categories, MMP, retropalatal and retroglossal Müller grades, and ESS grades (Table 2). Univariate analysis showed significant inverse correlations between min SaO_2 and age, AHI, BMI, neck and waist circumferences, ESS, OSA severity, BMI categories, MMP, retropalatal and retroglossal Müller grades, and ESS grades (Table 2).

Multivariate linear regression showed significant independent association between ST_{90} and AHI, ESS, and neck circumference (Table 3). The min SaO_2 was independently associated with AHI, ESS, BMI, and retropalatal and retroglossal Müller grades (Table 3).

When patients in each category of OSA severity were considered in subgroups who had the lowest (A) and highest (B) ST_{90} values, the median ST_{90} and CT_{90} were significantly different between subgroups A and B in all OSA severity categories (Table 4). Patient subgroups A and B also differed in median BMI (normal/simple snoring), AHI (mild and severe OSA), and ESS and MMP (severe OSA) (Table 4).

When patients in each category of OSA severity were considered in subgroups who had the lowest and highest min SaO_2 values, the median min SaO_2 and CT_{90} were significantly different between subgroups A and B in all OSA severity categories (Table 5). Patient subgroups A and B also differed in median AHI (normal/simple snoring), ESS (mild OSA), and AHI, ESS, BMI, MMP, neck and waist circumferences, and retroglossal Müller grade (severe OSA) (Table 5).

When patients were considered in subgroups who had CT_{90} <10% (n=205) and ≥10% (n=54), significant correlations between CT_{90} and ST_{90} and between CT_{90} and min SaO_2 were observed for CT_{90} <10% category (Figs. 1 and 2). In CT_{90} <10% category, the upper limit of ST_{90} was 36 minutes (Fig. 1). Only 1 of 205 patients showed min SaO_2 value <70% in the CT_{90} <10% category (Fig. 2). Three patients (5%) who had moderate OSA exceeded this threshold, but 51 of 95 patients (54%) who had severe OSA exceeded this threshold, therefore 54 patients were in CT_{90} ≥10% category.

Discussion

The traditional AHI and oxygen desaturation index parameters include the average number of apnea and hypopnea events per hour of sleep, regardless of duration and morphology of the apnea and hypopnea events that may have major effects on the induced physiologic stress.[11] Other workers suggested that the severity of OSA should be stratified by a combination of AHI and other hypoxia variables to explore the possible causes of the dissociation between the severity of hypoxemia and AHI in some OSA subjects.[12–14]

The ST_{90} and min SaO_2 are objective and easily available parameters that represent the duration and depth of nocturnal hypoxia. However, there is no consensus about the importance and superiority of these hypoxia parameters. A previous study about the clinical value of ST_{90} in the evaluation of chronic intermittent hypoxia in patients who had OSA showed a larger correlation coefficient between ST_{90} and AHI or ESS than min SaO_2.[12] In the present study, we

Table 2. Univariate analysis of factors affecting total sleep time with oxygen saturation <90% and minimum oxygen saturation.*

Variable		ST_{90}		min SaO_2	
		r	p≤†	R	p≤†
Age (y)		0.156	.02	-0.132	.04
Age (y)		0.156	.02	-0.132	.04
AHI (events/h)		0.772	.001	-0.748	.001
BMI (kg/m^2)		0.468	.001	-0.462	.001
Neck circumference (cm)		0.365	.001	-0.375	.001
Waist circumference (cm)		0.469	.001	-0.446	.001
ESS		0.344	.001	-0.319	.001
OSA severity	(1)	0.26 (0–6.93)	.001	90 (74–94)	.001
	(2)	0.83 (0–18.28)		87 (78–92)	
	(3)	4.83 (0.07–44.56)		83 (69–96)	
	(4)	45.5 (0.17–337.36)		75 (41–90)	
BMI (kg/m^2)	(1)	0.27 (0.03–68.96)	.001	89 (73–96)	.001
	(2)	1.3 (0–180.15)		86 (48–94)	
	(3)	7.88 (0.07–313.08)		83 (46–92)	
	(4)	51.77 (2.28–337.36)		73 (41–97)	
Tonsil size	(0)	36.82 (0.08–146.65)	NS	76 (68–93)	NS
	(1)	2.05 (0–261.76)		85 (41–96)	
	(2)	5.66 (0.03–337.36)		83 (46–93)	
	(3)	4.31 (0–122.08)		83 (70–90)	
MMP	(1)	0.88 (0.06–37.23)	.001	86 (75–92)	.001
	(2)	2.38 (0–313.08)		86 (46–96)	
	(3)	10 (0–337.36)		82 (41–93)	
	(4)	59.83 (10.2–145.16)		70 (48–81)	
Nasal obstruction	(1)	4.95 (0–286.03)	NS	84 (41–94)	NS
	(2)	4.56 (0–337.36)		84 (46–96)	
	(3-4)	1.14 (0.18–313.08)		86 (57–90)	
Retropalatal Müller grade	(1)	0.82 (0–36.82)	.002	87 (72–96)	.001
	(2)	2.28 (0–214.58)		86 (48–94)	
	(3)	6.81 (0–261.76)		83 (41–93)	
	(4)	18.90 (0–337.36)		80 (48–93)	
Retroglossal Müller grade	(1)	2 (0–168.2)	.001	86 (67–96)	.001
	(2)	3.95 (0–337.36)		84 (48–94)	
	(3)	16.47 (0.02–313.08)		79 (41–90)	
	(4)	83.61 (16.3–328.31)		70 (58–83)	
ESS	(1)	2 (0–222.81)	.002	86 (46–96)	.001
	(2)	3.95 (0–328.31)		85 (56–94)	
	(3)	11.07 (0.03–337.36)		81 (41–93)	
	(4)	111.16 (0.7–313.08)		66 (48–87)	

*Data reported as correlation coefficient r or median (range: minimum to maximum). †**NS:** not significant (p>0.05). **AHI:** apnea-hypopnea index; **BMI:** body mass index; **ESS:** Epworth sleepiness scale; min **SaO_2:** minimum oxygen saturation; **MMP:** modified Mallampati; **OSA:** obstructive sleep apnea; **ST_{90}:** total sleep time with oxygen saturation <90%.

observed a slightly higher absolute value of the correlation coefficient between ST_{90} and AHI or ESS than between min SaO_2 and AHI or ESS (Table 2). Another study showed that ST_{90} was strongly correlated with AHI and total apnea duration (r=0.770 and 0.776).[13] Furthermore, other workers showed that, after adjustment for BMI and other cardiovascular risk factors, ST_{90} was the strongest independent predictor of high-sensitivity C-reactive protein elevation, which is associated with OSA severity; the severity of OSA may be better stratified by combining AHI and nocturnal chronic intermittent hypoxia variables, such as ST_{90} and oxygen desaturation index, instead of AHI alone.[14]

In contrast, the 2007 American Academy of Sleep Medicine Manual for the Scoring of Sleep and Associated

Table 3. Multivariate linear regression of factors affecting total sleep time with oxygen saturation <90% and minimum oxygen saturation.*

Variable	Variable	r (95% CI)	p≤	R^2 (%)
ST_{90}	AHI	1.724 (1.468 to 1.981)	.001	55
	ESS	1.738 (0.719 to 2.756)	.001	
	Neck circumference	2.110 (0.020 to 4.201)	.05	
min SaO_2	AHI	-0.288 (-0.332 to -0.244)	.001	61
	ESS	-0.208 (-0.359 to -0.058)	.007	
	BMI	-0.238 (-0.428 to -0.048)	.02	
	Retropalatal Müller grade	0.976 (0.093 to 1.859)	.03	
	Retroglossal Müller grade	-1.231 (-2.387 to -0.075)	.04	

*Data reported as correlation coefficient r (95% confidence interval). **AHI:** apnea-hypopnea index; **BMI:** body mass index; **ESS:** Epworth sleepiness scale; **min SaO_2:** minimum oxygen saturation; **ST_{90}:** total sleep time with oxygen saturation <90%.

Table 4. Relation between measured variables and severity of obstructive sleep apnea for patients who had lowest and highest total sleep time with oxygen saturation <90%.*

Variable	Normal / simple snoring			Mild OSA			Moderate OSA			Severe OSA		
Subgroup	A	B	p≤†	A	B	p≤†	A	B	p≤†	A	B	p≤†
No. of patients	15	16		35	35		32	31		48	47	
ST_{90} (min)	0.13 (0–0.23)	0.7 (0.3–7)	.001	0.45 (0–0.8)	2.3 (1–18)	.001	1.6 (0.1–4.8)	13.4 (5–45)	.001	13.2 (0.2–47)	122 (49–337)	.001
CT_{90} (%)	0.03 (0–0.07)	0.25 (0–1.7)	.001	0.11 (0–0.2)	0.56 (0–5)	.001	0.3 (0–1.3)	2.9 (0–10)	.001	3.7 (0.04–19)	32.2 (11–75)	.001
AHI (events/h)	1.4 (0.3–4.4)	2.75 (0.8–4.9)	NS	8.7 (5–14.3)	11.4 (5–14)	.005	19.5 (15–28)	22.5 (15–28)	NS	42.7 (30.3–93)	67.9 (30–97)	.001
ESS	10 (0–17)	10 (0–17)	NS	8 (0–19)	9 (2–22)	NS	7.5 (0–19)	10 (0–18)	NS	10 (0–21)	15 (1–24)	.002
Age (y)	39 (20–66)	43 (26–73)	NS	42 (26–69)	44 (25–75)	NS	43 (30–66)	47 (26–74)	NS	49 (23–79)	46 (30–67)	NS
BMI (kg/m^2)	26 (21.9–29.6)	28.2 (22–42)	.05	29.9 (23–37)	30 (22–35)	NS	30 (25.3–42)	32.1 (23–41)	NS	32.95 (24–46)	34.1 (24–48)	NS
Tonsil size	1 (0–2)	2 (1–2)	NS	2 (0–3)	2 (1–2)	NS	2 (1–3)	2 (0–3)	NS	2 (0–3)	2 (0–3)	NS
MMP	2 (1–3)	2 (1–3)	NS	2 (1–3)	2 (1–3)	NS	2 (1–3)	2 (1–4)	NS	2 (1–4)	3 (2–4)	.04
Neck circumference (cm)	39.5 (36.5–42)	39.7 (36–46)	NS	41 (36–45)	40 (36–46)	NS	41 (37–45)	42 (35–48)	NS	42 (36–49)	43.5 (37–51)	NS
Waist circumference (cm)	97 (77–107)	106 (84–124)	.03	102 (84–118)	105 (86–124)	NS	105 (93–138)	110 (88–130)	NS	110 (96–140)	113 (88–140)	NS
Nasal obstruction grade	2 (1–3)	2 (1–3)	NS	2 (1–3)	2 (1–3)	NS	2 (1–3)	2 (1–2)	NS	2 (1–3)	2 (1–4)	NS
Retropalatal Müller grade	2 (1–4)	2 (1–4)	NS	2 (1–4)	2 (1–4)	NS	3 (1–4)	3 (1–4)	NS	3 (1–4)	4 (2–4)	NS
Retroglossal Müller grade	2 (1–2)	2 (1–3)	NS	2 (1–3)	1 (1–3)	NS	1 (1–3)	2 (1–3)	NS	2 (1–4)	2 (1–4)	NS

*Data reported as median (range: minimum to maximum). The subgroups A and B contained patients with lowest and highest ST_{90} values in the OSA severity category. †**NS:** not significant (p>0.05). **AHI:** apnea-hypopnea index; **BMI:** body mass index; **CT_{90}:** percentage of cumulative sleep time with oxygen saturation <90%; **ESS:** Epworth sleepiness scale; **MMP:** modified Mallampati; **OSA:** obstructive sleep apnea; **ST_{90}:** total sleep time with oxygen saturation <90%.

Events recommended that nocturnal hypoxia should be classified by min SaO_2,[10] and no changes in terminology or measurement in oxygen saturation (SpO2) were recommended in the 2012 update.[15] Nocturnal min SaO_2 may be an independent predictor of future carotid plaque burden, and other nocturnal SaO_2 parameters are not associated with carotid intima or media thickness or plaques, after adjusting for traditional cardiovascular disease risk factors.[16]

By analyzing both parameters separately in the present study, we observed that ST_{90} and min SaO_2 were both associated independently with AHI and ESS (Table 3). Furthermore, ST_{90} was independently associated with neck circumference, and min SaO_2 was independently associated with BMI (Table 3). Although the reliability of flexible pharyngoscopy with the Müller maneuver is controversial and potentially subjective, we observed an independent association between min SaO_2 and both retropalatal and retroglossal Müller grades.

A previous study evaluated the diagnostic potential of several novel parameters incorporating number, duration, and morphology of individual apnea and hypopnea events with complex formulas, to improve on limitations of the traditional AHI.[11] To provide clinically useful informa-

Table 5. Relation between measured variables and severity of obstructive sleep apnea for patients who had lowest and highest minimum oxygen saturation.*

Variable	Normal / simple snoring			Mild OSA			Moderate OSA			Severe OSA		
Subgroup	A	B	p≤†	A	B	p≤†	A	B	p≤†	A	B	p≤†
No. of patients	15	16		35	35		32	31		48	47	
Min SaO_2 (min)	87 (74–90)	92 (90–94)	.001	85 (78–86)	88 (86–90)	.001	81 (69–84)	87 (84–96)	.001	65.5 (41–75)	82 (75–90)	.001
CT_{90} (%)	0.2 (0–1.7)	0.04 (0–0.3)	.001	0.42 (0–5.4)	0.15 (0–1.7)	.001	2.5 (0.1–10.4)	0.3 (0–7.5)	.001	31.4 (3.9–75.5)	2.9 (0.02–37.9)	.001
AHI (events/h)	3.6 (0.8–4.9)	1.4 (0.3–4.4)	.003	10.5 (5.5–14)	9 (5–14.3)	NS	22.5 (15–28)	19.3 (15–28)	NS	63.8 (38.6–97)	41.5 (30.1–93)	.001
ESS	10 (0–17)	10 (3–17)	NS	9 (0–22)	9 (2–19)	.03	8 (0–18)	9 (0–19)	NS	15 (3–24)	10 (0–21)	.001
Age (y)	43 (26–73)	41 (20–66)	NS	45 (25–75)	41 (26–69)	NS	45 (26–66)	47.5 (31–74)	NS	44.5 (30–72)	48 (23–79)	NS
BMI (kg/m²)	27.7 (22–42)	26.1 (22–32)	NS	30.5 (23–35)	29.6 (22–37)	NS	32 (26–42)	30.8 (23–41)	NS	34.5 (24.4–48.4)	32.4 (24.1–41)	.002
Tonsil size	2 (1–2)	1 (0–2)	NS	2 (1–3)	1 (0–3)	NS	2 (0–3)	2 (1–3)	NS	2 (0–3)	2 (0–3)	NS
MMP	2 (1–3)	2 (1–3)	NS	2 (1–3)	2 (1–3)	NS	2 (1–4)	2 (1–3)	NS	3 (1–4)	2 (2–4)	.002
Neck circumference (cm)	39 (36–46)	39.7 (36–44)	NS	40 (36–45)	41 (36–46)	NS	42 (38–48)	41.7 (35–45)	NS	43.5 (39–51)	42 (36–49)	.001
Waist circumference (cm)	105 (84–124)	96.5 (77–113)	NS	104 (84–124)	102 (86–118)	NS	107 (92–138)	106 (88–130)	NS	114 (88–140)	110 (90–132)	.004
Nasal obstruction grade	2 (1–3)	2 (1–3)	NS	2 (1–3)	2 (1–3)	NS	2 (1–3)	2 (1–3)	NS	2 (1–4)	2 (1–4)	NS
Retropalatal Müller grade	2 (1–4)	2 (1–4)	NS	2 (1–4)	2 (1–4)	NS	3 (1–4)	2.5 (1–4)	NS	3 (1–4)	3 (2–4)	NS
Retroglossal Müller grade	2 (1–3)	1.5 (1–2)	NS	2 (1–3)	2 (1–3)	NS	2 (1–3)	1 (1–3)	NS	2 (1–4)	2 (1–4)	.004

*Data reported as median (range: minimum to maximum). The subgroups A and B contained patients with lowest and highest min SaO_2 values in the OSA severity category. †**NS:** not significant ($p>0.05$). **AHI:** apnea-hypopnea index; **BMI:** body mass index; **CT_{90}:** percentage of cumulative sleep time with oxygen saturation <90%; **ESS:** Epworth sleepiness scale; **min SaO_2:** minimum oxygen saturation; **MMP:** modified Mallampati; **OSA:** obstructive sleep apnea.

tion, we used a similar grouping system with easily available, objective hypoxia parameters ST_{90} and min SaO_2.

In patients within the OSA severity categories who were divided into subgroups A and B based on the values of ST_{90} and min SaO_2, both ST_{90} and min SaO_2 showed significant variation within OSA severity categories (Tables 4 and 5). However, we observed no significant differences in most physical variables between subgroup A and B in mild and moderate OSA (Tables 4 and 5). In contrast, in the severe OSA category, the subgroups A and B based on min SaO_2 differed significantly in several physical variables including BMI, MMP, neck and waist circumference and retroglossal Müller grades (Table 5). However, in severe OSA category, according to the ST_{90}, comparison of A and B subgroups showed no significant differences in physical variables aside from MMP grade (Table 4). Although all these patients were in the same (severe) OSA category, both hypoxia severity and physical abnormalities were associated with large variation in min SaO_2. These results suggest that severity of the physical abnormalities may be associated with the depth more than duration of hypoxia in severe OSA. The clinical utility of these findings may be interpreted by the success of surgical treatment in severe OSA.

In a study of 90 severe OSA patients who underwent multilevel surgery including modified tongue base suspension combined with uvulopharyngopalatoplasty, the ST_{90} may have enabled better identification of patients in whom surgical success was probable. The ST_{90} ≤36 min may be the best cutoff value for surgical success. They reported that surgical success was 100% in patients who had ST_{90} ≤36 min, but only 8% in patients who had ST_{90} >36 min.[17] However, another study of 119 OSA patients who underwent velopharyngeal surgery, including uvulopharyngopalatoplasty with transpalatal advancement pharyngoplasty, showed that CT_{90} rather than AHI was an independent predictor of surgical success.[18] It may be useful to categorize CT_{90} into level variables containing 4 levels (CT_{90}: grade 1, <10; grade 2, 10–20; grade 3, 20-40; grade 4 ≥40).[18]

Similar hypoxia levels were observed in both studies[17,18] as cutoff value of surgical success. In CT_{90} <10% category, the upper limit of ST_{90} was 36 minutes (Fig. 1). Furthermore, in the present study, only 1 of 205 patients showed min SaO_2 value < 70% in the CT_{90} <10% category (Fig. 2). These findings suggested that there is a relation between hypoxia parameters. It can be extrapolated that the cutoff value for CT_{90} <10% may correspond to

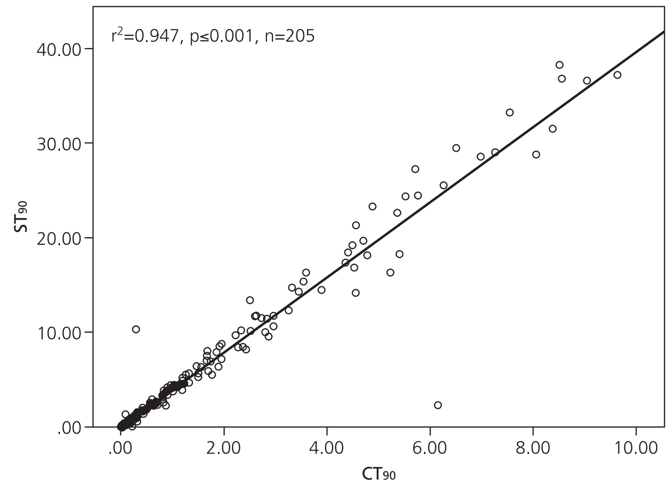

Fig. 1. Relation between percentage of cumulative sleep time with oxygen saturation <90% (CT_{90}) and sleep time with oxygen saturation <90% (ST_{90}). Variation of ST_{90} with CT_{90} in CT_{90} <10% category.

ST_{90} 36 min, and correspond to min SaO_2 70%. Surgical success rate may decrease markedly when this hypoxia threshold is exceeded, possibly because the balance between neurophysiologic feedback mechanisms and the absolute anatomic patency of the airway during sleep may be impaired remarkably beyond this threshold. In the present study, only 3 patients who had moderate OSA and 51 of 95 patients who had severe OSA exceeded this threshold (CT_{90} ≥10%).

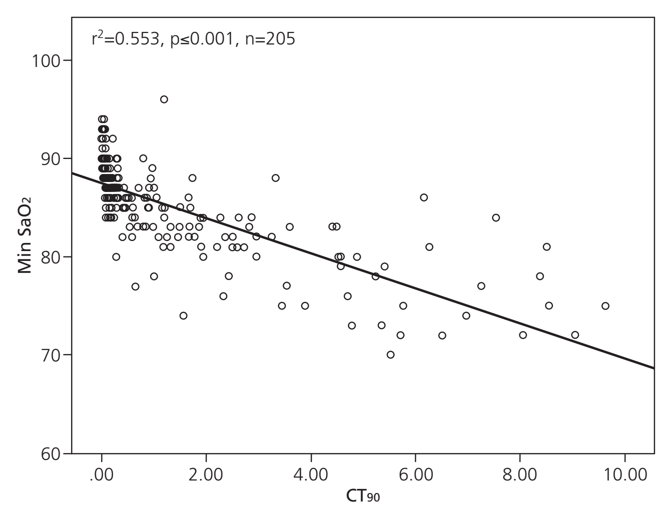

Fig. 2. Relation between percentage of time with oxygen saturation <90% (CT_{90}) and minimum oxygen saturation (min SaO_2). Variation of min SaO_2 with CT_{90} in CT_{90} <10% category.

Limitations of the present study include the retrospective design and potential for selection and referral bias associated with a single-institution analysis. In addition, the study lacked the follow-up data and analysis of other possible confounders such as anthropometric measurements, comorbidities, smoking, and inflammatory markers. Furthermore, the results may not be extended to women because the study included only men.

Conclusion

Hypoxia parameters (ST_{90}, CT_{90}, and min SaO_2) show significant variation within OSA severity categories and may provide useful information to clinicians about OSA disease severity and risk of health consequences. None of the physical parameters had clinically useful relations with hypoxia parameters in OSA patients except patients who had severe OSA. According to previously published[17,18] hypoxia thresholds, the probability of surgical success may be high for mild, moderate, and some severe OSA patients. However, for some moderate and severe OSA patients, surgical success may be limited, and these patients may be differentiated by hypoxia parameters. Clinicians should be aware of the relations between different hypoxia parameters to interpret study results and create appropriate treatment strategies.

Conflict of Interest: No conflicts declared.

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