



ASSOCIATION BETWEEN THE ANATOMICAL PROFILE AND THE SEVERITY OF OBSTRUCTIVE SLEEP APNEA IN A SAMPLE OF PERUVIAN PATIENTS.

ASOCIACIÓN ENTRE EL PERFIL ANATÓMICO Y LA SEVERIDAD DEL APNEA OBSTRUCTIVA DEL SUEÑO EN UNA MUESTRA DE PACIENTES PERUANOS

Wendy Edith Quispe Sapacayo ¹, Violeta Mirsia Valdez Pajuelo ¹, Rocio del Pilar Ramírez Campos ²

ABSTRACT

Introduction: Obstructive Sleep Apnea (OSA) is the total or partial limitation of the passage of air through the upper respiratory tract during sleep, it has two forms of presentation: central and obstructive (related to anatomical profile). **Objective:** To determine the relationship between the anatomical profile and severity of Obstructive Sleep Apnea in adult patients of a Private Clinic in Lima Norte, Lima, 2020-2022. **Methods:** Cross-sectional analytical study. We used medical records of patients diagnosed with OSA during the period 2020-2022 in a private clinic in Lima, Peru. Our variable was the severity of OSA, in addition to apnea-hypopnea per hour (AHI), in addition we also took oxygen desaturation index (ODI), Epworth Scale, CT90%, body mass index (BMI), minimum saturation and snoring and of the newborn reported in the clinical history. The response variable was OSA. **Results:** a total of 120 clinical histories were studied. The predominant OSA was mild (29.2%), followed by very severe (26.7%). In very severe OSA, patients with retrognathia had 3.0 higher frequency, those with long face had 30.0 lower frequency and those with short face had 4.0 higher frequency, compared to patients with normal face (40 vs 7 vs 41 vs 37; p<0.01). **Conclusions:** OSA is associated with the anatomical profile. The ANGLE scale was the one most associated with OSA compared to the Friedman Score. OSA was associated with BMI, IDO, minimum saturation, and maximum heart rate.

Keywords: Obstructive sleep apnea; Anatomical profile; Body mass index; Friedman score; Severity (Source: MESH-NLM)

RESUMEN

Introducción: La Apnea Obstructiva del Sueño (AOS) es la limitación del paso del aire total o parcial a través de las vías respiratorias superiores durante el sueño, tiene dos formas de presentación: central y obstructiva (relacionada con el perfil anatómico). **Objetivo:** determinar la relación entre el perfil anatómico y severidad del Apnea Obstructiva del Sueño en pacientes adultos de una Clínica Privada de Lima Norte, Lima, 2020-2022. **Método:** Estudio analítico transversal. Se utilizó historias clínicas de pacientes con diagnóstico de AOS durante el periodo del 2020-2022 en una clínica privada de Lima, Perú. Nuestra variable principal fue la severidad del AOS, índice apnea-hipopnea por hora (IAH), además también se tomó Índice de desaturación de oxígeno (IDO), Escala de Epworth, CT90%, índice de masa corporal (IMC), saturación mínima y ronquidos. La variable respuesta fue el AOS. **Resultados:** se trabajó un total de 120 de historias clínicas. El AOS que predominó fue el leve (29,2%), seguido del muy grave (26,7%). En el AOS muy grave; los pacientes con retrognatia tenían 3,0 mayor frecuencia, los de cara larga tenían 30,0 menor frecuencia y los de cara corta 4,0 mayor frecuencia en comparación con los pacientes con cara normal (40 vs 7 vs 41 vs 37; p<0,01). **Conclusiones:** El AOS se asocia al perfil anatómico. La escala de ANGLE fue la que más se asocio al AOS en comparación con el Score de Friedman. El AOS se asoció a el IMC, IDO, la saturación mínima y la frecuencia cardiaca máxima.

Palabras clave: Apnea obstructiva del sueño; Perfil anatómico; Índice de masa corporal; Score de Friedman, severidad. (Fuente: DeCS- BIREME)

¹ Universidad Peruana Unión, Lima, Perú.

² Universidad Nacional Mayor de San Marcos, Lima, Perú.

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INTRODUCTION

Obstructive Sleep Apnea (OSA) is established as the total or partial limitation of the passage of air through the upper respiratory tract during sleep, causing snoring, suffocation, a drop in the oxyhemoglobin saturation level (SaO₂) and microarousals⁽¹⁾. Causing an index of apnea-hypopnea (AHI) $\geq 15/h$, predominantly obstructive, that is sometimes accompanied by excessive sleepiness during the day, excessive tiredness, or unrefreshing sleep⁽²⁾. The severity of OSA increases when it is related to certain factors such as AHI, oxyhemoglobin saturation $< 90\%$ (hypoxemia), daytime sleepiness, obesity, and comorbidities^(3,4). OSA has been seen to increase in severity when the patient has risk factors such as upper airway obstruction, male sex, overweight (BMI), increased age, sedatives, alcohol, and tobacco⁽³⁾.

Worldwide, it represents a major public health problem due to its high prevalence, between 4 and 30%, between the ages of 40-60 years for both sexes⁽²⁾. It is estimated that 20% of the middle-aged adult population has mild OSA, and 80% of cases go undiagnosed^(5,6).

The main consequences of OSA are sleep fragmentation, cognitive impairment, intermittent hypoxia, and changes in intrathoracic pressure. These consequences are related to a higher risk of occupational and traffic accidents⁽⁷⁾. For this reason, in primary care, it is proposed to diagnose OSA when they present a high probability of hypersomnolence with an Epworth scale score ≥ 12 that can be evaluated by means of one or two channels based on oximetry and nasal pressure⁽⁸⁾.

In this context, the present study proposes identifying the association between the Anatomical profile and the severity of Obstructive Sleep Apnea in a sample of Peruvian patients.

METHODS

Design and study area

This study had an observational, analytical, and cross-sectional design.

Population and sample

The sample comprised the entire population of patients diagnosed with obstructive sleep apnea (OSA) treated at the Otorhinolaryngology Service from 2020 to mid-2022 in a private clinic in Lima, Peru. Information was

obtained through medical records during the established period. All patients underwent a cardiorespiratory polygraphy study. All patients had all the variables of interest. Thus, a total of 120 medical records were evaluated.

Variables and instruments

Patients with OSA with a score greater than 5 on the Epworth Sleepiness Scale and all the requested studies were included. All patients treated with psychotropic drugs were excluded, and other than those diagnosed with organic laryngeal disorders.

The OSA variable. It was determined by cardiorespiratory polygraphy, used as a complementary test for diagnosis and determines the degree of severity, giving us the index of apnea-hypopnea per hour (AHI), in addition, the Oxygen Desaturation Index (IDO), Epworth Scale, TC90%, body mass index (BMI), minimum saturation and snoring. The medical staff evaluated all this to determine the diagnosis of OSA. All these data were used to classify the variable as 1. Mild (AHI 5-14, CT90% 0, Epworth < 10 , BMI < 25 , no cardiovascular risk factors), 2. Moderate (AHI 15-29, CT90% 1-14, Epworth 10-14, BMI 25-29, ≥ 1 cardiovascular risk factor), 3. Severe (AHI 30-49, TC90% 15-29, Epworth 15-19, BMI 25-30-39, 1 cardio/cerebrovascular disease) and 4. Very severe (AHI ≥ 50 , TC90% ≥ 30 , Epworth ≥ 20 and drowsiness driving, BMI ≥ 40 , > 1 cardio/cerebrovascular disease).

The exposure variables that were taken were clinical bone bases (short face, long face, retrognathia, retromaxillary); cervical circumference; SCORE Friedman (I, II, III); Maximum heart rate and ANGLE Class (I, II 1, II 2, III). All these tests were performed at the clinic, so the information on all the patients was available. Sex (female, male), age, weight and height were also considered.

Procedures

The researchers, with prior permission, accessed the medical records, and the variables that were of interest for the present study were taken.



Statistical analysis

Statistical analysis was performed with STATA v17.0 software. For the descriptive analysis, the qualitative variables were summarized in proportions. In contrast, the quantitative variable was presented in the form of mean and standard deviation because it presented a normal distribution by analysis of bias, kurtosis, and histogram. In the bivariate analysis, the chi-square test was performed for the categorical variables, and in the case of the numerical variable, the Kruskal Wallis statistical test was chosen.

Ethical aspect

This study was approved by the North Lima Private Clinic and the ethics committee of the Faculty of Medicine of the Universidad Peruana Unión. In addition, all ethical research guidelines and indicated in the Declaration of Helsinki⁽¹⁰⁾.

RESULTS

The study used a total of 120 medical records. It was found that the mean age was 49.11 (13.45), the majority were male (77%), the mean BMI was 30.56 (5.16), the mean neck circumference it was 40.94 (8.54); Regarding the ANGLE scale, class II predominated (50%); the mean AHI was 32.67 (21.27); According to Epworth, the very serious presented 6.7%; the mean ODI was 31.1 (19.0); the mean for snoring was 1934.7 (1324.4); the mean of the TC 90% was 90.1 (105.4). Regarding the 90% categorized TC, the very serious predominated (64.2%); the mean minimum saturation was 72.6 (12.0); the mean maximum frequency was 113.8 (34.7). The predominant tonsillar volume was 25-70% (45.83). Regarding Mallampati, grade 4 presented 11.67%. Regarding the clinical bone bases, the one that predominated was the short face (42.5%) and the predominant OSA was the mild one (29.2%), followed by the very severe one (26.7%). (Table 1)

Table 1. Sociodemographic characteristics of the sample of patients with OSA.

Characteristics	n (%)
Age	49.11 (13.45)*
Sex	
Female	28 (23)
Male	92 (77)
BMI	30.56 (5.16)*
Neck circumference	40.94 (8.54)*
ANGLE Scale	
I	55 (46)
II 1	39 (33)
II 2	20 (17)
III	6 (5)
AHI	32.67 (21.27)*
Epworth	
Mild	53 (44.2)
Moderate	37 (30.8)
Severe	22 (18.3)
Very severe	8 (6.7)



Characteristics	n (%)
IDO	31.1 (19.0)*
Snoring	1934.7 (1324.4)*
CT 90	89.13 (106.1)*
Volume	
Normal	5 (4.17)
<25%	53 (44.17)
25-70%	55 (45.83)
50-65%	7 (5.83)
TC 90 categorized	
Mild	4 (3.3)
Moderate	30 (25.0)
Severe	9 (7.5)
Very severe	77 (64.2)
Mallampati	
Grade 1	22 (18.33)
Grade 2	43 (35.83)
Grade 3	41 (34.17)
Grade 4	14 (11.67)
Minimum saturation	72.6 (12.0)*
Maximum heart rate	113.8 (34.7)*
Clinical bone bases	
Short face	51 (42.5)
Long face	14 (11.7)
Normal	37 (30.8)
Retrognathia	17 (14.2)
Retromaxillary	1 (0.83)
OSA	35 (29.2)
Mild	28 (23.3)
Moderate	25 (20.8)
Serious	32 (26.7)
Very serious	

*mean (standard deviation)
Source of own elaboration



Regarding very serious OSA; patients with retrognathia had a 3.0 higher frequency, those with a long face had a 30.0 lower frequency and those with a short face had a 4.0 higher frequency compared to patients with a normal face (40 vs. 7 vs. 41 vs. 37; $p < 0.010$). According to Mallampati, those with grade 4 had a 32.73 higher frequency, those with grade 3 had a 27.5 higher frequency, those with grade 2 had a 7.19 higher frequency than those with grade 1 (41.82 vs. 36.59 vs. 16.28 vs. 9.09, $p = 0.001$). Of the patients who presented a tonsillar volume of 50-75%, those who presented a very

severe OSA were 42.86%. According to the Friedman Score, those with class III had a 10.2 higher frequency, and those with class II had a 7 lower frequency compared to those with class I (35.2 vs. 18 vs. 25; $p = 0.049$). According to the ANGLE scale, those in class III had a 20.6 higher frequency, those in class II 2 had a 42.3 higher frequency, and those in class II 1 had an 18.1 higher frequency compared to those in class I (12.7 vs. 30.8 vs. 55 vs. 33.3, $p < 0.001$). The other variables were not associated. (Table 2)

Table 2. Bivariate analysis of the characteristics associated with OSA classification in a Peruvian sample.

Characteristics	Diagnosis OSA				p-value
	Mild (n=35) n (%)	Moderate (n=28) n (%)	Severe (n=25) n (%)	Very severe (n=32) n (%)	
Age	50 (11.28)	49.71 (15.42)	52 (15.85)	45.34 (11.42)	0.224 ^{**}
Sex					0.317 [*]
Male	24 (26.09)	20 (21.74)	21 (22.83)	27 (29.35)	
Female	11 (39.29)	8 (28.57)	4 (14.29)	5 (17.86)	
BMI					0.096 ^{**}
Normal	3 (21.43)	4 (28.57)	6 (42.86)	1 (7.14)	
Overweight/obesity	32 (30.19)	24 (22.64)	19 (17.92)	31 (29.25)	
Neck circumference	38.47 (33.99)	41.22 (4.06)	40.84 (3.28)	43(15.04)	0.096 ^{**}
Mallampati					0.001[*]
Grade 1	14 (63.64)	2 (9.09)	4 (18.18)	2 (9.09)	
Grade 2	13(30.23)	15 (34.88)	8 (18.60)	7 (16.28)	
Grade 3	7 (17.07)	10 (24.39)	9 (21.95)	15 (36.59)	
Grade 4	8 (14.55)	11 (20)	13 (23.64)	23 (41.82)	
Minimum saturation	81.29 (7.25)	73.93 (12.92)	71.44 (9.02)	62.88 (10.22)	0.001^{**}
Maximum heart rate	114.69 (38.68)	110.96 (31.46)	105.32 (22.96)	122.09 (39.67)	0.1856 ^{**}
volume					0.001^{**}
Normal	1 (20)	3 (60)	1 (20)	0 (0)	
< 25%	23 (43.40)	11 (20.75)	4 (7.55)	15 (25.45)	
25-50%	10(18.18)	11 (20)	20 (36.36)	14 (25.45)	
50-75%	1 (14.29)	3 (42.86)	0 (0)	3 (42.86)	
AHI	9.41 (3.06)	22.11 (4.06)	40.35 (6.61)	61.33 (8.38)	0.000^{**}
Clinical bone bases					<0.010^{**}
Short face	10 (20)	8 (16)	12 (24)	21 (41)	
Long side	2 (14)	6 (43)	5 (36)	1 (7)	
Normal	20 (54)	9 (24)	5 (14)	8 (37)	
Retrognathia	3 (18)	4 (24)	3 (18)	7 (40)	
Retromaxillary	0 (0)	1 (100)	0 (0)	0 (0)	
Friedman Score					0.003^{**}
I	9 (56.3)	2 (12, 5)	1 (6.3)	4 (25)	

II	20 (40)	10 (20)	11 (22)	9 (18)	
III	6 (11.1)	16 (29.6)	13 (24.1)	19 (35.2)	
ANGLE					<0.001 **
I	28 (50.9)	11 (20)	9 (16.4)	7 (12.7)	
II 1	3 (7.7)	12 (30.8)	12 (30.8)	12 (30.8)	
II 2	3 (15)	3 (15)	3 (15)	11 (55)	
III	1 (16.7)	2 (33.3)	1 (16.7)	2 (33.3)	

° Performed with the Kruskal Wallis statistical test, significant p-value $p < 0.05$

* Performed with the chi-square statistical test of independence, significant p-value $p < 0.05$

** Performed with the Fisher statistical test, significant p-value $p < 0.05$

Source : Own elaboration.

Regarding the values of the AOS; BMI had a positive correlation of 0.309 ($p=0.001$), ODI had a positive correlation of 0.524 ($p<0.001$), TC90% had a positive correlation of 0.479 ($p<0.001$), snoring had a positive correlation of 0.271 ($p=0.003$) and the minimum saturation had a negative correlation of -0.409 ($p<0.001$). The maximum heart rate variable was not associated. (Table 3)

Table 3. Bivariate analysis of the characteristics associated with Epworth levels in a Peruvian sample.

	OSA Pearson's r	p value
BMI	0.309**	0.001
**	0.524**	0.001
Tc90	0.479**	<0.001
Snoring	0.271**	0.003
Minimum saturation	-0.409**	<0.001
Maximum	0.146	0.112

**Correlation is significant at level 0 .01 (2-sided).

DISCUSSION

The study found that the anatomical profile, such as the short face, retrognathia, and retromaxillary was associated with severe OSA; this was similar in other studies such as that of Tepedino M et al., done in Italy, where it was found that patients with severe OSA they presented low sagittal growth, low effective mandibular length, and low skull-basal length. The relationship between mandibular length was the only one por that presented a significant statistical association with the apnea-hypopnea index⁽⁹⁾. Another

study by Tyan et al. observed a positive correlation between measurements of the anatomical profile (face width ratio, tragion-ramus-stomion angle) with OSA⁽¹¹⁾. The soft tissues of the anatomical profile should also be taken into account in the evaluation ⁽¹¹⁾. In our study, tonsillar volume was associated with severe OSA. In other studies, it has been observed that patients with OSA showed a wider and flatter middle third and lower third of the face and a reduction in maxillary and mandibular length^(13,14). A possible explanation could be that mandibular growth could influence the severity of

OSA and in turn, the growth and position of the mandible, which would be influenced by the length of the skull base⁽⁹⁾; In a systematic review, the possibility of an association between jaw growth and severe OSA was demonstrated⁽¹⁵⁾.

In our study, an association was found between the Friedman Score and the severity of OSA. In a study by Friedman, he found a relationship between mild OSA and a low Friedman score; in the same way with, moderate to severe OSA, have a higher prevalence of the Friedman classification III and IV⁽¹⁶⁾. In a study where the adherence of the examiners to the Friedman Score for the staging of OSA was evaluated, a high adherence among examiners was observed, being very useful for evaluating OSA for clinical practice and research⁽¹⁷⁾. In the same way, the ANGLE Class and the Mallampati scale in our study are associated with the staging of OSA, various researchers use this classification to define the population class that they are going to study according to the severity of OSA⁽¹⁸⁻²⁰⁾.

In our study, a positive correlation was found between the values of OSA and BMI, IDO, minimum saturation, and maximum heart rate. In our study, AHI was associated with severe OSA, presenting a higher frequency in very severe OSA.

In other studies, it was observed that neck circumference was associated with Epworth and OSA severity^(22,23). In our study, the mean neck circumference was 40.94. In another study, no correlation was found between BMI and the mean percentage of SaO₂, indicating that the mean arterial oxygen saturation is similar between the different types of BMI⁽²⁴⁾.

A possible explanation is that general obesity, measured by BMI, generates more severe episodes of obstruction, which can be reflected in minimum oxygen saturation values, and a possible general worsening of OSA. Hypoxia stimulates the carotid chemoreceptors and causes a secondary sympathetic activation that increases blood pressure⁽²⁵⁾. In our study, the mean maximum heart rate was 113.84. In addition, sympathetic activations caused by hypoxic episodes in OSA patients persist during daytime wakefulness under normoxic conditions, which could cause persistent

sympathetic activation and lead to systemic hypertension and increased cardiac sympathetic tone⁽²⁶⁾.

OSA could modify lipid metabolism; in studies it has been observed that intermittent hypoxia increases the levels of angiotensin 4, which is a potent inhibitor of lipoprotein lipase, which would cause a decrease in the body's clearance of lipoproteins and increases the serum levels of fasting triglycerides and very low-density lipoprotein cholesterol⁽²⁷⁾. Higher consumption of total calories derived from protein and fat has also been observed in this type of patients⁽²⁸⁾ caused by lack of sleep that causes fatigue, which can lead to a lack of physical activity and increased caloric intake, leading to an increase in BMI and to severe OSA⁽²⁹⁾.

Being a cross-sectional study, it prevents establishing the temporal relationship between the dependent variable and the covariates of the study. On the other hand, the study did not use the gold standard (polysomnography) to diagnose OSA. But the diagnosis by cardiorespiratory polygraphy is also widely used. However, we consider that the study's findings are useful to obtain an overview of the anatomical profile and its association with obstructive sleep apnea.

CONCLUSIONS

In the present study, the results found show that OSA was associated with presenting clinical bone bases such as retromaxillary, retrognathia, short and long face. The ANGLE scale was the one most associated with OSA compared to the Friedman Score. OSA values were associated with BMI, IDO, minimum saturation, and maximum heart rate. Finally, obstructive sleep apnea is associated with the anatomical profile, its severity can increase according to the characteristics of the maxilla. Future studies should prospectively explore the severity of OSA, and thus learn more about this pathology in the Peruvian population.

If the current results are confirmed in future research, General Practitioners could be trained to provide an early diagnosis, with the use of the different scales and scores used in this work, to avoid underdiagnosis and thus not reach a very high OSA. serious.



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Correspondence: Violeta Valdez Pajuelo.

Address: Las Dalias 174 - Miraflores

Telephone number: 949336861

E-mail: violeta.valdezp@gmail.com

REFERENCES

- Mannarino MR, Di Filippo F, Pirro M. Obstructive sleep apnea syndrome. *Eur J Intern Med.* 2012;23(7):586–93. doi:10.1016/j.ejim.2012.05.013
- Mediano O, González Mangado N, Montserrat JM, Alonso-Álvarez ML, Almendros I, Alonso-Fernández A, et al. Documento internacional de consenso sobre apnea obstructiva del sueño. *Archivos de Bronconeumología.* 2022;58(1):52–68. doi:10.1016/j.arbres.2021.03.017
- Carrillo A. J, Vargas R. C, Cisternas V. A, Olivares-Tirado P, Carrillo A. J, Vargas R. C, et al. Prevalencia de riesgo de apnea obstructiva del sueño en población adulta chilena. *Revista chilena de enfermedades respiratorias.* 2017;33(4):275–83. doi:10.4067/S0717-73482017000400275
- Rapoport DM. POINT: Is the Apnea-Hypopnea Index the Best Way to Quantify the Severity of Sleep-Disordered Breathing? *Yes.* *CHEST.* 2016;149(1):14–6. doi:10.1378/chest.15-1319
- Saldías P. F, Leiva R. I, Salinas R. G, Stuardo T. L, Saldías P. F, Leiva R. I, et al. Estudios de prevalencia del síndrome de apneas obstructivas del sueño en la población adulta. *Revista chilena de enfermedades respiratorias.* 2021;37(4):303–16. doi:10.4067/s0717-73482021000300303
- Hidalgo-Martínez P, Lobelo R. Epidemiología mundial, latinoamericana y colombiana y mortalidad del síndrome de apnea-hipopnea obstructiva del sueño (SAHOS). *Rev Fac Med.* 2017;65(1 Sup):17–20. doi:10.15446/revfacmed.v65n1Sup.59565
- Almonte Estrada JM, Pagán Santos DA. Evolución clínica de pacientes con sospecha de síndrome de apnea obstructiva del sueño (SAOS) sometidos a cirugía electiva. [Thesis]. Universidad Nacional Pedro Henríquez Ureña; 2021 [citado el 9 de julio de 2022]. Disponible en: <https://repositorio.unphu.edu.do/handle/123456789/3596>
- Sánchez-Quiroga MÁ, Corral J, Gómez-de-Terreros FJ, Carmona-Bernal C, Asensio-Cruz MI, Cabello M, et al. Primary Care Physicians Can Comprehensively Manage Patients with Sleep Apnea. A Noninferiority Randomized Controlled Trial. *Am J Respir Crit Care Med.* 2018;198(5):648–56. doi:10.1164/rccm.201710-2061OC
- Tepedino M, Illuzzi G, Laurenziello M, Perillo L, Taurino AM, Cassano M, et al. Craniofacial morphology in patients with obstructive sleep apnea: cephalometric evaluation. *Braz J Otorhinolaryngol.* 2022;88(2):228–34. doi:10.1016/j.bjorl.2020.05.026
- van Delden JJM, van der Graaf R. Revised CIOMS International Ethical Guidelines for Health-Related Research Involving Humans. *JAMA.* 2017;317(2):135–6. doi:10.1001/jama.2016.18977
- Tyan M, Espinoza-Cuadros F, Pozo RF, Toledano D, Gonzalo EL, Ramirez JDA, et al. Obstructive Sleep Apnea in Women: Study of Speech and Craniofacial Characteristics. *JMIR mHealth and uHealth.* 2017;5(11):e8238. doi:10.2196/mhealth.8238
- Sutherland K, Schwab RJ, Maislin G, Lee RWW, Benediktssdottir B, Pack AI, et al. Facial Phenotyping by Quantitative Photography Reflects Craniofacial Morphology Measured on Magnetic Resonance Imaging in Icelandic Sleep Apnea Patients. *Sleep.* 2014;37(5):959–68. doi:10.5665/sleep.3670
- Lee RWW, Petocz P, Prvan T, Chan ASL, Grunstein RR, Cistulli PA. Prediction of Obstructive Sleep Apnea with Craniofacial Photographic Analysis. *Sleep.* 2009;32(1):46–52. doi:10.5665/sleep/32.1.46
- Liu Y, Lowe AA, Orthodont D, Fleetham JA, Park Y-C. Cephalometric and physiologic predictors of the efficacy of an adjustable oral appliance for treating obstructive sleep apnea. *American Journal of Orthodontics and Dentofacial Orthopedics.* 2001;120(6):639–47. doi:10.1067/mod.2001.118782
- Almeida KCM de, Raveli TB, Vieira CIV, Santos-Pinto A dos, Raveli DB. Influence of the cranial base flexion on Class I, II and III malocclusions: a systematic review. *Dental Press J Orthod.* 2017;22:56–66. doi:10.1590/2177-6709.22.5.056-066.oar
- Friedman M, Vidyasagar R, Bliznikas D, Joseph N. Does Severity of Obstructive Sleep Apnea/Hypopnea Syndrome Predict Uvulopalatopharyngoplasty Outcome? *The Laryngoscope.* 2005;115(12):2109–13. doi:10.1097/01.MLG.0000181505.11902.F7
- Friedman M, Soans R, Gурpinar B, Lin H-C, Joseph NJ. Interexaminer agreement of Friedman tongue positions for staging of obstructive sleep apnea/hypopnea syndrome. *Otolaryngology - Head and Neck Surgery.* 2008;139(3):372–7. doi:10.1016/j.otohns.2008.06.017
- Triplett WW, Lund BA, Westbrook PR, Olsen KD. Obstructive Sleep Apnea Syndrome in Patients With Class II Malocclusion. *Mayo Clinic Proceedings.* 1989;64(6):644–52. doi:10.1016/S0025-6196(12)65342-7
- Zhao T, Ngan P, Hua F, Zheng J, Zhou S, Zhang M, et al. Impact of pediatric obstructive sleep apnea on the development of Class II hyperdivergent patients receiving orthodontic treatment: A pilot study. *Angle Orthod.* 2018;88(5):560–6. doi:10.2319/110617-759.1
- Campos LD, Trindade IEK, Yatabe M, Trindade SHK, Pimenta LA, Kimbell J, et al. Reduced pharyngeal dimensions and obstructive sleep apnea in adults with cleft lip/palate and Class III malocclusion. *Cranio.* 2021;39(6):484–90. doi:10.1080/0886969634.2019.1668997
- Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. *JAMA.* 2000;284(23):3015–21. doi:10.1001/jama.284.23.3015
- Stradling JR, Crosby JH. Predictors and prevalence of obstructive sleep apnoea and snoring in 1001 middle aged men. *Thorax.* 1991;46(2):85–90. doi:10.1136/thx.46.2.85
- Pillar G, Shehadeh N. Abdominal fat and sleep apnea: the chicken or the egg? *Diabetes Care.* 2008;31 Suppl 2:S303-309. doi:10.2337/dc08-s272
- Ciavarella D, Tepedino M, Chimenti C, Troiano G, Mazzotta M, Foschino Barbaro MP, et al. Correlation between body mass index and obstructive sleep apnea severity indexes — A retrospective study. *American Journal of Otolaryngology.* 2018;39(4):388–91. doi:10.1016/j.amjoto.2018.03.026
- Leske J, Fletcher EC, Bao G, Unger T. Hypertension caused by chronic intermittent hypoxia—influence of chemoreceptors and sympathetic nervous system. *J Hypertens.* 1997;15(12 Pt 2):1593–603. doi:10.1097/00004872-199715120-00060
- Sharma N, Lee J, Youssef I, Salifu M, McFarlane S. Obesity, Cardiovascular Disease and Sleep Disorders: Insights into the Rising Epidemic. *Journal of sleep disorders & therapy.* 2017;6. doi:10.4172/2167-0277.1000260
- Kasisvathan V, Shalhoub J, Lim CS, Shepherd AC, Thapar A, Davies AH. Hypoxia-inducible factor-1 in arterial disease: a putative therapeutic target. *Curr Vasc Pharmacol.* 2011;9(3):333–49. doi:10.2174/157016111795495602
- Vasquez MM, Goodwin JL, Drescher AA, Smith TW, Quan SF. Associations of Dietary Intake and Physical Activity with Sleep Disordered Breathing in the Apnea Positive Pressure Long-term Efficacy Study (APPLES). *J Clin Sleep Med.* 2008;4(5):411–8. doi:10.5664/jcsm.27274
- Stelmach-Mardas M, Mardas M, Iqbal K, Kostrzewska M, Piorunek T. Dietary and cardio-metabolic risk factors in patients with Obstructive Sleep Apnea: cross-sectional study. *PeerJ.* 2017;5:e3259. doi:10.7717/peerj.3259

