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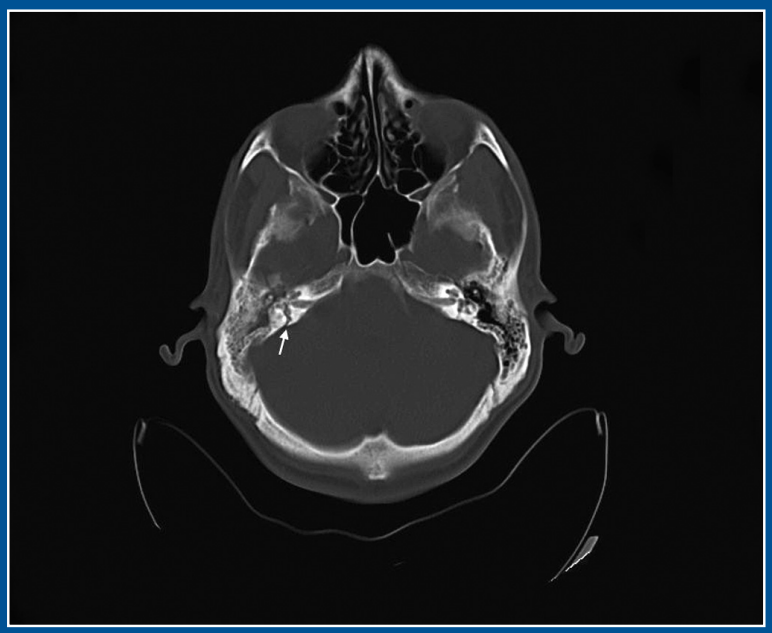

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Description

ENT Updates (formerly Journal of Medical Updates), is a periodical of the Continuing Education, and Scientific Research Association (CESRA), Turkey, which is published in both printed (p-ISSN 2149-7109) and electronic (e-ISSN 2149-6498) versions three times a year on April, August, and December. A peer-reviewed system is used to select manuscripts. The language of the journal is English. The journal is currently indexing and abstracting in Emerging Sources Citation Index (ESCI) by Thomson Reuters, TUBITAK ULAKBIM Turkish Medical Index, Proquest, EBSCO Host, Index Copernicus and Google Scholar.

Aims and Scope

The goal of the journal is to present and improve collective scientific knowledge and the scientific background dealing with otorhinolaryngological disorders and related subjects (allergy, pediatrics, neurology, psychiatry, neurosurgery, radiology, anesthesiology, pulmonology, etc.) via experimental and clinical studies, reviews, case reports, short communications and letters to the editor. The initial aim of this journal is to form a countrywide education platform and to share the recent information and learn about the treatment of various local or rare diseases in aware of the fact that a disease may be rare to a certain region while it is very common to another. The second aim of this journal and Continuous Education and Scientific Research Association (CESRA), a nonprofit organization serving for continuous education, is to represent our country in international arena of science and knowledge with the published papers. We aimed to undertake a novel effort in the international representation and attribution of published articles. That is why we have set an international editorial board from all over the world beside the national board spread to each corner of the country. The target readers of the ENT Updates include otorhinolaryngology specialists and residents as well as all other physicians working in the field of otorhinolaryngology or in related specialities.

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Clinical Research

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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 stud-

ies 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/m²)		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/m²)	(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 (SpO_2) 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/m^2)	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

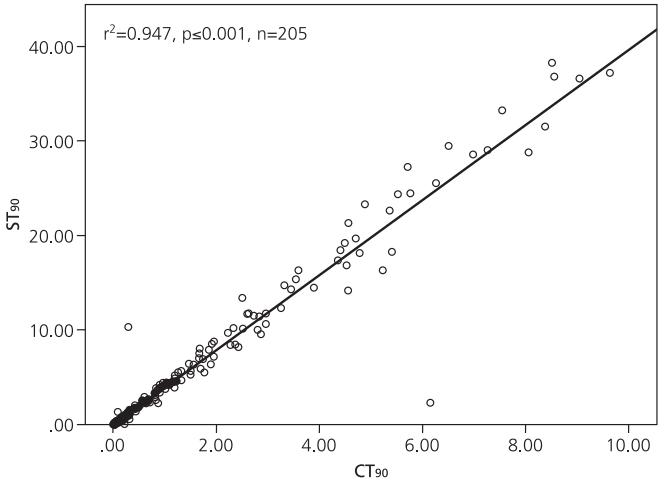

Fig. 1. Relation between percentage of cumulative sleep time with oxygen saturation <90% (CT_{90}) and sleep time with oxygen saturation <90% (ST_{90}). Variation of ST_{90} with CT_{90} in CT_{90} <10% category.

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%).

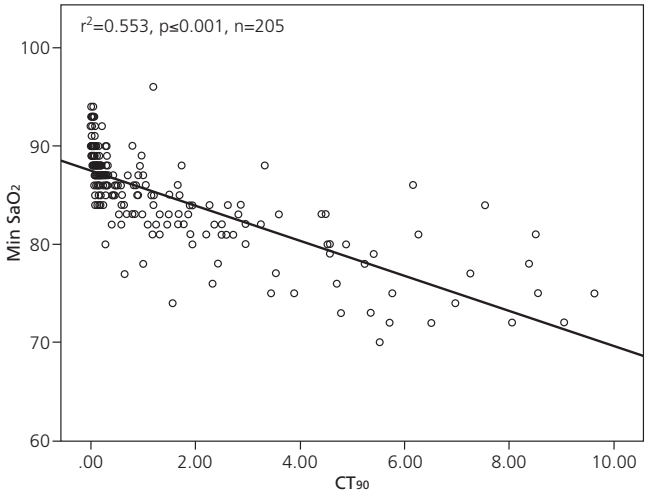

Fig. 2. Relation between percentage of time with oxygen saturation <90% (CT_{90}) and minimum oxygen saturation (min SaO_2). Variation of min SaO_2 with CT_{90} in CT_{90} <10% category.

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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Nasal response after exercise in swimmers, runners and handball players

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Abstract

Objective: The aim of this study was to investigate the effects of different physical activities on nasal response.

Methods: Young non-professional university teams (male, 20 to 24 years old) were enrolled in this study. Nasal functions were measured with an active anterior rhinomanometry and the saccharine transport method (nasal transport times, NTT) before and immediately after the exercise. After the initial measurements, the first group swam 30 minutes in the swimming pool. The second group (outdoor runners) ran 10 kilometers in approximately 30 minutes. The third group played handball for 30 minutes. The initial findings were compared statistically with the data obtained after exercise.

Results: When the reductions in nasal resistance were compared before and after exercise, the inspiration and expiration values of all groups were statistically significant. These three groups were similar regarding the comparison of nasal resistance change percentages. When the NTTs were compared before and after exercise, the decreases in the amount of time were statistically significant in all these three groups after exercise. When the change percentages of the decrease in nasal transport time were compared, the decrease in handball players was statistically significant compared to runners.

Conclusion: Nasal resistance reductions and the decreases in NTT were not affected by the type of sports being played or the air quality of the environment.

Keywords: Nasal resistance, active anterior rhinomanometry, nasal transport times, running, swimming, handball.

Özet: Yüzücülerde, koşucularda ve hentbol oyuncularında egzersiz sonrası nazal yanıt

Amaç: Çalışmanın amacı nazal yanıt üzerine farklı fiziksel aktivitelerin etkilerini araştırmaktır.

Yöntem: Bu çalışmaya genç amatör üniversite takımları (erkek 20–24 yaşlarında) katıldı. Nazal fonksiyonlar bir aktif anterior rinomanometreyle ölçüldü ve egzersizden önce ve hemen sonra sakkarin transport yöntemi (nazal transport zamanı, NTZ) uygulandı. İlk ölçümlerden sonra birinci grup yüzme havuzunda 30 dakika yüzdü, ikinci grup (açık hava koşucuları) yaklaşık 30 dakikada 10 km koştu, üçüncü grup 30 dakika hentbol oynadı. İlk bulguları istatistiksel olarak egzersiz sonrası elde edilen verilerle karşılaştırıldı.

Bulgular: Egzersiz öncesi ve sonrası nazal dirençteki azalmalar karşılaştırıldığında, tüm grupların inspirasyon ve ekspirasyon değerleri istatistiksel açıdan anlamlı idi. Bu üç grup nazal direnç değişikliği yüzdeleri açısından benzerdi. Egzersiz öncesi ve sonrası NTZ'ler karşılaştırıldığında, bu üç grubun tümünde egzersizden sonra NTZ'de azalmalar istatistiksel açıdan anlamlı idi. Nazal transport zamanındaki yüzde azalmalar karşılaştırıldığında koşuculara göre hentbol oyuncularının NTZ'sindeki azalma da istatistiksel açıdan anlamlı idi.

Sonuç: Nazal direnç ve NTZ'deki azalmalar ortamdaki havanın kalitesi ve yapılan sporun cinsinden etkilenmemiştir.

Anahtar sözcükler: Nazal direnç, aktif anterior rinomanometre, nazal transport zamanları, koşma, yüzme, hentbol.

Exercise today is becoming more and more popular not only for in pursuit of a healthy life but for recreational purposes. Related to sympathetic activity that notably increases during exercise, nasal resistance decreases and the rate and depth of breathing increase.[1,2] To meet the air requirement that increases during exercise, mouth breathing starts and harmful particles in the air go deep inside the lungs easily without getting caught in the filtration of the nose.[2]

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Due to the increasing need for air during exercise, outdoor athletes like runners are exposed more to harmful substances in the air, such as carbon monoxide, nitrogen oxide, sulphur dioxide, ozone and emission-derived particulate matter, etc.[3,4] Among athletes who are chronically exposed to these harmful air pollutant particles, exercise-induced bronchospasm, asthma, airway damage, and allergic rhinitis are seen more frequently.[5,6] It might be thought as a rule that indoor athletes are affected less by air pollution. Although this is rare, in indoor exercising places like ice arenas, skating athletes might often experience carbon monoxide and nitrogen dioxide (NO_2) induced airway disorders caused by fossil-fueled resurfacing machines and exercise-induced bronchospasm.[7] Swimming is recommended, especially at schools, for pregnant women, overweight people, and people with vertebra disease. Swimmers are exposed to (chlorine) chloramine and NCl_3 gases used to disinfect pools.[8] As a result, swimmers experience asthma, allergic rhinitis, non-allergic rhinitis, and lower airway hyperreactivity more frequently.[8]

Respiratory system diseases caused by harmful particles in the air have been discussed in many studies. However, the nasal response to different physical types of exercise is as important as the quality and content of the air inhaled by athletes in sports areas because, depending on the reduction in nasal resistance and changes in mucociliary activity during exercise, the respiratory tract will be affected more by the inhaled air in accordance with sports conditions. The aim of this study was to investigate and compare the effects of different physical activities on nasal response.

Materials and Methods

This prospective study was conducted in Faculty of Medicine, Eskişehir Osmangazi University between January and December 2013. This study was conducted according to the rules outlined in the Declaration of Helsinki. Signed informed consent was taken from all participants.

Study design

The study was commenced once ethics board approval was obtained. Young non-professional university teams were enrolled in this study. All subjects were male and between 20 and 24 years old. The study was conducted with the participation of three exercise groups. The first group included 20 swimmers to observe the effect of water. The second group included 20 runners doing outdoor sports, and the third group included 20 handball players doing indoor sports.

The participants in the study were non-smoker athletes who have never had nasal surgery and had no allergic symptoms. They were healthy individuals who had no septal deviation, nasal polyposis, sinusitis, or concha hypertrophy, with normal nasal endoscopy results. None of the patients were on any medication. They were all completely healthy.

Measurements

Active anterior rhinomanometry: Nasal resistances were measured with active anterior rhinomanometry before and immediately after exercise. The Homoth Rhino 2002 rhinomanometer (Hamburg, Germany) was utilized. All the measurements were performed three times and their average was taken. Nasal resistance was calculated as Pa-sec/ml according to the rules of the International Standards Committee.

Nasal transport times (NTT): The nasal transport time was also measured after rhinomanometric evaluations. Mucociliary transport measurement was performed by the same person using the saccharin transit time test described by Andersen et al.[9] The patients were situated in a seated position and their heads slightly extended. Five milligrams of granulated sodium saccharin was placed 1 cm inside the nostril using anterior rhinoscopy examination. The first sweet taste patients felt in their mouths was recorded in terms of its duration as seconds. The patients were not allowed to move their heads, swallow, sneeze, speak, or take a deep breath. If a patient had not yet experienced the sweet taste within 60 minutes, saccharin was placed on the tongue to make sure that the sense of taste existed and the measurement was postponed.

Methods

After the initial measurements, the first group swam 2 kilometers in 30 minutes. Their swimming speeds were set to reach a period of thirty minutes. The second group ran 10 kilometers in approximately the same amount of time. The third group played handball for 30 minutes. After these exercises in three groups, active anterior rhinomanometry and NTT were measured again.

Statistical analyses

Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (PASS) 2008 software (Utah, USA) programs were applied for the statistical analyses. While assessing the data, in addition to descriptive statistical methods (mean, standard deviation, median, frequency and ratio), a one-way ANOVA test was used in the between-group comparison of parameters showing normal distribution, while a Kruskal-Wallis test was used in the comparison of percentage changes according to group and the Mann-Whitney U test in the identification of the group causing the difference. In the in-group comparisons of parameters showing normal distribution, a t test (paired sample t test) was

Table 1. Inspiration measurements of active anterior rhinomanometry in the groups.

Inspiration measurements (Pa-sec/ml)		Runner	Swimmer	Handball player	p
		Mean±SD	Mean±SD	Mean±SD	
Left side	Before exercise	343.9±68	340.4±70.4	346.9±70.3	0.957*
	After exercise	475.0±90.1	445.5±74.4	452.3±76.6	0.485*
	p	0.001†,‡	0.001†,‡	0.001†,‡	
	Alteration (%)	40.8±26.2	34.4±28.6	33.7±26.9	0.481§
Right side	Before exercise	343.2±68.5	332.3±74.5	359.5±67.4	0.471*
	After exercise	447.1±69.5	456.7±82.3	451.6±71.5	0.921*
	p	0.001†,‡	0.001†,‡	0.001†,‡	
	Alteration (%)	33.4±24.2	41.5±30.2	28.8±26.7	0.406§
Left/Right	Before exercise	0.958†	0.334†	0.074†	
	After exercise	0.085†	0.448†	0.950†	

*One-way variance analysis, †Paired samples t test, ‡p<0.01, §Kruskal-Wallis test

used in dependent groups. The results were evaluated at a 95% confidence interval and a significance level of p<0.05.

Results

Three groups aged between 20 and 24 were included in the study. There were 20 runners in the first group, 20 swimmers in the second group, and 20 handball players in the third group.

Inspiration measurements of active anterior rhinomanometry in the groups were shown on Table 1 and Fig. 1. When the inspiration levels of athletes were compared, the values before the exercise in all three groups were similar on the right and left sides (p>0.05). The values after exercise were also similar on the right and left sides in the three groups (p>0.05). In each of the three groups separately, when the inspiratory values before and after exercise were compared, the change percentages on the left and right side increased in a statistically significant manner: runners (40.8%) – (33.4%), swimmers (34.4%) – (41.5%), and handball players (33.7%) – (28.8%) (p<0.01). When the inspiratory change percentages after exercise were compared with those recorded before exercise, there was no statistical difference between the left- and right-side change percentages (p>0.05). When the right and left nose were compared in runners, swimmers, and handball players, the inspiration levels of the left and right sides in the measurements performed before and after exercise were similar (p>0.05) (Table 1 and Fig. 1).

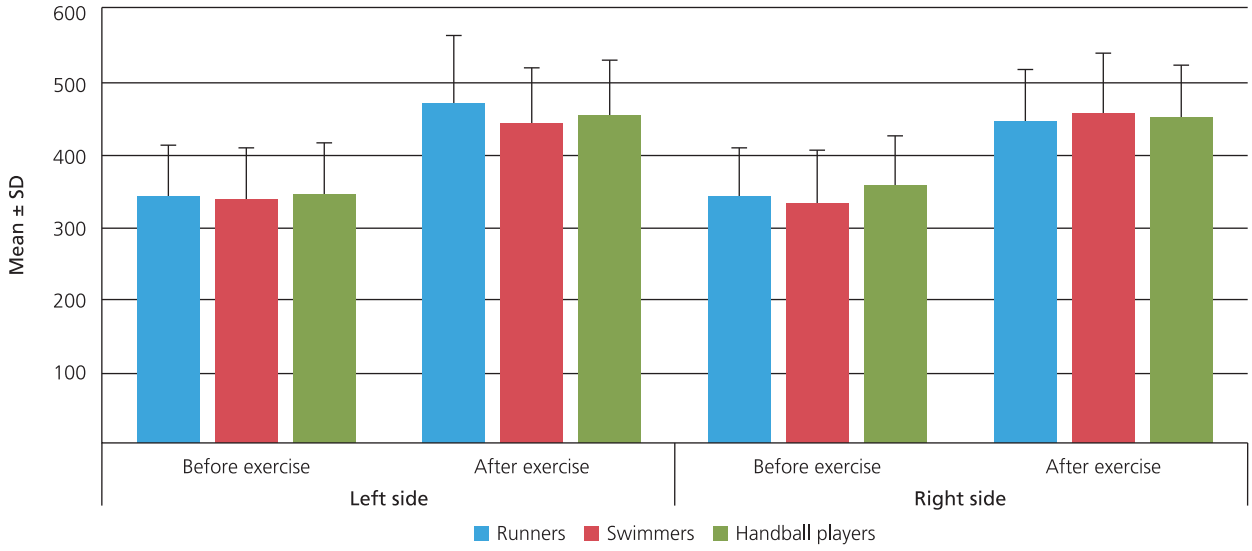

Fig. 1. Distribution of inspiration measurements of active anterior rhinomanometry. Values were given as Pa-sec/ml.

Table 2. Expiration measurements of active anterior rhinomanometry in the groups.

Expiration measurements (Pa-sec/ml)		Runner	Swimmer	Handball player	p
		Mean±SD	Mean±SD	Mean±SD	
Left side	Before exercise	357.2±63.9	353.8±66.4	361.4±67.8	0.935*
	After exercise	489.9±81.7	468.1±71.3	469.7±68.7	0.588*
	p	0.001†,‡	0.001†,‡	0.001†,‡	
	Alteration (%)	39.3±22.6	35.7±28.4	33.2±25.8	0.567
Right side	Before exercise	358.8±68.1	357.7±63.4	382.3±56.9	0.384*
	After exercise	460.3±60	477.1±69.9	475.2±61.4	0.661*
	p	0.001†,‡	0.001†,‡	0.001†,‡	
	Alteration (%)	31.4±22.8	35.6±21.7	26.4±21.8	0.428
Left/Right	Before exercise	0.909‡	0.633‡	0.040‡,§	
	After exercise	0.060‡	0.497‡	0.623‡	

*One-way variance analysis, †p<0.01, ‡Paired samples t test, §p<0.05

Expiration measurements of active anterior rhinomanometry in the groups were shown on Table 2 and Fig. 2. When the expiration levels of three groups were compared, the values before the exercise in all the three groups were similar on the right and left sides (p>0.05). The values after exercise were similar on right and left sides in the three groups (p>0.05). In each of the three groups separately, the change percentages in the expiration levels before and after exercise on the left and right sides were statistically significant for runners (39.3%) – (31.4%), swimmers (35.7%) – (35.6%) and handball players (33.7%) – (26.4%), respectively (p<0.01). When the percentage changes for expiration after exercise were compared with those measured before exercise, there was no statistical difference between the left- and right-side percentage changes (p>0.05). When the right and left nose were compared in runners, swimmers, and handball players, the expiration levels of the left and right sides in the measurements performed before and after exercise were similar (p>0.05). Although the change in the expiration measurements between the right side and left side in handball players was significant, this can be ignored (p<0.05) (Table 2 and Fig. 2).

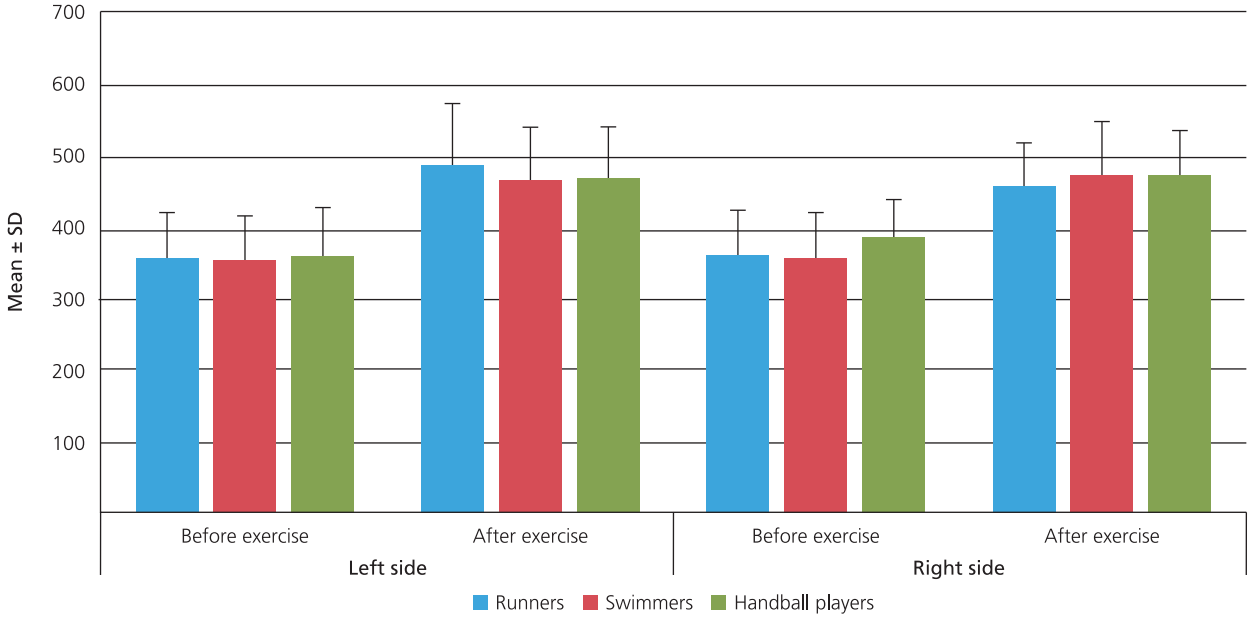

Fig. 2. Distribution of expiration measurements of active anterior rhinomanometry. Values were given as Pa-sec/ml.

Evaluation of groups' nasal transport time was shown on Table 3 and Fig. 3. When NTT is examined, the nasal transport times of runners, swimmers, and handball players before exercise are similar (p>0.05). The nasal transport times of runners, swimmers, and handball players after exercise are similar (p>0.05). In addition, the decrease in nasal transport time before and after exercise in each of the runners, swimmers, and handball players are 9.43%, 12%, and 24.75%, respectively, and the decrease in this time is statistically significant in all three groups (p<0.05). When the percentage changes in NTT were compared by pairwise comparison, the NTT decrease percentage of handball players were found to differ at a significant level compared to in runners (n=0.038). No statistically significant difference was observed between the times of runners and swimmers, and swimmers and handball players (p>0.05).

Table 3. Evaluation of groups' nasal transport time.

Nasal Transport time (second)	Runners	Swimmers	Handball players	p
	Mean±SD	Mean±SD	Mean±SD	
Before exercise	245.5±63.9	249.5±74.1	288.7±86.4	0.144*
After exercise	220.8±58.8	208.8±20.8	202.6±16.4	0.299*
P	b0.002†	0.006†,‡	0.001†,‡	
Alteration (%)	9.43±10	12.46±14.6	24.75±19.1	0.041§

*One-way variance analysis, †p<0.01, ‡Paired samples t test, §p<0.05

Discussion

Moistening air reaching the lower airway of the nose ensures heating. In addition, thanks to the nose's barrier feature, particles of specific sizes cannot pass through it and are cleared with mucociliary clearance.[10] To meet the air requirement which increases during exercise, nasal resistance decreases and the amount and speed of the air that passes through the nose increases.[1,2] Drying in the mucosa and thickened secretions cause changes in mucociliary transport mechanisms.[11] In addition, to meet the increasing air requirement, mouth breathing starts after a short time. As a result, by bypassing nasal filtration mechanisms, the air consisting of cold, unmoistened, and harmful particles reach the lungs directly and may cause lower respiratory diseases. Within the first 10 minutes of exercise, the reduction in nasal resistance is maximized and returns to a resting position 20 minutes after exercise.[12] This process is the time when the athlete is exposed the most to the particles in the air.

In the light of this information, we are more exposed to harmful particles in the air while exercising than compared to resting. In our study, the reduction in nasal resistance in inspiration and expiration among runners, swimmers, and handball players is statistically significant and similar. The similarity between the nasal response of athletes in outdoor, indoor, and swimming pool environments has shown us that the content of the inhaled air and the type of sports is not significant in nasal resistance. It has also been observed that the reduction in nasal resistance is more related to exercise.

There are too few studies that investigate NTT after exercise among healthy people. Ottaviano et al.[13] found increased NTT among swimmers compared to other athletes (tennis players, soccer players, runners, etc.) in their study. But in this study, NTT was measured, on average, 2.8 days after the last exercise. Passàli et al.[11] found in their study that the NTT of swimmers is longer than that of runners and skiers. However, the time interval when NTT was measured was not mentioned in this study. Unlike the studies of Ottaviano et al.[13] and Passàli et al.,[11] in our study, NTT was measured before and immediately after swimming and a significant decrease in NTT was observed in swimmers. Müns et al.[14] found a significant decrease in NTT in long-distance runners in their study. But they performed the measurements 1 week before and 1 week after exercise. Olseni et al.[15] could not find any difference in NTT after bicycle ergometer exercise. Wolff et al.[16] detected a slight increase in mucociliary clearance after exercising.

Our study is the first one to measure NTT before and immediately after exercise in athletes (runners, swimmers, and handball players). When NTT was compared before and immediately after exercise in runners, swimmers, and handball players in our study, the decrease was statistically significant in all three groups (p<0.05). The decrease percentages were similar between runners and swimmers, and swimmers and handball players. But the NTT percentage decreases of handball players were found to be significantly different from those of runners. Although observed in all

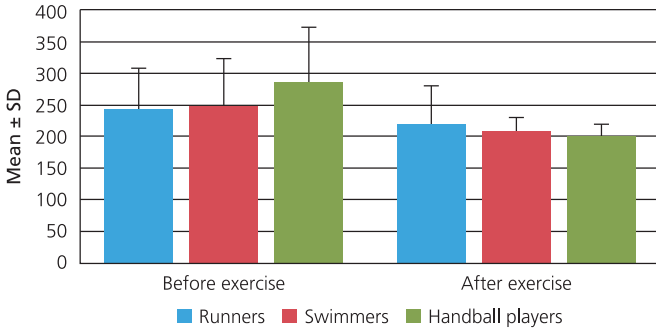

Fig. 3. Distribution of nasal transport time values before and after exercise. Values were given as Pa-sec/ml. Nasal transport time values were given as seconds.

three groups, the NTT decrease was the most prominent in handball players (indoor athletes). It might be assumed that the difference is caused by swimmers' exposure to chlorinated water and runners' exposure to polluted air.

There are still some shortcomings compared to our study. In most of the related studies, the athletes have respiratory system diseases (allergic rhinitis, asthma, etc.). In that case, it would not be accurate to measure the nasal resistance and NTT of athletes. As the athletes were selected out of completely healthy people in our study, we believe that their nasal functions were better measured. In other studies, it is either not mentioned how much later than exercising the NTT was measured or it was measured a long time after exercising. In our study, NTT measurements were performed immediately after exercising. Also differing from other studies, our study included rhinomanometric measurements that were performed immediately after exercise, so the changes during exercise were evaluated more accurately.

Conclusion

Reduction in nasal resistance and decreases in NTT are not affected by the type of sports or the air quality of the environment. As the athletes of all exercise types are more exposed to the air in the environment based on their resting conditions, the content of the inspired air while exercising is as important as resting.

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Conflict of Interest: No conflicts declared.

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Computed tomography analysis of sinonasal anatomical variations and relationship with the maxillary sinus retention cysts

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Abstract

Objective: The purpose of the present study was to investigate the relationship of sinonasal anatomic variations (SAVs) with maxillary sinus retention cysts (RCs) on paranasal sinus tomography.

Methods: Our study included 202 patients who applied to the ENT outpatient clinic with fascial pain, nasal obstruction and postnasal drip complaints between September 2014 and February 2016 and underwent CT of paranasal sinus on coronal plane. The patients who had maxillary RCs in their CT scan comprised the study group while the patients who did not have RCs in their CT scan comprised the control group. The CT scans of these two groups were examined and recorded for the SAVs. The statistical analysis of the SAVs for these two groups was conducted using the Mann-Whitney U test.

Results: The presence of septal deviation from SAVs and pneumatized uncinate in patients found to have maxillary sinus retention cyst was considered statistically significant ($p<0.05$). The sex in patients with right maxillary sinus RCs was considered statistically significant ($p<0.05$). The presence of pneumatized uncinate in patients with left maxillary sinus RCs was considered statistically significant ($p<0.05$).

Conclusion: In our study, the statistical relationship between SAV and maxillary sinus retention cysts may show that SAVs may be effective in the etiology of maxillary sinus retention cysts. This result has to be verified by more detailed studies.

Keywords: Sinonasal variation, retention cysts, computed sinus tomography.

Özet: Sinonazal anatomik varyasyonların bilgisayarlı tomografi ile analizi ve maksiller sinüsteki retansiyon kistleriyle ilişkisi

Amaç: Paranazal sinüs tomografisi çekilmiş olan hastalardaki sinonazal anatomik varyasyonlar (SAV) ile maksiller sinüs retansiyon kistleri arasındaki ilişki araştırıldı.

Yöntem: Çalışmaya Eylül 2014 ile Şubat 2016 tarihleri arasında Kulak Burun Boğaz polikliniğine fasiyal ağrı, nazal obstrüksiyon, postnazal akıntı şikayetleri ile başvuran ve koronal planda paranazal sinüs bilgisayarlı tomografi (PSBT) çekilmiş 202 hasta dahil edildi. PSBT'sinde retansiyon kisti saptanan hastalar çalışma grubu olarak, retansiyon kisti saptanmayan hastalar ise kontrol grubu olarak ayrıldı ve iki grubun PSBT'leri incelenerek sinonazal anatomik varyasyonlar saptandı. Çalışma ve kontrol grubu SAV'lar bakımından Mann-Whitney U testi ile analiz edildi.

Bulgular: Maksiller sinüslerinde retansiyon kisti tespit edilen hastaların SAV'lardan olan septum deviasyonu ve pnömatize unsinatın bulunması istatistiki olarak anlamlı olarak bulundu ($p<0.05$). Sağ maksiller sinüslerinde retansiyon kisti bulunan hastalarda cinsiyet ($p<0.05$) istatistiksel olarak anlamlı bulundu. Sol maksiller sinüslerinde retansiyon kisti bulunan hastalarda pnömatize unsinatın bulunması ($p<0.05$) istatistiksel olarak anlamlı bulundu.

Sonuç: Çalışmamızda SAV ile maksiller sinüsteki retansiyon kistleri arasındaki istatistiki ilişki retansiyon kistlerinin etyolojisinde SAV'ların etkili olduğunu gösterebilir. Bu konuda araştırmacılar tarafından detaylı çalışmalar yapılmalıdır.

Anahtar sözcükler: Sinonazal varyasyon, retansiyon kistleri, bilgisayarlı sinüs tomografisi.

Benign mucosal cysts of the maxillary sinus are generated from obstructions in the mucosal gland ducts.[1] Generally, they are asymptomatic, and they are diagnosed incidentally on plain graph or computerized tomography.[2] A radiologic image is generally originated from the maxillary sinus floor and rises up like a rising sun. If it is filled the

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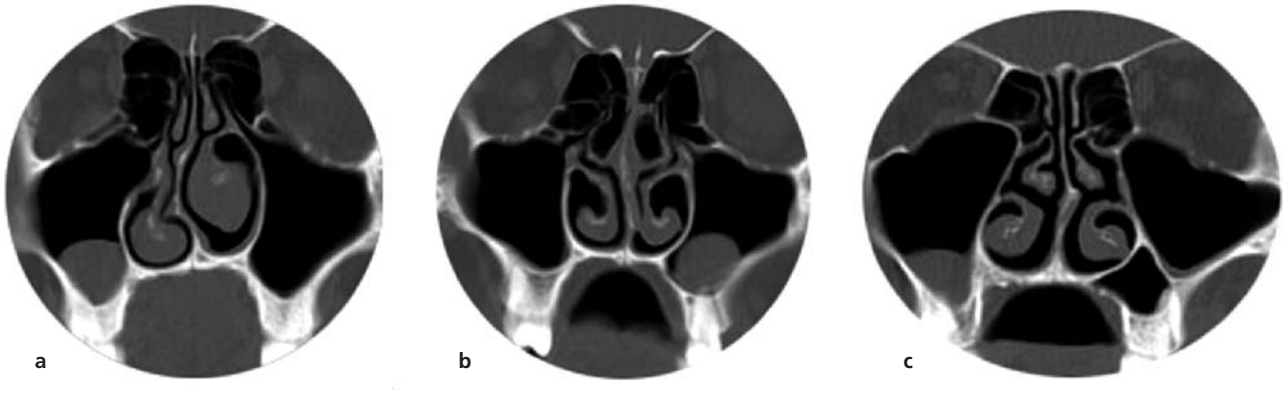

Fig. 1. Paranasal sinus tomography views of a patient's maxillary sinus. (**a**) View showing the nasal septal deviation + retention cyst on the floor of the maxillary sinus. (**b**) View showing the concha bullosa + retention cyst on the floor of the maxillary sinus. (**c**) View showing the reverse concha + retention cyst on the floor of the maxillary sinus.

sinus completely, it can lead to fascial and periorbital pain and the cyst content is a clear yellow liquid.[3] If it obstructs the sinus ostium, it leads to sinus infection.[4]

Some cysts may grow in the maxillary sinus without any complaints. If there is no complication due to the retention cysts (RCs), patient monitoring is appropriate.[5] Sinonasal anatomic variations (SAVs) play the most important role in the pathogenesis of diseases, and paranasal sinuses comprise the area in which SAVs are seen most frequently in humans.[6,7]

Because recurrent sinusitis might represent a putative risk factor associated with the development of maxillary RCs, surgery is aimed at restoring ventilation and drainage of the dependent maxillary sinus.[8] The most common anatomic variations impair ventilation and drainage of the sinuses with narrowing the ostiomeatal complex, nasal septal deviation (NSD), excessive pneumatized agger nasi cells, concha bullosa, paradoxical middle turbinate, uncinate process pneumatization, and Haller cells.[9–11] In our study, we investigated whether there was an effect of SAVs on the increase of maxillary sinus retention.

Materials and Methods

Our study was conducted retrospectively between 01.09. 2014 and 09.02.2016 with patients who sought treatment for facial pain, nasal obstruction, and postnasal drip complaints at our ENT outpatient clinic. All of the 202 patients were examined with coronal paranasal sinus computed tomography (CT). At the same center, we performed tomography scans, which were examined by a radiology expert. Maxillary sinus RCs were found in 39 patients, and these patients were considered as the study group (Fig. 1). The remaining (163) patients (for whom we did not find RCs) were considered as the control group. The paranasal sinus tomographies of the two groups were examined, and the SAVs like NSD, concha bullosa, Haller cells, agger nasi cells, reverse concha and pneumatized uncinate were determined and recorded.

Patients who had chronic nasal and sinus diseases like allergy, sinusitis, and nasal polyp and those who had a previous nose or paranasal surgery were excluded from the study. This study was conducted with the permission of the hospital's ethics committee (10.03.2016/19).

Statistical analysis

Data were analyzed with SPSS for Windows. The qualitative data are given by numbers and percentages; the data of the quantitative variables are expressed as medians. Patients who had RCs on maxillary sinus BT were determined as the study group, while those who did not have RCs were determined as the control group. SAVs were determined by examining the paranasal sinus CT of the two groups. For the study and control groups, the Mann-Whitney U test was used in terms of SAVs. A value of $p<0.05$ was considered significant.

Results

There were 14 women (35.9%) and 25 men (64.1%) in the study group, and 89 women (54.6%) and 74 men (45.4%) in the control group. The age of the patients ranged between 11 and 85 years. The mean age was 34.02±13.073 years. There were 39 patients with RCs on one or both maxillary sinuses. The number of right maxillary sinus RCs was 18, and the number of left maxillary sinus RCs was 25.

Table 1. Sex and SAVs distribution of the study group and control group and their statistical analysis.

	Study group	Control group	p value*
Nasal septal deviation	22	113	**0.012**
Concha bullosa	15	57	**0.683**
Haller cell	3	12	**0.944**
Agger nasi cell	6	26	**0.931**
Reverse concha	4	10	**0.364**
Pneumatized uncinate	4	3	**0.010**

*One way ANOVA

Table 2. The pneumatized uncinate was significantly higher in the left maxillary sinus retention cyst (+) group (p<0.001).

	Study group	Control group	p value*
Nasal septal deviation	5	52	0.331
Concha bullosa	6	50	0.658
Haller cell	1	9	0.815
Agger nasi cell	3	25	0.774
Reverse concha	2	7	0.360
Pneumatized uncinate	3	2	0.001

*One way ANOVA

The number of both maxillary sinus RCs was 4. Statistical analysis was conducted and it was observed that maxillary sinus RCs were found significantly more often in men (p<0.036). On the side in which NSD and pneumatized uncinate were seen, the number of RCs was more likely to be higher (p<0.05), (p<0.05) (Table 1). Right maxillary sinuses were statistically analyzed in the study group and control group, and RCs were more common in men (p<0.05) (Fig. 2). Left maxillary sinuses were compared between the study and control group, and pneumatized uncinate was seen significantly more frequently in the study group (p<0.001) (Table 2).

Discussion

When we looked at other variables like NSD, concha bullosa, Haller cells, agger nasi cells and reverse concha pneumatized uncinate values, significant differences were not observed (p>0.05). Patients with left sinus RCs were significantly different from the control group in terms of pneumatized uncinate (p<0.001). When we looked at other variables like NSD, concha bullosa, Haller cells, agger nasi cells and reverse concha, no significant differences were seen (p>0.05).

Although maxillary sinus cysts have benign clinical course, sometimes they give rise to clinical problems. In the literature, maxillary sinus RC-related publications are limited. The etiology of the maxillary sinus cyst has not been understood well yet. In our study, the rate of male patients in the maxillary sinus cyst-positive group was significantly higher compared with that of the control group (p<0.05). In the study by Omezli et al.,[10] the same result was obtained in terms of sex. In patients with RCs on the maxillary sinuses, the NSD and pneumatized uncinate seemed to be more, which shows that SAVs can be one of

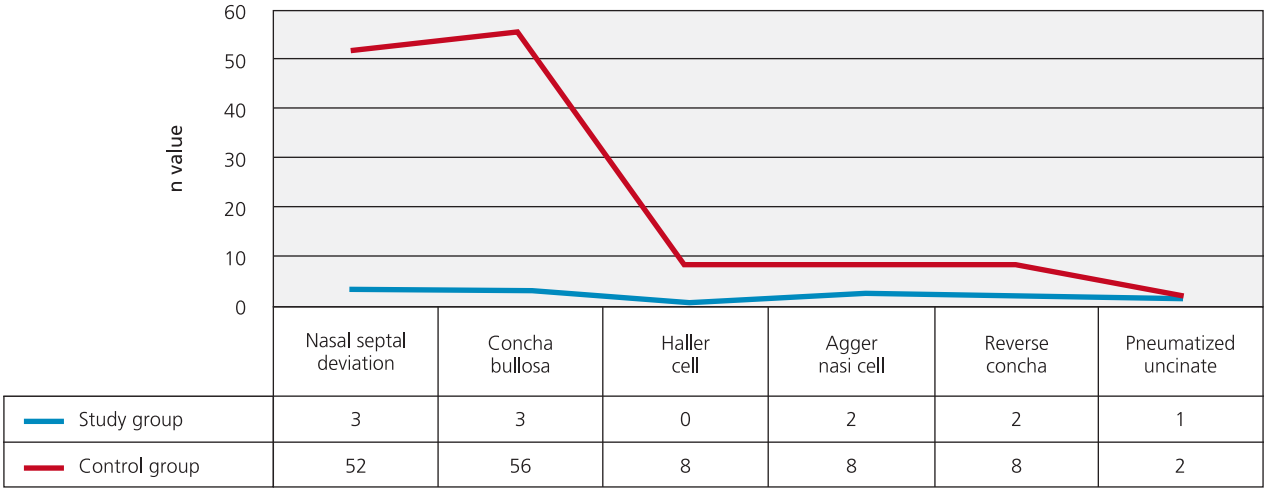

Fig. 2. There was a significant difference in terms of sex in the right maxillary sinus retention cyst (+) group.

the reasons for RCs. Right and left maxillary sinus cysts were considered separately, and significant differences were observed in terms of sex. Significant differences were found on the left side only in terms of pneumatized uncinate. When maxillary sinuses were examined, and each one was analyzed as a single party, the reason why only the number of left pneumatized uncinate was higher may be due to the number of cases. In this regard, there is a need for more studies. In the study by Yousem,[6] the severity and degree of SAVs directly increased the severity of inflammation rather than the presence of SAVs. In the study of Huizing, they emphasized that if the SAVs increase, the mucosal contact area to the level of mucociliary movement decreases or immobilizes ciliary activity and leads to paranasal sinus pathology.[7]

In the study of Harar et al. conducted on paranasal sinus CT of 500 possible chronic sinusitis patients, the incidence of maxillary sinus cyst was 22%.[9] In the sinus cyst-positive group, the incidence of sinus inflammatory disease was 52.7% while the inflammatory sinus disease ratio was 41.3% in the sinus cyst-negative group. The difference between the 2 groups was significant ($p<0.05$). As a result, they emphasized that chronic rhinosinus plays a critical role in the formation of mucosal cysts.[11] Omezli et al.[10] conducted their study in Ordu and Erzurum, two centers with different climatic conditions; 17,659 panoramic graphics were analyzed in that study and the ratio of maxillary sinus RC prevalence in the Black sea region was 1.6% while it was 0.4% in Eastern Anatolia. The mild climate and low altitude significantly increased the probability of developing mucosal cysts in the maxillary sinus ($p<0.05$).

When SAVs were compared between the study and control groups, significant differences were observed in terms of pneumatized uncinate, NSD, and patient's sex ($p<0.05$). No significant differences between the two groups were observed in terms of concha bullosa, Haller cells, agger nasi cells and reverse concha ($p>0.05$). In patients with right sinus RCs there were significant differences in terms of sex ($p<0.05$).

Conclusion

Although maxillary sinus RCs are seen frequently in ENT and dental practice, their etiology is still not understood well. In previous studies, sinus inflammation, sex, climate, humidity and altitude were pointed out as etiologic factors. In our study, we tried to look at this clinical situation from the point of SAVs and we found that SAVs such as NSD and pneumatized uncinate were seen significantly more in the sinus cyst (+) group. Our cases are quantitatively limited and these results need to be confirmed with larger series.

Conflict of Interest: No conflicts declared.

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Surgical intervention for traumatic facial paralysis: an analysis of 15 patients

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Abstract

Objective: The aim of the present study was to analyze patients who underwent facial nerve decompression.

Methods: A retrospective data analysis was performed on 15 patients operated between January 2005 and January 2015. All patients were evaluated with high-resolution temporal computed tomography, House-Brackmann grading system, and electrodiagnostic tools (electromyography or electroneurography).

Results: There were 8 female and 7 male patients with a mean age of 20.56 (range: 2 to 59) years. All of the patients underwent facial decompression surgery via a transmastoid approach.

Conclusion: Transmastoid approach in patients with facial nerve injuries within the first genu and the digastric ridge is appropriate, and the increase in the amplitude observed in the postoperative EMG records obtained from musculus orbicularis oculi may be considered as significant indicator of nerve recovery that occurs before clinical improvement.

Keywords: Traumatic facial paralysis, transmastoid approach, electromyography.

Özet: Travmatik fasiyal paraliziye yönelik cerrahi: 15 hastanın analizi

Amaç: Bu çalışmanın amacı fasiyal sinir dekompresyonu yapılan hastaları analiz etmektir.

Yöntem: 2005 Ocak – 2015 Ocak tarihleri arasında cerrahi geçiren 15 hastanın verileri geriye dönük incelendi. Bütün hastalar yüksek rezolüsyonlu temporal tomografi, House-Brackmann derecelendirme sistemi, elektrodiagnostik testler elektromiyografi ya da elektronörografi) ile değerlendirilmiştir.

Bulgular: Çalışmaya yaş ortalaması 20.56 (aralık: 2–59) yıl olan 8 kadın ve 7 erkek hasta katılmıştır. Hastaların tümüne transmastoid yolla fasiyal dekompresyon uygulanmıştır.

Sonuç: Transmastoid yaklaşım fasiyal sinir birinci dirseği ve digastric *ridge* arasında hasar olanlarda uygun olmaktadır. Postoperatif elektromiyografi bulgularındaki orbikularis okuli kasındaki amplitüd artışı klinik iyileşme öncesinde sinirdeki iyileşmenin anlamlı indikatörü olarak bulunmuştur.

Anahtar sözcükler: Travmatik fasiyal paralizi, transmastoid yaklaşım, elektromiyografi.

Temporal bone fractures primarily result from head trauma secondary to traffic accidents and falls.[1] Temporal bone trauma can result in facial paralysis, which occurs in 5–10% of patients, depending on the type of fracture. The other manifestations of temporal trauma are hearing loss (sensorineural, conductive or mixed) and cerebrospinal fluid leakage.

Temporal bone fractures are usually classified as longitudinal, transverse or mixed based on the course of the fracture line according to the long axis of the petrous bone.[1]

The timing and type of surgery employed for patients with traumatic facial paralysis from temporal bone trauma are very important and can be challenging at times.[2] Electrodiagnostic tests and temporal bone imaging techniques provide important parameters that affect the decision regarding surgery and can be used to predict facial functional outcomes.[2]

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Materials and Methods

This was a retrospective review of the data from 15 patients who underwent facial nerve decompression in the Gaziantep University Otolaryngology Department between January 2005 and January 2015. The local ethics committee approved the study. All patients presented with facial paralysis immediately after the trauma. All patients were evaluated with high-resolution temporal computed tomography (HRCT) and the House-Brackmann grading system (HBG), and electrodiagnostic tools [electromyography (EMG) or electroneurography (Enog), if possible] were used to evaluate the facial function.

Surgical technique

All patients underwent facial decompression surgery via a transmastoid approach. After a standard mastoidectomy, the facial nerve was decompressed from the second genu to the digastric ridge, a posterior tympanotomy was performed, the incudostapedial joint was separated and the incus was removed. Then, the decompression was continued from the second genu to the geniculate ganglion. After finding and repairing the injured side, the operation was complete. There was no need to perform a middle fossa approach in these patients because of the site of the injuries.

Results

Seven of the patients were male and 8 were female, and their ages ranged from 2–59 (average 20.56) years. All patients had unilateral fractures; 8 had transverse fractures, 3 had mixed fractures and 4 had longitudinal-type fractures. **Fig. 1** shows the transverse type of temporal bone fracture.

The following types of trauma occurred: 8 patients were in traffic accidents (3 were motorcycle accidents), 5 patients fell from a height and 2 patients were struck by a falling television. Seven patients had total sensorineural hearing loss (>120 dB), 4 patients had moderate mixed-type hearing loss (average air conduction between 38–50 dB) and 2 patients had mild conductive hearing loss (average air conduction between 28–35 dB). Two patients had normal hearing. In thirteen patients, the laceration was found in the tympanic segment; in 2 patients, the laceration was found in the 1st genu; and in 2 patients, the laceration was found in the 2nd genu of the facial nerve. The intraoperative findings correlated with the HRCT findings that were obtained before the operation. Ossicular chain reconstruction with incus transposition or bone cement was performed for the conductive hearing loss. A transmastoid approach was planned based on the site of the lesion of the facial nerve.

The intraoperative findings, was summarized in **Table 1**. The timing of the surgery ranged from 2 days to 3 months after the injury (average of 39.38 days), as shown in **Table 1**. The main findings were edema, granulation tissue and a partial or complete split of the facial nerve.

Three patients underwent Enog and 12 patients underwent EMG prior to the operation. Four patients had total axonal degeneration, and the remaining patients had no voluntary motor unit potential (MUP). The preoperative and postoperative House-Brackmann grading system is summarized in **Table 2**. Five patients had House-Brackmann grade 2 facial paralysis and 10 patients had House-Brackmann Grade 3 facial paralysis during the postoperative follow-up.

An electrophysiological evaluation was performed 6 months after the surgery. There were no major complications after the surgery.

Discussion

This study reviewed 15 patients with traumatic facial paralysis. Traffic accidents were the cause of the trauma in 8 patients (3 of them were motorcycle accidents), falls from a height were the cause of trauma in 5 patients and strikes from a falling television were the cause of trauma in 2 patients. The number of falls was relatively high because sleeping on the roof is a common habit in the southeastern region of Turkey. According to Ulrich[3] and McHugh,[4] temporal bone fractures can be classified as longitudinal, transverse and mixed according to the axis of the petrous pyramid. In our study, 8 fractures were transverse, 4 were

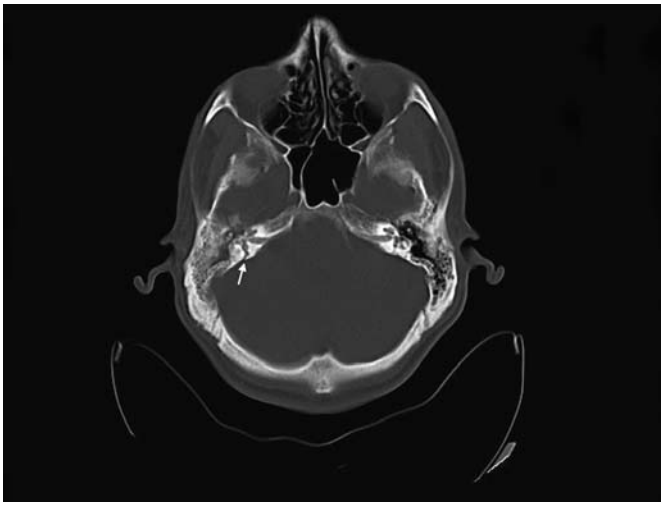

Fig. 1. Thirty-year-old male with transverse temporal bone fracture (Number 2 patient in the table). This temporal bone HRCT shows right side transverse temporal bone fracture includes labyrinth (arrow).

Table 1. Intraoperative findings of the patients underwent facial decompression.

	Site	Fracture	Approach	Hearing loss	Facial nerve findings (location & nerve condition)		
					Lesion location	Operative findings	FN integrity
1	RE	TF	TM	SNHL	TS	Fractured bony fragments and edema	Intact
2	RE	TF	TM	SNHL	TS	Granulation tissue	Intact
3	LE	MF	TM	SNHL	TS	Partial laceration and fibrosis and edema	Intact
4	RE	LF	TM	MIXED	TS-MS	Completely split, granulation and edema	Impaired
5	RE	MF	TM	SNHL	LS-TS	Bony fragments, partial laceration, edema and fibrosis	Intact
6	RE	LF	TM	CHL	TS	Completely split, fibrosis	Impaired
7	RE	LF	TM	Normal hearing	TS-MS	Completely split, edema	Impaired
8	LE	TF	TM	SNHL	TS	Completely split, granulation tissue	Impaired
9	RE	TF	TM	SNHL	TS	Partial laceration and fibrosis, granulation tissue	Intact
10	LE	TF	TM	SNHL	TS	Completely split and fractured bony fragments	Impaired
11	RE	TF	TM	SNHL	GG-TS	Granulation tissue and edema	Intact
12	LE	TF	TM	SNHL	TS	Granulation tissue and edema	Intact
13	LE	LF	TM	CHL	GG-TS	Fractured bony fragments and fibrosis	Intact
14	RE	TF	TM	SNHL	TS	Partial laceration and edema	Intact
15	LE	MF	TM	CHL	TS	Completely split, granulation tissue and edema	Impaired

CHL: conductive hearing loss; **GG:** geniculate ganglion; **LE:** left; **LF:** longitudinal-type fracture; **LS:** labyrinthine segment; **MF:** mixed fracture; **MS:** mastoid segment; **RE:** right, **SNHL:** sensorineural hearing loss; **TF:** transverse fracture; **TM:** transmastoid; **TS:** tympanic segment.

longitudinal and 3 were mixed-type fractures. In two of the patients with longitudinal fractures, there was disruption of the facial nerve.

Some controversies remain regarding the timing of and the approach used for surgery. The type of injury, the onset of paralysis, the localization of the injury, comorbidities (cranial injuries) and the results of the electrophysiologic tests are the main determinates for both the timing of and the approach used for the surgery. Horizontal segment and geniculate ganglion injuries can be exposed by the transmas-

Table 2. Intraoperative findings of the patients underwent facial decompression.

Patient No	Timing	EMG/ENoG Pre-op	Loss (%)	EMG Post-op (6 months-1 years)	Pre- op HBG	Post- op HBG
1	7 days	Total axonal degeneration	…	mOOc; amp R; 1.1, L; 3.0 mV	5	2
2	2 months	mOOc; amp R; 0.1, L; 1.6 Mv/No voluntary MUP	93%	mOOc; amp R; 0.9, L; 2,9 mV/voluntary MUP+	6	3
3	2 days	Total axonal degeneration	…	mOOc; amp R; 2.3 , L; 1.1 mV	5	2
4	2.5 months	mOOc; amp R; 0.3, L; 2.0 Mv/No voluntary MUP	85%	mOOc; amp R; 1.0, L; 2.3 mV	5	3
5	3 months	mOOc; amp R; 0.3, L; 2.7 Mv/No voluntary MUP	88%	mOOc; amp R; 1.2, L; 2.9 Mv/voluntary MUP+	5	2
6	1 month	mOOc; amp R; 0.3, L; 2.2 Mv/No voluntary MUP	86%	mOOc; amp R; 1.4, L; 2.9 Mv/voluntary MUP+	5	3
7	4 days	Total axonal degeneration	…	mOOc; amp R; 0.7, L; 2.8 Mv/voluntary MUP+	6	3
8	1 month	mOOc; amp R; 2.3, L; 0.2 Mv/No voluntary MUP	95%	mOOc; amp R; 2.1, L; 0.9 mV	6	3
9	1.5 month	mOOc; amp R; 0.3, L; 1.7 Mv	82%	mOOc; amp R; 0.9, L; 1.9 Mv	5	3
10	2 months	mOOc; amp R; 0.2, L; 3.0 Mv/No voluntary MUP	93%	mOOc; amp R; 1.4, L; 3.4 Mv/voluntary MUP+	6	3
11	1 month	mOOc; amp R; 0.3, L; 3.4 Mv/No voluntary MUP	91%	mOOc; amp R; 2.1, L; 3.7 Mv/voluntary MUP+	6	3
12	1.5 month	mOOc; amp R; 2.0, L; 0.1 Mv	95%	mOOc; amp R; 2.2, L; 1.2 Mv	5	2
13	1.5 month	mOOc; amp R; 1.6, L; 0.3 Mv/No voluntary MUP	81%	mOOc; amp R; 2.1, L; 0.9 Mv	5	2
14	2 months	mOOc; amp R; 0.2, L; 3.1 Mv/No voluntary MUP	93%	mOOc; amp R; 1.2, L; 3.3 Mv/voluntary MUP+	5	3
16	1.5 month	mOOc; amp R; 2.4, L; 0.3 Mv/No voluntary MUP	87%	mOOc; amp R; 2.7, L; 1.2 Mv/voluntary MUP+	6	3

amp: amplitude; **L:** left; **mOOc:** musculus orbicularis oculi; **MUP:** motor unit potential; **Mv:** microvolt; **R:** right

toid approach.[5–7] The majority of the patients in our series had transverse fractures that were associated with the involvement of part of the facial nerve between the first genu and the digastric ridge. Edema, the formation of granulation tissue, and the presence of bone chips in the facial nerve were the major intraoperative findings. Transmastoid facial nerve decompression was performed in our series based on the preoperative HRCT and intraoperative findings. We preferred to perform a posterior tympanotomy to inspect the middle ear and decompress the mastoid segment of the facial nerve. Conductive hearing loss was restored by ossicular chain reconstruction. All of the patients had HBG-6 initially, and the rate of recovery was measured by EMG and HBG. Ten of the 15 patients recovered to HBG III, and 5 recovered to HBG II. According to the EMG results, there was an increase in the MUP and amplitudes of the orbicularis oculi muscle.

The small number of patients evaluated is the major limitation of this study; however, the authors propose that using the transmastoid approach in patients with facial nerve injuries within the first genu and digastric ridge is appropriate. The timing is another challenging issue; however, the patient who underwent surgical intervention after 3 months had HBG II and voluntary MUP 6 months after the surgery.

Conclusion

The authors propose that the transmastoid approach in patients with facial nerve injuries within the first genu and the digastric ridge is appropriate, and the increase in the amplitude observed in the postoperative EMG records obtained from musculus orbicularis oculi may be considered as significant indicator of nerve recovery that occurs before clinical improvement.

Conflict of Interest: No conflicts declared.

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Effects of topical hyaluronic acid (Sepragel®/Hylan B) on mucosal healing after endoscopic sinus surgery

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Abstract

Objective: To investigate the effects of hyaluronic acid (HA) (Sepragel® Hylan B; Genzyme Co., Cambridge, MA, USA) on the mucosal healing of patients who undergone functional endoscopic sinus surgery (FESS) for chronic rhinosinusitis and/or nasal polyposis.

Methods: A total of thirty-six patients were included in the study. Patients had received topical administration of HA soaked sponges to the middle meatus on one side of their nasal cavities intra-operatively at the end of the procedures. Other side of the middle meatus was free of any treatment or packing to create a control group. Postoperative endoscopic examination was performed at the 1st, 4th and 12th weeks in order to score mucosal findings regarding synechiae, mucosal hypertrophy and polyp formation on both sides. Mucosal findings were scored from 0 to 3 points (0: lesion free, 1: mild, 2: moderate, 3: severe).

Results: Average scores of the mucosal cavities were compared and it was found to be significantly low for the HA administered mucosa ($p<0.05$). Synechia formation and mucosal hypertrophy at the 1st, 4th and 12th weeks were significantly low for the Hylan B group compared to the control group ($p<0.05$ for both findings).

Conclusion: Topical HA has preventive effects on synechia formation and mucosal hypertrophy.

Keywords: Functional endoscopic sinus surgery, hyaluronic acid, chronic rhinosinusitis, nasal polyposis, synechia.

Özet: Topikal hyaluronik asidin (Sepragel®/Hylan B) endoskopik sinüs cerrahisi sonrası mukozal iyileşme üzerindeki etkisi

Amaç: Çalışmanın amacı kronik rinosinüzit ve/veya nazal polip tedavisi için fonksiyonel endoskopik sinüs cerrahisi (FESC) uygulanan hastalarda hyaluronik asidin (HA) (Sepragel® Hylan B; Genzyme Co., Cambridge, MA, ABD) mukozal iyileşme üzerine etkisini araştırmaktır.

Yöntem: Çalışmaya toplam 36 hasta dahil edildi. Cerrahi prosedürler hastaların bir taraf orta meatuslarına HA emdirilmiş spongel'in lokal uygulanması ile sonlandırıldı. HA uygulanmayan diğer nazal kavitelere herhangi bir tedavi ya da tampon uygulaması yapılmadı ve çalışmanın kontrol grubu olarak takipleri yapıldı. Her iki nazal kavite mukozal sineşi, hipertrofi ve nazal polip oluşumu yönünden postoperatif 1., 4. ve 12. haftalarda endoskopik muayene ile incelendi. Mukozal bulgulara muayene sonrası 0 ile 3 arasında puan verildi (0: lezyon yok, 1: hafif derece lezyon, 2: orta derece lezyon, 3: şiddetli derece lezyon).

Bulgular: Her iki taraf nazal kavite ortalama puanları karşılaştırıldı ve puan mukozasına HA uygulanan nazal kavitede istatistiksel olarak anlamlı derecede düşük bulundu ($p<0.05$). Sineşi oluşumu ve mukozal hipertrofi bulguları, 1., 4. ve 12. haftalarda HA grubunda kontrol grubundan istatistiksel olarak anlamlı derecede düşük bulundu ($p<0.05$).

Sonuç: Topikal hyaluronik asit uygulaması sineşi ve mukozal hipertrofinin üzerine önleyici etkilere sahiptir.

Anahtar sözcükler: Fonksiyonel endoskopik sinüs cerrahisi, hyaluronik asit, kronik rinosinüzit, nazal polip, sineşi.

Surgical management of chronic rhinosinusitis and nasal polyposis has evolved and become an inevitable end point for the treatment of cases which are resistant to medical interventions.[1] Related to the technical advances, blinded conventional surgical methods such as intranasal ethmoidectomy have been replaced with image-guided endoscopic and more functional methods.[2] Functional endoscopic sinus surgery (FESS) is a set of minimally invasive techniques in which paranasal air cells and ostia are opened under direct visualization.[3] As all other surgical procedures, FESS is not a complication-free surgery. From minor to major, various complications such as minor bleeding, periorbital edema,

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cerebrospinal fluid rhinorrhoea and orbital injury may occur during or after the surgery.[4,5] The main goal of FESS is to eradicate diseased mucosa, restore sinus ventilation and maintain a healthy normal functioning mucosal ciliary activity.[6] Unfortunately, after the extirpation process, denuded edematous mucosal surfaces proximate and unfavorable synechia formation may occur. Uncontrolled synechia formation of the middle meatus or frontal recess area may result with recurrent disease or iatrogenic sinonasal pathologies. In order to inhibit the risky approximation of highly adhesive raw surfaces, modifications in surgical methods or systemic and topical administrations of chemical agents such as corticosteroids have been proposed.[7]

Recently, physicians have been tried to adapt viscoseparative biomaterials between denuded surfaces in body cavities to prevent fibrin formation and fibroblast ingrowth.[8] As an example of these biomaterials, hyaluronic acid (HA) is a natural polysaccharide (glycosaminoglycan composed of repeated disaccharides of D-glucuronic acid and N-acetyl-glucosamine) in the extracellular matrix of living organism, such as connective and epithelial tissues.[9] HA has important bioactivities, such as decreased adhesion formation and increased epithelial regeneration and it has various clinical applications from dry eye syndrome to wound healing.[10,11]

In the present study, we aimed to investigate the effects of HA on the mucosal healing of patients undergone endoscopic sinus surgery for chronic sinusitis with or without nasal polyposis.

Materials and Methods

Study design

Ethical committee of the hospital has approved the study and all patients had given written consent. Twenty-one male and 15 female adult patients with chronic sinusitis with or without polyposis who are resistant to medical therapy and required FESS (bilateral ethmoidectomy without middle turbinectomy, with or without antrostomy and with or without nasal septoplasty, and with or without frontal sinusotomy) were recruited to this study. None of the patients had previous nasal or endoscopic sinus surgery. Patients were asked about any food hypersensitivity and none had declared chicken hypersensitivity (Sepragel® is derived from rooster material).

Surgical procedures and follow-up

All procedures were performed under general anesthesia by the senior author of this study. At the end of the procedures, one side of the ethmoid cavities was filled with approximately 6 to 12 mL "Hylan B". Sepragel® sinus (Genzyme Co., Cambridge, MA, USA) is a sterile, non-pyrogenic, transparent, viscoelastic gel composed of cross-linked molecules of hyaluronan. Hyaluronan is a bioabsorbable material that functions to fill a cavity to keep mucosal surfaces separate during the healing process. Other side of the middle meatus was free of any treatment or packing. Patients received postoperative oral antibiotic (second generation cephalosporin) for 10 days. Topical nasal steroids were not administered. Patients were also instructed not to take any medication (included over the counter drugs) unless approved by the senior author of the study.

Outcome parameters

The physicians performed postoperative endoscopic controls of the cavities at the 1st, 4th and 12th weeks after the procedures. During the examination, cavity was refilled with Sepragel®, based on the amount of remaining Hylan B in the cavity. Cavities were scored in terms of the presence and degree of "synechia, mucosal hypertrophy and polyp formation" shown in Table 1. Examiner graded the pathology from 0 to 3 points. "0" indicates "no visible lesion", "1" indicates "mild lesion", "2" indicates "moderate lesion" and "3" indicates "severe lesion". Each patient was graded with a minimum "0", maximum "9" total points and grading was repeated at the 1st, 4th and 12th weeks.

Statistical analysis

Statistical analysis was performed with "SPSS 15.0 (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL, USA) for Windows XP". Median values of the total scores of groups (Hylan B group and control group) were compared using Wilcoxon Signed Ranks statistical analysis. $p<0.05$ was considered statistically significant.

Results

Of the 36 patients, 21 were male and 15 were female with a mean age of 41.64±3.26 (range: 22 to 62) years. Of the 36

Table 1. Endoscopic evaluation of nasal cavity.

Endoscopic examination	Score
No visible lesion	0
Mild lesion	1
Moderate lesion	2
Severe lesion	3

patients, 20 had chronic rhinosinusitis without nasal polyposis and 16 had nasal polyposis. All patients had bilateral endoscopic anterior and posterior ethmoidectomy. Five patients had simultaneous septoplasty with ethmoidectomy.

No operative or postoperative complication occurred and no side effects were observed related to Hylan B. Table 2 showed postoperative mucosal grading. Synechia formation at the 1st, 4th and 12th weeks was significantly less for the Hylan B group compared to the control group ($p<0.05$). Mucosal hypertrophy at the 1st and 4th weeks was significantly less for the Hylan B group compared to the control group ($p<0.05$). The degree of the polyp formation was not significant at the 12th week between the groups ($p>0.05$). Statistical results are summarized in Table 3.

Table 2. Postoperative mucosal grading.

Grade	Synechia	Mucosal hypertrophy	Polyp formation
Grade 0	No	No	No
Grade 1	Mild	Edema	Mucosal hypertrophy
Grade 2	Moderate	Moderate mucosal hypertrophy	Mild polyposis
Grade 3	Total obstruction	Severe mucosal hypertrophy	Severe polyposis

Table 3. Median scores (1st week $p<0.05$; 4th week $p<0.05$; 12th week $p<0.05$).

	1st week		4th week		12th week	
	Control	Hylan B	Control	Hylan B	Control	Hylan B
Synechia	0.31	0.15	0.43	0.09	0.26	0
Mucosal hypertrophia	1.08	0.61	1.17	0.44	0.56	0.42
Polyp formation	_	_	0.05	0.048	0.62	0.61

Discussion

Rhinologists are frequently experienced with the blockage of the middle meatus after endoscopic sinus surgery. Unfortunately, this is usually come out with the recurrent disease and revision procedures. Numerous methods with varying results have been proposed to deal with this issue.[12] Medialization of the middle turbinate with transseptal suturing or iatrogenic adhesion creation, middle turbinate reductions (complete or partial), antrostomy stents and various spacers such as non-absorbable packing materials or Silastic® etc. have been tried in order to widen middle meatus and ethmoidectomy cavity.[13,14] These measures share a common role to keep away the denuded mucosal surfaces of the lateral side of the middle turbinate and ethmoid cavity. In this study, we aimed to use Sepragel® sinus (Hylan B) with the same goal.

The Hylan B molecules fill the sinus cavity and act as a spacer without an inflammatory response and adverse reactions. As well as the spacer effect of the Hylan B, anti–inflammatory effect of the molecule is seems to be important to obtain our results. Because our short-term observations (at the 1st and 4th week) revealed that "mucosal hypertrophy and edema" at the 1st and 4th week was significantly less for the Hylan B group compared to the control group. In agreement with our observations, Kimmelman et al. showed that Hylan B applied cavities in their study group revealed significantly less mucosal edema especially at the 4th week.[7] These findings may ascribe to the anti-inflammatory effects of Hylan B, which was already showed by previous in vitro and in vivo studies.[15,16]

We also observed another important effect of Hylan B in our patients that it significantly reduces synechia formation in the area of middle meatus especially at the 1st, 4th and 12th weeks compared to the control group. This was already observed in the study of Kimmelman et al.[7] However, our observations are the results of much longer follow-up period and revealed that even at the postoperative 12th week, Hylan B has a significant protective effect on preventing synechia formation. Another important aspect of the follow-up procedure is long-term findings of nasal mucosa about the nasal polyp formation. Our results indicated that there is no significant difference between the groups about recurrence of the nasal polyps at the postoperative 12th week. Although Hylan B has been shown to be effective to reduce inflammation in various tissues, nasal polyp seems to have more complicated etiology that does not explain solely with inflammatory reaction.

Although Sepragel® is non-pyrogenic and sterile, the application of Hylan B to the ethmoid cavity has a potential of being infected. As well as Kimmelman et al., we did not experience any postoperative infectious complication in our study group. Additionally, no unfavorable side effect of Hylan B was observed both in our and Kimmelman's study.[7] Various minor complications have been reported after the clinical application of HA.[8] However, these reports were about the non-nasal application of the HA.[17,18] According to our and literature findings, it is possible to accept intranasal application of HA as a safe procedure.

Conclusion

Outcomes of our study have demonstrated that topical HA is effective in preventing synechia formation on paranasal mucosa after endoscopic sinus surgery in long-term. While the preventive effect of HA on mucasal hypertrophy is significant in short-term, preventive effect is insignificant on the recurrence of nasal polyposis in long-term.

Conflict of Interest: No conflicts declared.

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Evaluation of mean platelet volume and neutrophil to lymphocyte ratio as a diagnostic indicator in patients with recurrent aphthous stomatitis

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Abstract

Objective: Recurrent aphthous stomatitis (RAS) is a chronic inflammatory disease of oral mucosa characterized by recurrent painful ulcers. Despite it is a condition seen frequently, its etiology and pathogenesis are not known fully. Its etiology is reportedly idiopathic or multifactorial. Mean platelet volume (MPV) indicates thrombocytic activation, while neutrophil/lymphocyte rate (NLR) is an indicator of chronic inflammation, and both of them can be measured during routine whole blood analysis. The aim of this study is to investigate MPV and NLR values in patients with RAS and the control group.

Methods: A total of 39 patients with RAS and 34 control subjects were included in the study.

Results: When the patient and the control groups were compared, MPV, ESR, CRP and vitamin B12 values were significantly higher in the patient group while NLR, WBC, hemoglobin, neutrophil and lymphocyte values were not significantly different between both groups.

Conclusion: It was shown that MPV can be used as a diagnostic indicator in patients with RAS.

Keywords: Recurrent aphthous stomatitis, mean platelet volume, neutrophil/lymphocyte ratio.

Özet: Rekürren aftöz stomatitli hastalarda bir tanı indikatörü olarak ortalama trombosit hacmi ve nötrofil/lenfosit oranının değerlendirilmesi

Amaç: Rekürren aftöz stomatit (RAS) oral mukozanın tekrarlayan, ağrılı ülserlerle karakterize, kronik inflamatuar bir hastalığıdır. Sık görülen bir durum olmasına karşın etyolojisi ve patogenezi tam olarak bilinmemektedir. Etyolojisinin idiyopatik veya multifaktöryel olduğu belirtilmektedir. Ortalama trombosit hacmi (MPV) trombosit aktivasyonunu gösteren, nötrofil lenfosit oranı (NLR) ise kronik inflamasyon göstergesi olan ve her ikisi de rutin tam kan tetkiklerinde ölçülebilen değerlerdir. Bu çalışmanın amacı RAS'lı ve kontrol grubu hastalardaki MPV ve NLR değerlerini araştırmaktır.

Yöntem: Bu çalışmaya 39 RAS'ı bulunan ve 34 kontrol grubu hasta dahil edildi.

Bulgular: Hasta ve kontrol grubu karşılaştırıldığında MPV, ESR, CRP, vitamin B12 değerlerinin hasta grubunda kontrol grubuna göre anlamlı derecede yüksek çıktı ve NLR, WBC, hemoglobin, nötrofil, lenfosit değerleri arasında her iki grup arasında anlamlı fark bulunmadı.

Sonuç: Ortalama trombosit hacminin, RAS'lı hastalarda tanısal bir gösterge olabileceği ortaya konuldu.

Anahtar sözcükler: Reküren aftöz stomatit, ortalama trombosit hacmi, nötrofil lenfosit oranı.

Recurrent aphthous stomatitis (RAS) is an inflammatory disease of the oral mucosa characterized by painful, multiple, well-defined lesions with a necrotic center surrounded by erythematous halo, observed especially in children and adolescents.[1] The etiopathogenesis of RAS is not fully known, but is accepted as idiopathic or multifactorial. Among etiological factors genetic, immunological, hormonal, nutritional or hematological deficiencies and some environmental causes (trauma, stress, medications, and microorganisms) are blamed.[1–3]

Mean platelet volume (MPV) in full blood counts provides information on the size and activity of platelets and is evaluated as a marker of platelet dysfunction. Larger platelets are more active and prone to aggregation and

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thus are thought to perhaps cause endothelial dysfunction.[4] MPV correlates well with platelet function and activation and is stated to be an indicator of inflammation in chronic diseases.[5–7] Neutrophil to lymphocyte ratio (NLR), like MPV, can be determined in full blood counts. NLR is used as a marker of systemic inflammation.[8] The relationship of NLR with diseases progressing with chronic inflammation such as cardiovascular diseases, malignancy, ulcerative colitis and hepatic cirrhosis has been shown and it is stated to have prognostic importance for these diseases.[9,10]

The aim of this study is to reveal the relationship between values of MPV and NLR, used recently as indicators of inflammatory processes, in recurrent aphthous stomatitis and to investigate the correlation with some other parameters.

Materials and Methods

Our study was completed with permission from the Clinical and Laboratory Ethics Committee of Faculty of Medicine, Abant İzzet Baysal University dated 30/04/2015 numbered 2015/22-39. All patients participating in the study were given detailed information and their written consent was obtained.

The study included a total of 73 patients who attended Dermatology and Otorhinolaryngology Clinics of İzzet Baysal Training and Research Hospital, Abant İzzet Baysal University between January 2014 and July 2015. Of these, 39 patients (13 male, 26 female) attended for at least a year, with oral aphthous ulcer complaint recurring at least 3 times per year and diagnosis of recurrent aphthous stomatitis and 34 were the patients (9 male, 25 female) of the control group.

All patients with recurrent aphthous stomatitis diagnosis were investigated for Behçet's disease. Among patients in both patient and control group, those with Behçet's disease, using medications containing iron and vitamins, with chronic diarrhea, aspirin use, diabetes mellitus, asthma, chronic obstructive pulmonary disease, peripheral and cerebral vein disease, hematological disorders, cirrhosis, portal hypertension, inflammatory bowel disease, obesity and malignancy or diseases that may cause platelet function disorders were excluded from the study. The control group comprised patients attending the Dermatology and Ear, Nose and Throat clinics of our hospital with complaints other than RAS and anemia. Exclusion criteria for the RAS group were applied to the control group.

All venous blood samples were taken between 08:00–10:00 in the morning after 12 hours starvation in EDTA blood tubes and analyses were completed within 2 hours. Blood samples of patients were measured for erythrocyte sedimentation rate, C-reactive protein (CRP), folic acid, vitamin B12 and full blood counts for white blood cells (WBC), MPV, NLR and hemoglobin (Hgb). Reference values for our laboratory are given in Table 1. Additionally in the patient group the age at first appearance of aphthous lesion, duration, and recurrence of aphthous lesion per year were recorded and history of smoking was recorded in both groups.

Statistical analyses were completed using the SPSS 16.0 program (SPSS Inc., Chicago, IL, USA). Numerical data were assessed by Kolmogorov-Smirnov test to see if they were normally distributed or not. Categorical data were expressed as frequency and percent, and numerical data were expressed as average and standard deviation. Normally distributed data were compared with Independent samples t-test and abnormally distributed data were compared with Mann Whitney-U test between control and patient group. Categorical data were compared with chi-square test between groups. The Spearman analysis was used to analyze correlation among the age at first appearance of aphthous lesion, duration, and recurrence of aphthous lesion per year in the patient group.

Table 1. Demographic and laboratory parameters in patients and control groups; reference values of laboratory.

	RAS (n=39)	Control (n=34)	Reference values	p value
Age	32.74±11.92	29.94±5.84	-	0.217
Mean platelet volume (MPV) (fL)	8.96±1.27	8.29±1.32	0–99.9	0.032
WBC (K/uL)	6.64±1.9	7.21±2.11	4.5–11	0.226
Neutrophil (K/uL)	4.23±1.77	4.39±1.83	1.8–7.3	0.705
Lymphocyte (K/uL)	1.89±0.46	2.05±0.69	1.1–5.1	0.244
NLR	2.12±0.65	2.26±1.02	-	0.479
Hemoglobin (Hgb) (g/dL)	13.93±1.56	13.35±2.12	11.5–17.5	0.183
Erythrocyte sedimentation rate (ESR) (mm/sa)	14 (1–37)	5.5 (1–36)	0–30	0.003*
C-reactive protein (CRP) (mg/dL)	2.2 (0.2–32.5)	0.2 (0–22)	0.01–0.5	0.000*
Vitamin B12 (pg/mL)	328 (104–1004)	287.5 (155–535)	145–914	0.033*
Folic acid (ng/mL)	8 (3–20)	5.4 (2.7–11)	3.1–19.9	0.000*

*These values were calculated with Mann-Whitney U test and the other values were calculated with independent samples t-test.

Results

In our study the mean age in the recurrent aphthous stomatitis group of 39 patients (13 male, 26 female) was 32.74±11.92 years with mean age in the control group of 34 patients (9 male, 25 female) of 29.94±5.84 years in a total of 73 patients. There was no statistically significant difference between the patient and control group in terms of age or sex (p=0.217). The demographic characteristics and laboratory findings of patients are given in Table 1. According to these results, while there was a significant difference between the patient and control groups in terms of MPV, erythrocyte sedimentation rate (ESR), CRP, vitamin B12 and folic acid values, the difference in NLR, Hgb, WBC, neutrophil and lymphocyte values was not significant (Table 1). The mean values of all data with significant difference were higher in the RAS group. There were 7 patients in the patient group and 4 in the control group with a history of smoking and when examined for history of smoking the difference between the two groups was not seen to be significant (p=0.461). The mean age at first appearance of oral aphthous lesion was calculated as 25.28±11.97 years. There was no correlation found between initial age of oral aphthous lesions (years), disease duration (months), and aphthous lesion incidence (number/year) and MPV and NLR values (Fig. 1).

Discussion

Recurrent aphthous stomatitis affects 10–20% of the general population, it is more common in children and young adults and is among the most common ulcerative mucosal diseases in the oral cavity.[11,12] Due to frequent occurrence and negative effects on the quality of life of patients, it continues to be a significant health problem. The disease has three different clinical variants described; minor aphthous ulcers, major aphthous ulcers and herpetiform ulcers.[13] In 80–90% of RAS patients, minor aphthous ulcers are the most common clinical variant. Lesions are smaller than 1 cm, shallow ulcers that are less than 10 in number. They are common in the regions of lip mucosa, buccal mucosa and floor of the mouth. These lesions tend to heal without leaving a scar within 2 weeks. Major aphthous ulcers are more rarely observed as deep and painful ulcers larger than 1 cm. Locations are generally lips, soft palate and tonsils. Healing of ulcers may take 6 weeks and frequently leaves scars. The rarest form of herpetiform ulcers occurs as numerous small vesicular style ulcers. Ulcers are 1–2 mm in size, with a tendency to combine and form larger irregular ulcers. Generally they heal within two week without leaving a scar.[14] The etiopathogenesis of RAS is still not fully understood. However, it is thought to form due to the effect of many factors. Some researchers have proposed that RAS develops associated with an immune system function disorder. It may accompany systemic diseases such as agranulocytosis, neutropenia, inflammatory bowel disease, gluten enteropathy, B vitamin deficiencies and HIV disease and apart from these may occur with stress, trauma, iron, folic acid and B12 vitamin deficiencies.[11,12] Currently as no certain etiological factors have been found, we cannot promise curative treatment for RAS. The aim of treatment is to provide pain control, speed up healing and reduce the incidence of recurrence.[15] Biopsies taken from RAS patients have found the presence of T cells and polymorphonuclear leukocytes in lesions, leading to the consideration that these cells play a role in pathogenesis.[16] Additionally in Behçet''s disease, with similar etiopathogenesis to RAS, hypersensitivity of T lymphocytes to a variety of antigens was not identified, with increased platelet and neutrophil activity was shown in blood parameters.[17–19]

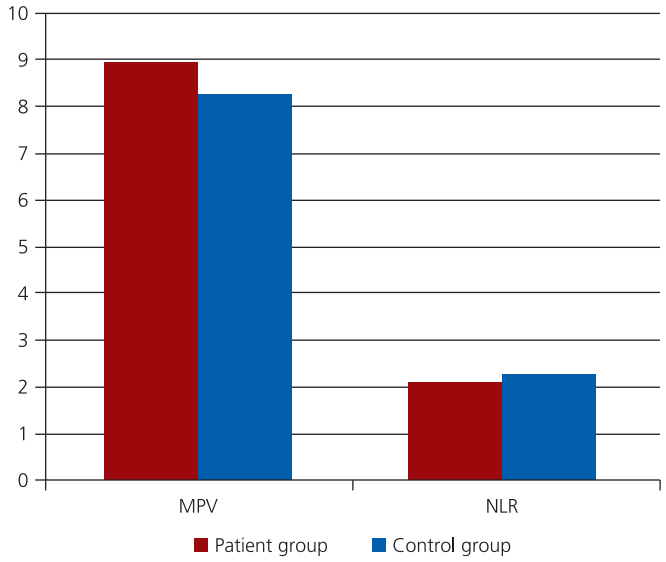

Fig. 1. Values of MPV and NLR in RAS and control group. **MPV:** mean platelet volume, **NLR:** neutrophil to lymphocyte ratio.

Neutrophil to lymphocyte ratio has come to the agenda in recent years as an easy and practical method measured in blood that provides important information to determine diagnosis and prognosis of a variety of diseases. NLR is used as a marker of inflammation evidence in many diseases.[20] In a study by Wang et al.,[21] in patients with angiography independent of NLR, it was shown to be a predictor of mortality and cardiovascular diseases. Recently, NLR has begun to be used to measure severity of inflammation in a variety of diseases like cardiovascular diseases, malignancies and dia-

betes.[22] In a study by Demir et al.,[23] NLR was related to inflammation linked to myocardial ischemia while another study by Muhammed Suliman et al.[24] stated that NLR was an inexpensive method to show inflammation in acute coronary diseases. In our study, we did not find a significant difference between patient and control groups in terms of NLR values. The lack of significant difference in our study for this parameter, used recently to evaluate chronic inflammation evidence, may lead to the consideration that NLR cannot be shown to be a very reliable indicator of inflammation in RAS, or that it may be linked to other inflammatory processes in control group patients that we did not identify.

Mean platelet volume is a value easily evaluated in blood samples by clinicians. It correlates well to platelet function and activation and is stated to be a significant indicator of inflammation in chronic diseases.[5–7,25] The relationship between MPV and Behçet's disease was shown in a study by Acikgoz et al.[26] Immunological mechanisms play a major role in the etiopathogenesis of Behçet's and RAS diseases. Hypersensitivity of T lymphocytes to a variety of antigens plays a significant role in the pathogenesis of these diseases. Additionally, among blood parameters, Behçet's patients' platelet and neutrophil activities are shown to increase.[17–19] Evaluated as a significant marker of inflammation in chronic diseases, MPV was found to be significantly high in psoriasis patients compared to a control group with a positive relationship to psoriasis disease index score in studies by Karabudak et al.[27] and Canpolat et al.[28] on psoriasis and psoriatic arthritis patients. Unlike these studies, the study by Kisacik et al.[25] identified low MPV levels in patients with rheumatoid arthritis and ankylosing spondylitis related with high levels of inflammation. A study by Ekiz et al. on RAS and Behçet's patients showed that MPV and ESR values were significantly high in the patient group compared to the control group. They identified MPV values as an evidence of inflammation in these diseases; however, they did not find a significant difference between both diseases.[4] In our study, the MPV values were found to be high by a significant degree in the patient group compared to the control group. This supports the knowledge that MPV is an easy and cheap marker of inflammation as stated in many studies in the literature. Additionally, ESR and CRP are the acute phase reactants. CRP is thought to be an inflammatory marker and affects the development of inflammation.[29] In our study, ESR and CRP values were found to be significant higher in the RAS group compared to the control group and this supports RAS as an inflammatory process. Our study is the first to evaluate two different inflammation markers like MPV and NLR, cheaply and easily obtained from full blood counts, together in RAS patients with a disease with chronic inflammatory characteristics. In our study, though MPV was found to be significantly high showing similar characteristics to literature studies, NLR was not found to be significant contrary to studies in the literature.

Conclusion

Though the etiopathogenesis of RAS, common in society and negatively affecting quality of life, is not fully known, it is a chronic inflammatory disease. MPV was evaluated with the literature and shown to be a simple, easy and cheap inflammation marker for use in evaluation of these patients.

Conflict of Interest: No conflicts declared.

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Clinical and histopathological presentations of sinonasal cancers in Komfo Anokye Teaching Hospital

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Abstract

Objective: To determine the incidence, clinical and histopathological presentations of the paranasal sinus tumors in Komfo Anokye Teaching Hospital, Kumasi, Ghana.

Methods: All cases of sinonasal cancers diagnosed between January 2007 and December 2012 were retrospectively reviewed.

Results: Of the 68 patients (38 males, 30 females) whose charts were reviewed, the median age was 49 (range: 14 to 84) years. The common clinical presentations were epistaxis (23%), nasal mass (20%), headache (12%), nasal blockage (12%), nasal discharge (11%), proptosis (9%), cheek swelling (8%), and epiphora (5%). The most common histopathological subtypes were squamous cell carcinoma (39.6%) and adenocarcinoma (25%).

Conclusion: Sinonasal tumors are frequent in male adults and present with epistaxis, nasal mass, blocked nose and nasal discharge, while squamous cell carcinoma remains the common histopathological type.

Keywords: Paranasal sinus, tumor, clinical, histopathological.

Özet: Komfo Anokye Eğitim Hastanesinde sinonazal kanserlerin klinik ve histopatolojik özellikleri

Amaç: Çalışmanın amacı Gana Kumasi'deki Komfo Anokye Eğitim Hastanesinde paranazal sinüs tümörlerinin insidansı, klinik ve histopatolojik özelliklerini belirlemektir.

Yöntem: Ocak 2007 ile Aralık 2012 arasında tanı konmuş tüm sinonazal kanser olguları retrospektif olarak gözden geçirilmiştir.

Bulgular: Altmış sekiz hastanın (38 erkek, 30 kadın) dosyaları gözden geçirilmiş olup yaş ortalaması 49 (aralık: 14–84) idi. Olağan klinik belirtiler burun kanaması (%23), nazal kitle (%20), baş ağrısı (%12), burun tıkanıklığı (%12), burun akıntısı (%11), proptoz (%9), yanak şişliği (%8) ve epifora (%5) idi. En sık görülen histopatolojik alt-tipler yassı epitel hücreli karsinom (%39.6) ve adenokarsinom (%25) idi.

Sonuç: Sinonazal tümörler sıklıkla yetişkin erkeklerde görülmekte olup hastalar burun kanaması, nazal kitle, tıkalı burun ve burun akıntısı ile başvurmaktadırlar. Yassı epitel hücreli karsinom hâlâ sık görülen histopatolojik tiptir.

Anahtar sözcükler: Paranazal sinüs, tümör, klinik, histopatolojik.

Sinonasal cancers are malignant neoplastic lesions of the nose and the paranasal sinuses. Sinonasal cancers are rare neoplastic lesions accounting for less than 1% of all malignancies and about 3% of all head and neck cancers.[1–3] These lesions tend to affect mostly Africans, the Japanese and the Arabs.[4,5]

Kuijpens et al. reported of a greater incidence of sinonasal cancers in males than in females with a male-to-female ratio of 2:1.[1] Arnold et al. reported in a similar retrospective study of a male-to-female ratio of 2:1.[6] The patients' ages ranged between 28 and 92 years with a median age at diagnosis of 64 years. Likewise, Betlejeweski et al. found in another study a male-to-female ratio of 1.5:1, with ages ranged between 50 and 69 years.[7] Fasunla and Lasisi also reported of male to female ratio of 2:1, with ages ranged between 4 and 69 years.[8] Brobby also reported of a similar study male-to-female ratio of 1.5:1 with ages ranged between 36 and 79 years.[9]

Sinonasal cancers are associated with significant otorhinolaryngologic morbidity and mortality in West Africa.[5] The symptoms of sinonasal cancers depend on site and the extent of disease and may initially include nasal obstruction, epistaxis, or symptoms consistent with chronic sinusitis such as headache, rhinorrhoea while

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small tumors may be asymptomatic.[10] Koivunen et al. reported nasal obstruction (35%), epistaxis (18%) and observable or palpable tumor (12%) in the cases studied.[11] Fasunla and Lasisi found epistaxis, obstruction and nasal discharge in all cases (100%), check swelling (92.7%), cheek pain and paraethesia (69.5%) and toothache (56.5%).[8] In another study by Waldron et al., the most common presenting symptoms were pain (59%), oral symptoms (40%), facial swelling (38%), nasal obstruction (35%) and epistaxis (25%).[12] Myers et al. also reported pain (34%), nasal obstruction (34%), expansile mass (29%), epistaxis (23%), numbness in the area innervated by the maxillary component of the trigeminal nerve (V2 distribution) (14%), epiphora (11%) and diplopia (11%).[2]

Sinonasal cancers can present a histological diversity pattern, the most common being squamous cell carcinoma, adenocarcinoma, lymphoma, melanoma, sarcoma and adenoid cystic carcinoma. Arnold et al. found squamous cell carcinoma with 30.9%, melanoma (19.5%), and adenocarcinoma (17.1%) of the patients.[6] Others were esthesioneuroblastoma (8.9%), lymphoma (5.7%), undifferentiated carcinoma (4.9%), adenoid cystic carcinoma (4.9%), plasmocytoma (3.3%), fibrosarcoma (1.6%), leiomyosarcoma (1.6%) and metastatic disease (1.6%) in the cases studied. Kuijpens et al. found squamous cell carcinoma as the most frequent histological type in 46.0%, followed by adenocarcinoma (15.0%), melanoma (8.0%) and olfactory neuroblastoma (3.5%).[1] Myers et al. also reported squamous cell carcinoma (51.0%), adenoid cystic carcinoma (12.0%) and adenocarcinoma (11.0%).[2] Madison Michael et al. revealed squamous cell carcinoma (64.0%), adenocarcinoma (18.0%), adenoid cystic carcinoma and undifferentiated carcinoma (9.0%) in a histological analysis of sinonasal tumors.[13]

This study was conducted in view of the fact that less literature has been reported on sinonasal cancers within West Africa sub-region and Ghana in particular.

Materials and Methods

Study design

The study has been conducted in accordance with the principles of the Helsinki Declaration and approved by the local Institutional Review Board. Medical records of the sinonasal cancer patients admitted to Eye, Ear, Nose and Throat Clinic of Komfo Anokye Teaching Hospital between January 2007 and December 2012 were analyzed retrospectively.

Outcome parameters

Data including age, sex, clinical presentations and histological diagnosis were obtained from patients' medical records for the study.

Statistical analysis

Data were analyzed using the IBM Statistical Package for Social Sciences v16 (SPSS Inc., Chicago, IL, USA). Parametric tests were applied to data of normal distribution and non-parametric tests were applied to data of questionably normal distribution. Data are expressed as mean±SD or median (interquartile range), as appropriate. Statistical significance was assumed for $p<0.05$.

Results

Of the 68 patients (38 males, 30 females) whose charts were reviewed, the median age was 49 (range: 14 to 84) years. With regard to age distribution, 5 (7.4%) patients were between 11 and 25 years, 16 (23.5%) patients were between 26 and 40 years, 30 (44.1%) patients were between 41 and 55 years, 6 (8.8%) patients were between 56 and 70 years and 11 (16.3%) patients were between 71 and 85 years.

The clinical presentations of the patients varied in respect to the stage of the lesion at presentation. In this study, 23 (33.8%) patients presented with epistaxis, 12 (17.6%) patients with headache, 8 (11.8%) patients with cheek swelling, 12 (17.6%) patients with nasal blockage, 11 (16.2%) patients with nasal discharge, 9 (13.2%) patients with proptosis, and 5 (7.4%) patients with epiphora. A total of 20 patients (29.4%) were presented with nasal mass.

The patients' histological reports analyzed revealed variety of cancers including squamous cell carcinoma in 27 (39.6%) patients, adenocarcinoma in 17 (25.0%) patients, malignant melanoma and lymphoma in 6 (8.8%) patients each. Besides, there were undifferentiated carcinoma in 7 (10.3%) patients, fibrosarcoma in 3 (4.4%) patients, adenoid cystic carcinoma and olfactory neuroblastoma were found in one (1.5%) patient.

Discussion

Sinonasal cancers can be diagnosed in all ages, nonetheless are rare in children. In this study, 68 cases of sinonasal cancers were found in the age range 14 to 84 years with median age of 51 and peak age group of 41 to 55 (44.1%) with a male-to-female ratio of 1.3:1.

The distribution in this study was lower than the findings in Poland by Betlejewski et al.[7] where majority of cases

(55) were between 50 and 69 years and Zyłka et al.[14] who reported 50.8% of all the patients aged above 60 years, with the most common age group being 71–80 years (33.3%).

Carrau et al.[15] found sinonasal cancers mostly in patients between 50 and 70 years of age and Myers et al.[2] reported of a higher incidence at 60 years.

Fasunla and Lasisi[8] in Nigeria reported of occurrence of sinonal cancers in the age ranged between 4 and 69 years with the peak age of 50 years.

The lower median age of occurrence in this study may be due to the lower life expectancy in Ghana which is about 57 years.

The sex distribution in this study was similar to other studies reported in the literature where sinonasal cancers seemed to be frequent in males than females.

A male to female ratio of 1.3:1 was in concordance to that of Betlejewski et al.[7] (1.5:1), Brobby[9] (1.5:1), Fasunla and Lasisi[8] (2:1), Kuijpens et al.[1] (2:1) and Arnold et al.[6] (2:1). The higher incidence in males than females may be due to the fact that males may be more exposed to certain conditions that may contribute to the insurgence of the disease. For instance, with the exposure of sawn dust, inhalation of fume from heavy metals, smoking and alcoholism may predispose individuals to such condition.

The clinical presentations in this study were epistaxis (28%), headache (12%), cheek swelling (8%), nasal blockage (12%), nasal discharge (11%), epiphora (5%), proptosis (9%) and nasal mass (20%).

Most of the literatures reviewed reported of epistaxis, nasal obstruction, nasal discharge, check swelling and nasal mass as some of the common presentations in sinonasal cancers. These symptoms may vary from patient to patient depending on the stage of the lesion. Myers et al.[2] reported of nasal obstruction (34%), expansile mass (29.0%), epistaxis (23.0%) and epiphora (11.0%). Koivunen et al.[11] also reported of nasal obstruction (25.0%), epistaxis (18.0%) and palpable tumor (12.0%) whereas Fasunla and Lasisi[8] reported of nasal obstruction and discharge (100%), cheek swelling (92.7%), cheek pain and paraesthesia (69.5%) and toothache (56.5%). This really indicates that patients who present with nasal blockage, epistaxis, nasal mass and others might be possible candidates of sinonasal tumors.

In this study, the most common histological presentation was squamous cell carcinoma (39.6%) followed by adenocarcinoma (25.0%), malignant melanoma and lymphoma (8.8%). Besides, there were undifferentiated carcinoma and fibrosarcoma (7.4%), and adenoid cystic carcinoma and olfactory neuroblastoma (1.5%).

Likewise, the most of the studies reported in the literature revealed squamous cell carcinoma as the most common histological feature of sinonasal cancers followed by adenocarcinoma.

Madison Michael et al.[13] reported squamous cell carcinoma (64.0%) and adenocarcinoma (18.0%), Kuijpens et al.[1] also reported 46.0% and 15.0%, Myers et al.[2] reported 51.0% and 11.0% while Arnold et al.[6] reported 30.9% and 17.1%, respectively. All these studies confirm the higher incidence of squamous cell carcinoma in sinonasal cancers.

Conclusion

Although sinonasal cancers are rare, they constitute almost 3.0% of all head and neck cancers. They affect mostly adults and they are frequently seen in males than females often present with epistaxis, nasal mass, blocked nose and nasal discharge, whilst the common histological feature is the squamous cell carcinoma. It is therefore important to investigate properly patients who present with some of these symptoms for sinonasal cancers.

Conflict of Interest: No conflicts declared.

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Level IIb lymph node metastasis in transglottic laryngeal squamous cell carcinoma

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Abstract

Objective: To evaluate the clinical and pathologic parameters associated with level IIb metastasis in transglottic laryngeal carcinoma.

Methods: A total of 238 laryngeal squamous cell carcinoma patients admitted to our tertiary center and surgically treated between January 2006 and January 2014. Of these 238 patients, 134 patients with transglottic laryngeal SCC were enrolled in the study. The type of neck dissection, the location of histopathologically proven metastatic lymph nodes, clinical N and T stages were reviewed. Palpable lymph nodes were accepted clinically cN(+) and the opposite as cN(-).

Results: Of the 134 patients, 116 were diagnosed as cN(-), and 18 were as cN(+). Level IIb metastasis was diagnosed in 12 patients in the cN(+) group, and in two patients in the cN(-) group. Histopathological level IIb metastasis was shown in 14 of 134 patients, representing 16 of 268 neck dissection specimens. Level IIb metastasis was shown in the ipsilateral specimens in 12 patients and contralateral specimens in two patients. Forty-one of 134 patients presented cartilage invasion, and nine of them were diagnosed with level IIb metastasis.

Conclusion: Thyroid cartilage invasion, the presence of level IIa invasion and advanced stage disease are the risk factors for level IIb metastasis. Therefore, level IIb should not be neglected during neck dissection in transglotticlaryngeal carcinoma.

Keywords: Level IIb, lymph node metastasis, transglottic, laryngeal squamous cell carcinoma.

Özet: Transglottik larinks skuamöz hücreli karsinomlarda level IIb lenf nodu metastazı

Amaç: Çalışmanın amacı transglottik laringeal karsinomda level IIb metastazı ile ilişkili klinik ve patolojik paremetreleri araştırmaktır.

Yöntem: 2006 Ocak ve 2014 Ocak arasında üçüncü basamak kliniğimizde parsiyel veya total larenjektomi uygulanan 238 hastanın medikal kayıtları retrospektif olarak tarandı. Bu 238 hastadan transglottik larinks skuamöz hücreli karsinomu olan 134'ü bu çalışmaya dahil edildi. Boyun diseksiyonu tipi, histopatolojik lenf nodları ve lokalizasyonları, klinik N evresi ve T evresi verileri değerlendirildi. Palpabl lenf nodlarının varlığında klinik olarak boyun pozitif cN(+) olarak kabul edildi.

Bulgular: Yüz otuz dört hastanın 116'sı cN(-) ve 18'i cN(+) olarak saptandı. Level IIb metastazı cN(+) grupta 12 hastada, cN(-) grupta 2 hastada bulundu. Histopatolojik level IIb metastazı 134 hastanın 14'ünde ve 268 boyun diseksiyonu spesmeninin 16'sında saptandı. Level IIb metastazı ipsilateral spesimenlerin 12'sinde ve kontralateral spesmenlerin 2'sinde gösterildi. 134 hastanın 41'inde tiroid kartilaj invazyonu mevcuttu ve bu hastaların 9'unda aynı zamanda level IIb metastazı vardı.

Sonuç: Larinks kanserlerinde tiroid kartilaj invazyonu, level IIa metastazı ve ileri evre olması level IIb metastazı için risk faktörü olarak bulundu. Bu nedenle transglottik karsinomlarda level IIb diseksiyonu ihmal edilmemelidir.

Anahtar sözcükler: Level IIb, lenf nodu metastazı, transglottik, larinks skuamöz hücreli karsinomu.

The treatment of laryngeal squamous cell carcinoma (SCC) is based on proper design of therapeutic strategies aimed to control cervical lymph node metastasis. Cervical nodal metastasis is one of the most important prognostic factors in carcinoma of the larynx.[1] The incidence of clinically detectable lymph node metastasis in laryngeal carcinoma is high, and the levels II, III, and IV are the most commonly involved lymphatic groups in carcinoma of the larynx.

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Understanding of the lymphatic spread of the laryngeal SCC is important for performing selective neck dissection (SND).

Since the first description of neck dissection, it has been the most common treatment option for cervical lymph node metastases of laryngeal cancer. Recently, surgical treatment of neck metastasis has evolved to provide oncologic efficacy while reducing morbidities. Despite all efforts to preserve, the spinal accessory nerve (SAN) may still be damaged because of various intraoperative factors and causes an extensive decrease in the quality of life. Previous studies showed that the severity of postoperative shoulder syndrome is directly proportional to the extent of neck dissection. These studies indicated 18% to 77% frequency of shoulder syndrome in functional neck dissection while 29% to 39% in SND.[2–4] The clearance of the lymph nodes lying posterior and superior to the SAN might traumatize SAN. These lymph nodes were named as "level IIb" by Suen et al.[5] If these lymph nodes are not cleared, the SAN dysfunction can be decreased.[6–8]

The preservation of the IIb region is reported to be possible in N0 cases of laryngeal cancer. However, level IIb metastasis can be observed in laryngeal SCC carcinomas. Consequently, determination of high-risk patients for level IIb metastasis may allow the surgeon to perform SND, in which the lymph nodes at greatest risk of metastasis are resected. So, in low-risk patients, further dissection of level IIb may be avoided.

The aim of this study was to evaluate the clinical and pathologic parameters associated with level IIB metastasis in transglottic laryngeal carcinoma.

Materials and Methods

Study design

This retrospective study has been conducted in accordance with the principles of the Helsinki Declaration and approved by the local Institutional Review Board. A total of 238 laryngeal squamous cell carcinoma patients admitted to our tertiary center between January 2006 and January 2014 and treated with total or partial laryngectomy with or without neck dissection constituted the study group. Of these 238 patients, 134 patients with transglottic laryngeal SCC were enrolled in the study. The term transglottic was used for tumors that invaded supraglottic, glottic, and subglottic regions and displayed a vertical progression.

Surgical approach to the neck

To determine the type of neck dissection, frozen sections were examined intraoperatively. If the lymph nodes of the ipsilateral SND II-IV material were diagnosed as metastatic on frozen section, level V was added to the neck dissection, and contralateral SND II-IV was also performed. If metastasis was diagnosed postoperatively, radiation therapy was applied.

Outcome parameters

The evaluated data included the type of neck dissection, the histopathological metastatic lymph nodes and their locations, clinical N stage, and T stage. Estimations were made according to the American Joint Committee for Cancer (2002). Palpable lymph nodes were accepted clinically cN(+) and the opposite as cN(-). Cases were examined in terms of level IIb metastasis.

Statistical analyzes

Data were analyzed using the Statistical Package for Social Sciences (SPSS) software version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Parametric tests were applied to data with normal distribution and non-parametric tests were applied to data with questionably normal distribution. The distribution of categorical variables in both groups was compared using Fisher's exact test. Data are expressed as mean±SD or median (interquartile range), as appropriate. Statistical significance was assumed for $p<0.05$.

Results

The study group consisted of 128 men and six women. The mean age was 62.32 (range: 42 to 76) years. The mean follow-up was 49 (range: 12 to 96) months.

Total laryngectomy was performed in 118 patients, supracricoid laryngectomy in 13 patients, and near-total laryngectomy in three patients. Bilateral neck dissection was performed in all patients with a total of 268 neck dissections. Metastasis to level IIb was diagnosed in 16 neck dissection specimens of 14 patients.

Of the 134 patients, 12 were diagnosed as stage T2, 75 as T3, and 47 as T4. Of the 134 patients, 116 were diagnosed as cN(-), and 18 were as cN(+). Metastasis to level IIb was diagnosed in 12 patients in the cN(+) group and in 2 patients in the cN(-) group. The relationship between level IIb metastasis and clinical N stage was found to be statistically significant. Of the 14 patients with level IIb metastasis, one patient was diagnosed as stage T2, three patients were as T3, and 10 patients were as T4.

Histopathological level IIb metastasis was shown in 14 of 134 patients, representing 16 of 268 neck dissection specimens. Level IIb metastasis was shown in the ipsilater-

al specimens in 12 patients and contralateral specimens in 2 patients. There was no isolated level IIb involvement. For patients who had ipsilateral level IIb metastasis, ipsilateral level IIa, ipsilateral level III, and contralateral level IIa metastasis were also observed. For patients who had contralateral level IIb metastasis, level IIa and level III metastasis were also observed ipsilaterally and contralaterally. Two patients were cN(-), and 12 were cN(+).

Forty-one of 134 patients presented cartilage invasion and 9 of them were diagnosed with level IIb metastasis. A total of 32 patients had ipsilateral level IIa metastasis. Of these 32 patients, 12 had ipsilateral level IIb metastasis. Of these 14 patients, 12 had isolated ipsilateral level IIb metastasis and 2 isolated ipsilateral and contralateral level IIb metastasis. A total of two patients were diagnosed with bilateral level IIb metastasis. All of these patients had ipsilateral level IIa metastases.

Discussion

The present study aimed to define the risk of level IIb lymph node metastasis in transglottic laryngeal carcinomas. Determination of the high-risk patients for level IIb lymph node metastasis can guide surgeons for further dissection of level IIb. Performing neck dissection only to these high-risk patients may reduce overtreatment and shoulder syndrome.

The lymphatic drainage of glottic and supraglottic larynx area is mainly toward the lymph nodes in levels II, III, and IV. Laryngeal carcinomas metastasize primarily to levels II and III before other lymph node regions according to the current understanding of the lymphatic drainage pathway.[9] However, the role of level IIb lymph nodes in laryngeal carcinoma is less clear. Various studies have shown that metastases are rarely found in level IIb in laryngeal carcinoma.[8–16] Metastases in level IIb are often associated with level IIa metastases.[9] In the present study, 14 (10.4%) of 134 patients diagnosed with transglottic laryngeal SCC, 16 level IIb metastases were detected as a result of 268 neck dissections. 32 patients had ipsilateral level IIa metastases, and 14 of them had ipsilateral level IIb metastases. Two patients had both contralateral level IIa and level IIb metastases.

Koybasioglu et al. reviewed 49 patients with laryngeal SCC and reported that level IIb lymph nodes were negative in all of the dissection materials.[8] Of these 49 patients, neck staging was N0 in 29 patients, N1 in 17 patients, and N2 in three patients. They concluded that level IIb should not be added to lateral neck dissection to avoid damage to the SAN.

Sezen et al. reviewed 98 neck dissections performed in 63 laryngeal carcinomas and reported six level IIb metastases in 63 cases.[17] However, all six cases were cN(+), and metastases in level IIb were not found in cN(-) cases. Of the studied six patients, five were supraglottic cancers and one was subglottic cancer. The T stages were T3 or T4 in all cases. To be brief, these authors revealed that level IIb can be conserved in cN0 cases. In the present study, 116 of 134 with transglottic laryngeal SCC patients were diagnosed as cN(-), and 18 were as cN(+). Metastasis to level IIb was diagnosed in 14 necks in the cN(+) group and two necks in the cN(-) group. One of the patients with level IIb metastasis was T2, three patients were T3, and 10 patients were T4.

Dundar et al. reported their results of neck dissections for the treatment of 81 patients with laryngeal SCC for whom 148 SNDs and modified radical neck dissection type II were performed.[18] In five of the 148 neck dissection specimens was metastasis found in level IIb. In the present study, 40 of 81 patients were diagnosed as transglottic laryngeal SCC, with four of them diagnosed as level IIb metastasis. However, Wiegand et al. reported transglottic carcinomas in 12 of 73 patients, with no presence of level IIb metastasis.[19]

In our single institution series of transglottic laryngeal carcinoma, cartilage invasion, advanced stage and level IIa metastasis were found to be associated with level IIB metastasis. In cases with advanced stage tumors and/or cartilage invasion, the omittance of level IIb dissection to protect SAN may result in a diminished surgical success.

Conclusion

According to our results, thyroid cartilage invasion, the presence of level IIa invasion and advanced stage disease are the risk factors for level IIb metastasis. Therefore, level IIb should not be neglected during neck dissection in transglottic carcinoma.

Conflict of Interest: No conflicts declared.

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The effects of depression and anxiety levels on the status of recovery in patients with idiopathic sudden sensorineural hearing loss

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Abstract

Objective: To compare the severity of anxiety and depression symptoms in idiopathic sudden sensorineural hearing loss (ISSHL) patients with (n=33) and without (n=17) recovery, and healthy control group.

Methods: This study was conducted on ISSHL inpatients (n=50) and a healthy control group (n=52). Severity of the anxiety and depression symptoms was assessed using the State-Trait Anxiety Inventory (STAI) and Beck Depression Inventory (BDI) during admission. Hearing data of all 50 cases obtained at baseline and after the treatment (at the end of the 4th week) were gathered from the audiological evaluation form of each patient.

Results: The rates of ISSHL patients with and without recovery were 66% and 34%, respectively. The mean BDI and STAI-II scores of the patients with ISSHL were significantly higher than those of the control group (11.4±8.6 vs. 6.8±4.3 and 41.6±7.3 vs. 36.7±8.4, respectively; p<0.05). Among the ISSHL patients, there was a moderate and significant positive correlation between the BDI and STSI-II scores (r=0.617, p<0.05). The mean BDI, STAI-I, and STAI-II scores of the control group were significantly lower than those of the recovery and no recovery groups (p<0.05). However, the recovery and no-recovery groups did not show any difference in terms of mean BDI, STAI-I and STAI-II scores (p>0.05).

Conclusion: ISSHL patients had a more depressive and anxious mood compared to the healthy controls. However, anxiety and depressive mood had no effect on the recovery status of the ISSHL patients. Physicians also need to pay attention to the status of anxiety and depressive symptoms in patients with ISSHL.

Keywords: Idiopathic sudden sensorineural hearing loss, anxiety, depression.

Özet: Depresyon ve anksiyete düzeylerinin idiyopatik ani sensorinöral işitme kaybı olan hastaların iyileşme durumlarına etkileri

Amaç: Çalışmanın amacı ani idiyopatik sensorinöral işitme kaybı olup iyileşen (n=33) ve iyileşmeyen (n=17) hastalarda ve sağlıklı kontrollerde anksiyete ve depresyon semptomlarının şiddet derecesini karşılaştırmaktır.

Yöntem: Bu çalışma hastanede yatan sensorinöral işitme kayıplı hastalarla (n=50), sağlıklı kontrol grubunda (n=52) gerçekleştirildi. Anksiyete ve depresyon semptomlarının şiddet derecesi hastaneye kabul sırasında uygulanan Durumsal Sürekli Kaygı Envanteri (STAI) ve Beck Depresyon Envanteri (BDI) ile değerlendirildi. Başlangıçta ve tedavi sonrasında (4. haftanın sonunda) her bir hastanın odyolojik değerlendirme formundan 50 olgunun tüm işitme verileri elde edildi.

Bulgular: ISSHL hastalarının %66'sı iyileşmiş, %34'ü iyileşmemişti. ISSHL hastalarının ve kontrol deneklerin ortalama BDI ve STAI-II skorları sırasıyla 11.4±8.6 vs. 6.8±4.3 ve 41.6±7.3 vs. 36.7±8.4 (p<0.05) olup, ISSHL hastalarının değerleri kontrol grubundan anlamlı derecede daha yüksek idi. ISSHL hastalarında BDI ve STSI-II skorları arasında orta derecede ve anlamlı pozitif korelasyon mevcuttu. (r=0.617, p<0.05). Kontrol grubunun ortalama BDI, STAI-I ve STA-I-II skorları, iyileşen ve hiç iyileşmeyen gruplara göre anlamlı derecede daha düşüktü (p<0.05). Ancak iyileşmiş ve hiç iyileşmemiş gruplar arasında ortalama BDI, STAI-I ve STAI-II skorları açısından anlamlı farklılık gözlemlenmedi (p>0.05).

Sonuç: Sağlıklı kontrollere göre ISSHL hastaları daha depresif ve endişeli bir ruh hali içindeydi. Ancak anksiyete ve depresif ruh hali ISSHL hastalarının iyileşme durumunu hiçbir şekilde etkilememiştir. Doktorlar ISSHL hastalarının anksiyete ve depresif semptomlarına da dikkat etmelidir.

Anahtar sözcükler: İdiyopatik ani sensorinöral işitme kaybı, anksiyete, depresyon.

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Idiopathic sudden sensorineural hearing loss (ISSHL), which is usually a unilateral condition, is considered as an otological emergency. It may range from slight impairment of hearing to virtual deafness. Although the clinical definition of ISHHL is not strictly clear, hearing loss of at least 30 dB in three consecutive frequencies in the standard pure tone audiogram over 72 hours or less stands is the most commonly used definition.[1–4] Understanding the factors contributing to recovery in ISSHL is an important challenge in ear, nose and throat (ENT) practice. In this context, being at a younger age, male gender, shorter elapsed time between the onset of hearing loss and initiation of treatment, lower self-reported depressive symptoms and upward-sloping or cupeloid audiogram are reported to be associated with better outcomes.[5,6]

Depression is one of the leading causes of disability worldwide.[7] Poor self-care and adherence to medical regimens, amplification of somatic symptoms and disability, high medical care utilization, and increased morbidity and mortality from medical illness have been associated with depression[8] while anxiety is a significant factor contributing to disability, morbidity, and mortality.[7] As the literature shows a high level of comorbidity between depression and anxiety,[9,10] it may be necessary to evaluate anxiety while studying the effects of depression on recovery from a physical illness.

In patients having no hearing problem before the onset of ISSHL, unilateral hearing loss can be a very sudden change[11] causing stress, anxiety and fear. Several studies have investigated the relationship of mood, anxiety and physical illnesses, and reported that patients with depression, other mood states or anxiety have poorer treatment outcomes.[5] In the current literature, there is a limited number of studies on the association between treatment outcomes in ISSHL and level of depression and anxiety. The aim of the present study was to compare the level of self-reported anxiety and depression in ISSHL patients with and without recovery after administrating a treatment and following-up for a period of four weeks.

Materials and Methods

Study population

This cross-sectional study was conducted on inpatients with ISSHL at the ENT clinic of our university hospital. Before starting the study, an approval was obtained from Human Research Ethics Committee of our university. All patients (n=63) treated between October 2014 and May 2015 were offered to participate in the study. After obtaining written informed consents, the final study population consisted of 50 patients.

Acute-onset hearing loss without any recognizable cause, untreated sudden hearing loss having a sensorineural origin, application to hospital within 7 days of onset, not being lost to follow-up during recovery, having a hearing level of 30 dB over at least three frequencies, normal hearing in the contralateral ear (a 40 dB HL air conduction pure-tone average [PTA] at 0.25, 0.5, 1, 2, 4, and 8 Hz frequencies), having no prior hearing loss or ear surgery in the affected ear and lack of impairment of the cranial nerves (except cranial nerve VIII)[12] were the inclusion criteria.

The exclusion criteria were having a history of trauma, ontological surgery or barotrauma during the previous 4 weeks, having cerebellopontine angle pathology, congenital cochlear malformations, neurological disorders, recent use of ototoxic drugs, having a neoplasm during the previous 2 years, or having another major disorder (such as hypertension, coronary artery disease, liver or renal dysfunction, diabetes mellitus, chronic obstructive pulmonary disorder, etc.) or any ontological disorder such as otitis media during the previous 4 weeks and receiving a psychiatric treatment. The data on the inclusion and exclusion criteria were gathered from the patients, first degree relatives and patients' files.

Healthy controls

Fifty-two (52) age- and gender-matched control subjects were recruited from the university hospital. None of them was on any form of prescribed psychiatric medication. None of the healthy volunteers had any of the exclusion criteria listed above. The data on the exclusion criteria and prescribed psychiatric medications were gathered from the participants, first degree relatives, and participants' files.

Study measures

The State-Trait Anxiety Inventory (STAI)[13] is a widely used self-evaluation questionnaire measuring the state and trait anxiety. It contains two subscales composed of 20 items. The state (STAI-I) subscale measures the anxiety associated with any specific situation or time-period at the moment of the questionnaire) while the trait (STAI-II) subscale measures the relatively stable anxiety which show how a person feels on a day-to-day basis. A 4-point Likert scale is used to rate the responses. The total state and total trait anxiety scores vary from 20 to 80 points. A higher score shows a higher anxiety level while a lower score shows a lower anxiety level. The Turkish validation of the STAI was conducted by Öner and Le Compte in 1983.[14]

Beck Depression Inventory (BDI)[15] is a self-evaluation scale. It consists of 21 items to evaluate the level and severity of depression symptoms. It provides a quadruple Likert-type measurement. The points assigned to each item vary between 0 to 3 while the total points vary between 0 and 63. The Turkish validation and reliability check of BDI was performed by Hisli.[16]

Hearing data of all 50 cases obtained by AC-40 Interacoustics Clinic Audiometer (Interacoustics, Assen, Denmark) at baseline and after the treatment (at the end of the 4th week) were gathered from the audiological evaluation form of each patient.

Study procedure

The patients were given the BDI, STAI-I and II forms on the first day of hospitalization at the ENT clinic. The STAI and BDI forms were evaluated by a senior psychiatrist (DGM).

ISSHL was defined as a hearing loss of 30 dB or more over at least 3 contiguous frequencies in 72 hours.[3]

During their initial visits, a complete clinical history was obtained from the patients and standard audiological examinations consisted of pure-tone tests were performed. Then, all the patients were given the same treatment protocol with i.v. methylprednisolone (1 mg/kg per day, Prednol-L ampoule; Mustafa Nevzat Drug Industry, Istanbul, Turkey), tapering the dose 10 mg every 3 days within the following days. While being on corticosteroids, the patients were administered H2 receptor inhibitor ranitidine 1x11 ampoule i.v. (Ulcuran ampoules 50 mg/2 ml iv; Yavuz Drug Industry, Istanbul, Turkey), oral vitamin B1 (2x250 mg thiamine hydrochloride) and B6 (250 mg pyridoxine hydrochloride; Nerox B tablet; Abdi İbrahim Pharmaceutical Company, Istanbul, Turkey) for three months. Then, 100 mg pentoxfylline (Vasoplan AMP 100 mg/5 ml; Mustafa Nevzat Drug Industry, Istanbul, Turkey) was added into 500 ml Voluven (Fresenius Kabi AG, Bad Homburg, Germany) and administered by intravenous infusion every other day for eight days.

All ISSHL patients underwent a pure-tone speech audiometry. Pure tone thresholds were obtained for air conduction at 250 Hz, 500 Hz, 1 kHz, 2 kHz, 4 kHz, and 6 kHz and for bone conduction at 250 Hz, 500 Hz, 1 kHz, 2 kHz, and 4 kHz. The methods recommended by the Hearing Committee of the American Academy of Otolaryngology Head and Neck Surgery were used to report the audiological data obtained. In order to follow-up the treatment responses of the patients, the audiological evaluation was carried out every other day and repeated for 4 weeks after the end of the treatment. Using the Siegel criteria, a classification was made based on the treatment outcomes and the pure tone averages obtained during the follow-ups after one month term.[17,18] Patients having ISSHL were divided into two subgroups by taking into account whether their PTAs recovered (complete, partial and slight recovery) or not.

Statistical analysis

All the variables were summarized using descriptive statistics. The data obtained were analyzed using the Statistical Package of Social Science (SPSS Inc., Chicago, IL, USA) version 22.0 for Windows and presented as mean ± SD and percentage as appropriate. The mean BDI, STAI-I and STAI-II scores of the ISSHL and the control groups were compared by the Student's t-test. The correlations between the BDI, STAI-I, and STAI-II scores were analyzed using the Pearson's correlation coefficients. The gender rates and the mean BDI, STAI-I, and STAI-II of the patients and the control groups were compared with chi-square test and one-way analysis of variance (ANOVA), respectively. Tukey's multiple comparison procedure was performed when significant main effects were present. $P<0.05$ was regarded as significant.

Results

Sixty-three inpatients with ISSHL were found to be eligible to participate in the study. After refusal of five patients to participate in the study and eight patients being excluded from the study for not meeting the inclusion criteria, the final study population consisted of 50 patients. In terms of age and gender, there was no difference between the patient and the control groups. The average ages of the patient and the control groups were 38.3±13.19 and 35.2±7.83 years, respectively. 30 (60%) of those in the patient groups and 26 (50%) of those in the control group were male. Following the treatment, the recovery rate was 33 (66%) in the patient group.

The comparison of the ISSHL patients and the control groups in terms of pre-treatment anxiety and depression levels is shown in Table 1. The mean BDI and STAI-II scores were significantly higher in patients with ISSHL when compared to the control group (Table 1). Among ISSHL patients, the BDI and STSI-II scores showed a moderate correlation and a significant correlation, respectively ($r=0.617$, $p<0.05$).

The gender rates of the patient groups and the control group were similar (p>0.05) (Table 2).

The mean BDI, STAI-I and STAI-II scores of the control group were significantly lower than those of the recovery and no-recovery groups (p<0.05). However, there was no difference between the recovery and no-recovery groups in terms of the mean BDI, STAI-I and STAI-II scores (p>0.05) (Table 3).

Discussion

Our aim was first to evaluate the pre-treatment depression and anxiety levels of the patients having ISSHL and then to compare the patient groups (recovery and no-recovery groups) and healthy controls in terms of the said levels. Our study revealed that the depression and anxiety levels of the ISSHL patients were higher when compared to the healthy controls. However, when ISSHL patients recovering and not recovering after the treatment were compared, the depression and anxiety levels were found to be similar.

The hearing loss observed in ISSHL cases is a sudden change. Most of the times, the patients experiencing a sudden hearing loss do not have a history of such a loss.[1] For this reason, this extraordinary event causes anxiety in such patients. Hearing loss may lead to difficulties in communication and learning, reduce productivity, and increase depression, anxiety and social isolation.[19] Due to social isolation, the level of psychiatric symptoms may be higher in people having hearing impairment.[5,20,21]

Various studies have investigated the prognostic significance of depression or anxiety in patients having physical illnesses such as myocardial infarction, cancer or asthma. In some studies, recovery has been reported to be negatively affected by anxiety or depression.[7,12,22] Similarly, a limited number of studies have evaluated the effects of only depression or only anxiety on the prognosis of ISSHL.[5,23] In the current study, we have evaluated both the depression and the anxiety levels of ISSHL patients during the pre-treatment period and found a positive relation between depression and anxiety levels. Moreover, we used an anxiety instrument (STAI-II) found to be correlated with depression levels in many studies; however, the depression and anxiety levels before the treatment were similar in the recovery and no-recovery groups. This result is in conflict with the previous findings.[5,24] The major reason of having such a result can be related with having a limited number of participants. Another reason can be the non-evaluation of the depression and anxiety levels of the recovery and no-recovery groups after the treatment. Evaluating the depression and anxiety levels only at the beginning of the treatment but not evaluating afterwards is one of the major limitations of the present study. An important finding of our study is that both the trait anxiety and the depression levels were higher in the ISSHL group when compared to the healthy controls. STAI-I (trait anxiety), which is a widely used anxiety instrument, is considered as a measurement tool for the general negative effect. Although being an anxiety specific instrument stands as a drawback, STAI-II has been proven to be a good instrument in assessing the general psychopathology. Recent studies have shown the importance

Table 1. Comparison of the pre-treatment anxiety and depression levels of ISSHL patients and healthy controls.*

	Patients (n=50)	Control (n=52)
BDI	11.4±8.6†	6.8±4.3
STAI-I	39±11.4	35±9.4
STAI-II	41.6±7.3‡	36.7±8.4

*The data are presented as the mean ± standard deviation. The data were compared using the Student's t-test. †,‡p<0.05 vs. control.

Table 2. Comparison of gender ratios in the recovery, no-recovery and control groups.*

	Recovery (n=33)	No-recovery (n=17)	Control (n=52)
Female	13 (65%)	7 (35%)	26 (50%)
Male	20 (66.7%)	10 (33.3%)	26 (50%)

*The data are presented as percentages. The data were compared using the chi-square test.

Table 3. Comparison of depression and anxiety of the recovery and no-recovery groups having sudden hearing loss and the control group.*

	Recovery (n=33)	No-recovery (n=17)	Control (n=70)
Beck depression inventory	10.9±8.9	11.9±8.4	6.8±4.3†
STA-I	37.9±10.5	40.6±13.4	35.4±9.4
STA-II	40.9±6.9	43.9±6.8	36.7±8.4‡

*The data are presented as the mean ± standard deviation. The data were compared using the ANOVA. †,‡Significantly lower compared to the recovery and no-recovery groups (p<0.05).

of this tool as a marker that predicts high impairment and comorbidity in anxiety and depression disorders.[25–27] Finding a higher level of anxiety and depression in ISSHL patients compared to the healthy controls shows the importance of evaluating the psychiatric dimension in ISSHL patients. The results we obtained show both the effects of anxiety and depression on the prognosis of ISSHL and the importance of evaluating the psychiatric dimension in these patients. We consider this situation in another dimension; it has been emphasized in the literature that inflammation may have a role in the etiology of depression and anxiety and similarly in the etiology of ISSHL.[28–30] In a study on the efficiency of TNF-α inhibitor on depression and anxiety in individuals having a chronic physical disease, Abbott et al.[29] have shown that the said TNF-α inhibitor treatment decreases depression in patients having a chronic disease. Similarly, Demirhan et al.[31] have shown that TNF-α inhibitor treatment can be effective in the treatment of ISSHL patients. As a result, taking into account that depression, anxiety and ISSHL may have similar pathophysiologies and that our results showed a higher level of anxiety and depression in ISSHL patients when compared to the controls, one may postulate that evaluation of the psychiatric dimension in ISSHL patients is important.

Our study had some limitations that need to be taken into consideration in future studies. First of all, our sample was composed of only inpatients, which may raise the concern of generalizability. Secondly, the present study was based on a cross-sectional data that cannot be used to determine causal relationships. It would be beneficial to determine the depression and anxiety levels after the treatment. Thirdly, the questionnaires used to evaluate anxiety and depression were self-reported instruments not yielding an objective data. Lastly, our small sample size prevented us to generalize the results to the overall ISSHL population. Based on the limitations of the present study, we suggest conducting studies on larger populations composed of both outpatients and inpatients.

As a conclusion, our results demonstrate that patients with ISSHL have higher levels of depression and anxiety when compared to healthy controls. The comparison between recovery and no-recovery groups showed no difference in terms of depression and anxiety symptoms. Future studies are required to determine the impact of depression and anxiety on the pathogenesis of ISSHL.

Conflict of Interest: No conflicts declared.

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Case Report

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Ultrasonographic features of pharyngoesophageal diverticulum in a case misdiagnosed as a thyroid nodule: a case report and review of the literature

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Abstract

Ultrasonography technique is generally used for head and neck lumps. As pharyngoesophageal diverticula reach large sizes, it might project toward the thyroid gland which can be confused with thyroid nodule during thyroid ultrasonography, leading to unnecessary fine needle aspiration biopsy. In this report, we present a case of pharyngoesophageal diverticulum that mimicked thyroid nodule in ultrasonography together with literature knowledge and ultrasonographic signs.

Keywords: Diverticulum, nodule, thyroid, ultrasound.

***Özet:* Tiroid nodulü olarak yanlış tanı alan faringoözefageal divertikül olgusunun ultrasonografik özellikleri: Olgu sunumu ve literatürün gözden geçirilmesi**

Baş ve boyun şişlikleri için genellikle ultrasonografi tekniği kullanılır. Faringoözefagael divertikül büyük boyutlara ulaştığında, tiroid beze yansıyabilir, ultrasonografi sırasında tiroid nodül ile karıştırılabilir, gereksiz ince iğne aspirasyon biyopsisine neden olabilir. Bu çalışmada, ultrasonda tiroid nodülünü taklit eden faringoözefageal divertikül olgusunu, literatür bilgisi ve ultrasonografik işaretlerle birlikte sunduk.

Anahtar sözcükler: Divertikül, nodül, tiroid, ultrason.

Killian-Jamieson diverticulum is an infrequent, pulsion type of diverticulum which derived from the anterolateral wall of the cervical esophagus in a gap below the cricopharyngeus and lateral to the longitudinal tendon of the esophagus. Zenker's diverticulum originates from the posterior wall of the pharyngoesophageal part in a midline zone of weakness above the cricopharyngeus.[1]

Diverticulums can mimic thyroid nodule in ultrasonography due to its large size. In this paper, we discuss cases of Killian-Jamieson diverticulum that originate from the esophagus and mimic thyroid nodule, and we present ultrasonographic findings together with literature knowledge in order to prevent unnecessary biopsies.

Case Report

A 62-year-old female patient was referred from the endocrinology department ward to the ultrasonography unit of radiology clinic for the evaluation of a biopsy because of her previous ultrasonography results, performed at an external center. The women had occasional difficulty in swallowing, no family history of thyroid disease, negative laboratory tests and a normal physical examination. A thyroid ultrasonography was carried out with 10 MHz linear transducer and showed a heterogeneous nodular lesion (21×16 mm) with hypoechoic borders posterior to the left lobe of thyroid gland and a hyperechogenic center that casted shadow behind (Fig. 1). Diverticulum was suspected

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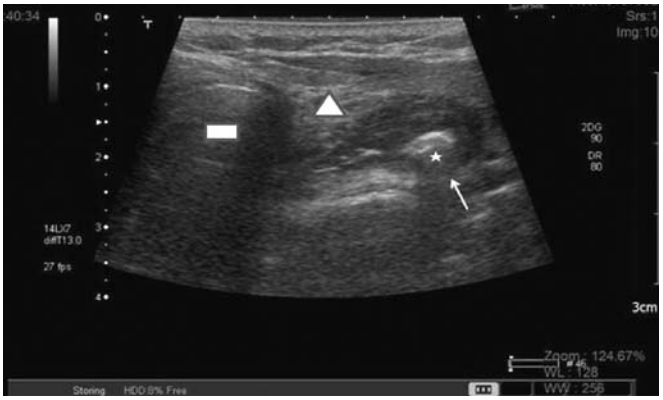

Fig. 1. In the axial section US image, there is centrally hyperechogenic lumen (asterix) and peripherally hypoechoic (arrow) diverticulum located laterally at left. Triangle is on the thyroid tissue and rectangle is on the trachea.

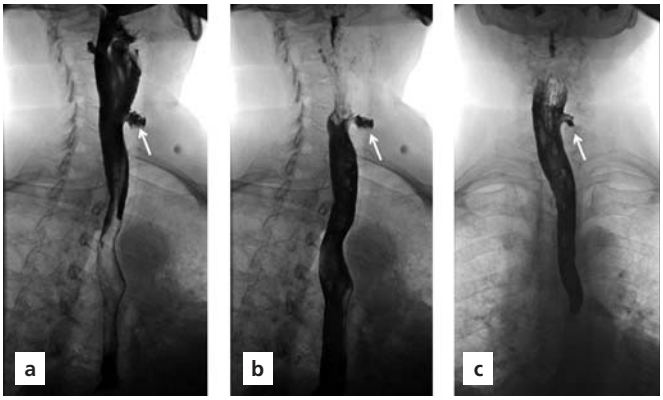

Fig. 2. Laterally located diverticulum is observed at left, at oblique (**a** and **b**) and AP (**c**) radiograms (arrow).

because of its relation to the esophagus at axial sections. When the patient was asked to swallow, the shape of the diverticulum changed. To confirm diverticulum the patient underwent barium esophagography examination. The barium examination revealed an esophageal diverticulum at C5–6 level, located left to the median line, which was filled with barium contrast agent (Fig. 2).

Discussion

This gap was first described by Killian as corresponding to the area where the recurrent laryngeal nerve enters the pharynx. This finding was later confirmed by Jamieson and is now termed the Killian-Jamieson triangle.[2–4]

Diagnosis of diverticulum is made upon detection of diverticular filling of contrast agent at the pharyngoesophageal junction in barium esophagography, together with the weight loss, regurgitation, cough, and aspiration symptoms of the patient.[5]

Diverticulum may mimic thyroid nodule in ultrasonographic examination because of its large size and location toward the thyroid leading to inadvertently fine needle aspiration biopsy (FNA). According to the review of literature, some patients underwent FNA after the initial diagnosis of thyroid nodule.[6–8] Therefore it is important to know the ultrasonographic appearance of diverticulum in order to prevent unnecessary FNA. Killian-Jamieson diverticulum cases with ultrasound findings were demonstrated in Table 1.

Important signs of diverticulum during ultrasonography are motion of air bubbles inside the diverticulum, changes in shape during swallowing, and observation of the connection to the esophagus in dynamic examination. Additionally, presence of peripheral echogenic line,

Table 1. US examination of pharyngoesophageal diverticulum cases in the literature.

Case	Ultrasound finding	Sex	Diverticulum size (cm)	Age (years)	FNA application (+)/(-)	Number of cases
Mercer et al.[15]	Hypoechoic lesion containing some bright foci/ left side	F	NA	58	(-)	1
Pang et al.[16]	Hypoechoic nodule with internal-hyperechoic foci and hypoechoic rim	M	1	54	(-)	1
Kim et al.[17]	Bilateral hyperechoic lesion	M	NA	71	(-)	1
Kim et al.[18]	Echogenic masses with echogenic foci and hypoechoic rim	7/6	1.5	41-70	7(+)/6(-)	13
Mimatsu K[14]	Hypoechoic lesion containing echogenic foci	F	4	74	(-)	1
Cildag MB (Present case)	Heterogeneous nodular lesion with hypoechoic rim and hyperechogenic center	F	2	62	(-)	1

F: female; **M:** male

hypoechoic rims and central or peripheral echogenic foci are signs suggesting that this structure originates from gastrointestinal system.[9,10]

Because of the echogenic foci inside, this structure could be confused with thyroid nodules contain punctuate microcalcification foci as found in papillary thyroid carcinoma. Air bubbles inside the diverticulum create comet-tail artifact or reverberation artifact in ultrasonography. This appearance is due to presence of air, water or debris inside the diverticulum. The diverticulum can change shape by compression of the probe or by swallowing.[11,12]

The aspects of a Killian- Jamieson diverticulum and a Zenker's diverticulum are similar; they cannot be differentiated on ultrasonography but can be differentiated on barium esophagography.[13] Barium esophagography is still considered the gold standard test for diagnosis of diverticulum. It reveals filling of contrast near the pharyngoesophageal junction, close to posterior aspect of distal pharynx. This is best observed at lateral view, at the level of C5–6 vertebrae during swallowing.

Misdiagnosis of diverticulum includes thyroid nodules, adenomas, thyroid abscess, parathyroid hyperplasia or adenoma, lymphadenopathy, pharyngeal or paratracheal air abscess.[14] Asymptomatic small diverticula are followed up with imaging techniques in combination with clinical evaluations, whereas surgical treatment is considered in cases with clinically serious dysphagia, weight loss, aspiration and recurrent pulmonary infections.

In conclusion, although pharyngoesophageal diverticulum is seen rarely, it may be confused with thyroid nodule during thyroid ultrasonography. Therefore, it is important to know the ultrasonographic signs of diverticulum in order to prevent unnecessary biopsies.

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