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ORIGINAL ARTICLE

Upper airway assessment in obstructive sleep apnea patients: can computed tomography with lateral cephalometry replace drug-induced sleep endoscopy (DISE)?

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KEYWORDS
Obstructive sleep apnea;
Drug-induced sleep endoscopy;
DISE;
Computed tomography with lateral cephalometry

Abstract
Objective: To evaluate the association between results from drug-induced sleep endoscopy (DISE) and computed tomography with lateral cephalometry (CTLC) of the pharynx in obstructive sleep apnea (OSA) patients, regarding the same anatomic level, in order to understand if CTLC could replace DISE in selected patients.
Study design: Cross-sectional.
Setting: Tertiary hospital.
Methods: A total of 71 patients who attended the Sleep Medicine Consultation in the Otorhinolaryngology Department of Hospital CUF Tejo between 1.6.2019 and 30.9.2021, performed a polysomnographic sleep study and were elected to undergo DISE and CTLC of the pharynx for diagnostic purposes were selected. Obstructions at the same anatomic levels – tongue base, epiglottis and velum - were compared in both exams.
Results: Patients with reduction of epiglottis-pharynx space on CTLC had also a complete obstruction at epiglottis level on the VOTE classification of DISE (p = 0,027). Reduction of velum-pharynx space or tongue base-pharynx space were not related to complete obstruction of the velum (P = 0,623) or the tongue base (p = 0,594) found in DISE. Those with two or more space reductions had a tendency to multilevel obstruction observed in DISE (p = 0.089).

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Conclusion: When evaluating the obstruction level(s) of an OSA patient, efforts should be made to perform DISE, since CTLC measures, though regarding at the same structures, dont́ correlate completely with obstructions observed in DISE.

PALABRAS CLAVE
Apnea obstructiva del sueño;
Endoscopia del sueño inducida por fármacos;
DISE;
Tomografía computarizada con cefalometría lateral

Evaluación de la vía aérea superior en pacientes con apnea obstructiva del sueño: ¿puede la tomografía computarizada con cefalometría lateral reemplazar endoscopia del sueño inducida por fármacos por fármacos?

Resumen
Objetivo: Evaluar la asociación entre los resultados de la endoscopia del sueño inducida por fármacos (DISE) y la tomografía computarizada con cefalometría lateral (TCCL) de faringe en pacientes con apnea obstructiva del sueño (AOS), en el mismo nivel anatómico, para comprender si la TCCL podría reemplazar DISE en pacientes seleccionados.
Diseño del estudio: Transversal.
Lugar: Hospital de tercer nivel.
Métodos: Un total de 71 pacientes que acudieron a la Consulta de Medicina del Sueño en el Servicio de Otorrinolaringología del Hospital CUF Tejo entre el 1.6.2019 y el 30.9.2021, a los que se les había realizado un estudio polisomnográfico del sueño y fueron elegidos para realizar DISE y TCCL de faringe con fines diagnósticos, fueron seleccionados. Las obstrucciones en los mismos niveles anatómicos (base de la lengua, epiglotis y velo) se compararon en ambos exámenes.
Resultados: Los pacientes con reducción del espacio epiglotis-faringe en TCCL también tenían una obstrucción completa a nivel de epiglotis en la clasificación VOTE de DISE ($p = 0,027$). La reducción del espacio velo-faringe o base de la lengua-faringe no se relacionó con la obstrucción completa del velo ($P = 0,623$) o de la base de la lengua ($p = 0,594$) encontrada en DISE. Aquellos con dos o más reducciones de espacio presentaron tendencia a la obstrucción multinivel observada en DISE ($p = 0,089$).
Conclusión: Al evaluar el o los niveles de obstrucción de un paciente con AOS, se debe intentar realizar DISE, ya que las medidas de TCCL, aunque se refieren a las mismas estructuras, no se correlacionan completamente con las obstrucciones observadas en DISE.

Introduction

Obstructive sleep apnea (OSA) is the most common sleep disorder, characterized by episodes of recurrent partial or complete obstruction of the upper airway during sleep, which lead to episodes of apnea, hypopnea or microarousals related to respiratory effort.[1] Risk factors include advanced age, male gender, obesity and craniofacial dysmorphia. OSA is responsible for the surge of well-known symptoms such as daytime hypersomnolence, headaches, insomnia, difficulties in concentration, memory and mood and, if not properly addressed and treated, increases the risk of adverse events, such as traffic accidents, neuropsychiatric dysfunction, brain and cardiovascular morbidity, pulmonary hypertension, type 2 diabetes and metabolic syndrome.[2,3]

Mild OSA is defined by an Apnea-Hypopnea Index (AHI) between 5 and 15 events per hour and it's treatment is only recommended in the presence of OSAS (Obstructive Sleep Apnea Syndrome) characterized by: AHI > 5 associated with symptoms such as daytime hypersomnolence or in the presence of 2 or more symptoms among: repeated asphyxia during sleep, feeling of unrefreshing sleep, recurrent awakenings during sleep, daytime fatigue, difficulty concentrating. OSA treatment is recommended for moderate ($15 < AHI < 30$) or severe ($AHI > 15$) OSA, even without symptoms, due to the increased cardiovascular risk.[3]

Itś worth to mention that some authors consider these definitions, based exclusively in the AHI to be very limited, since they dont́ reflect the disease heterogenicity.[4,5] Mediano et al.[6] recommend taking into account, besides AHI: time with oxyhemoglobin saturation below 90%, as a reflection of hypoxemia; daytime sleepiness; degree of obesity measured by body mass index and comorbidities (risk factors or cardiovascular disease) that have been related to OSA, like arterial hypertension (especially if it is resistant to treatment or has a non-dipper pattern), type 2 diabetes mellitus, dyslipidemia, coronary heart disease, stroke, heart failure or atrial fibrillation.

Positive airway pressure (PAP) is the primary therapy for individuals with symptomatic OSA of any severity. Other

treatment options include oral appliances, particularly for individuals with mild to moderate OSA. Lifestyle modification, hypoglossal nerve stimulation and positional therapy are also considered valid alternatives.[7,8] Surgical intervention in the upper airway is suitable for select patients and is often recommended for symptomatic patients unable to tolerate PAP therapy.[9–11]

The variety of surgical options available to treat OSA is profuse, each one aiming to address specific anatomical problems causing the obstruction. Site-specific and targeted surgery can and must be offered these days.[12] This is only possible with rigorous and correct patient selection and adequate upper airway evaluation methods.

Drug-induced sleep endoscopy (DISE) is the investigation of choice in the surgical assessment of sleep disordered breathing. It allows for a dynamic and three-dimensional endoscopic evaluation of the airway and identifies areas of collapse, thereby informing both on the selection of surgical techniques and conservative measures, such as mandibular advancement splints. However, it has some disadvantages: (1) it involves sedation and therefore has inherent anesthetics risks, (2) so far, no consensus could be reached on a scoring and classification system and (3) it requires a trained team and a specially equipped room available.[12–14]

An alternative to DISE, when the previous topics were a problem (for instance in an office with no conditions to safely perform DISE, like in primary care settings, or when the patient is being evaluated by a non-ENT doctor) could be computed tomography with lateral cephalometry of the pharynx (CTLC). It is a standardized and accessible exam to evaluate anatomical craniofacial relationships, it allows precise measurements of cross-sectional areas at different levels as well as 3D reconstruction and volumetric assessment of the upper airway.[15–17] We hypothesized that CTLC could replace DISE in selected patients and in specific situations if the results of both exams showed significant correlation in three common obstruction sites: the velum, the tongue base and the epiglottis.

Hence, the aim of this study was to evaluate the association between DISE and CTLC results in obstructive sleep apnea (OSA) patients, regarding the same anatomic level's evaluation, in order to understand if CTLC could replace DISE in selected patients.

Methods

Study population

This cross-sectional study enrolled a consecutive series of subjects who attended the Sleep Medicine Consultation in the Otorhinolaryngology Department of Hospital CUF Tejo (Lisbon, Portugal) by one author (CC) in a 27 months period, between 1.6.2019 and 30.9.2021. All subjects were 18 years of age or older, had OSA symptoms, performed a polysomnographic sleep study level II or III, and were elected to undergo drug-induced sleep endoscopy (DISE) and a computed tomography with lateral cephalometry (CTLC) of the pharynx for diagnostic purposes. Patients with incomplete data were excluded.

This study was approved by Hospital CUF Tejo ethics committee.

Table 1 VOTE classification structure used routinely and the one used in this study outlined in darker.

STRUCTURE	DEGREE OF OBSTRUTION	CONFIGURATION		
		A-P	LATERAL	CONCENTRIC
Velum				
Oropharynx lateral walls				
Tongue base				
Epiglotis				

A-P, anterior-posterior

Drug-Induced Sleep Endoscopy (DISE)

DISE was performed on all subjects by the evaluating surgeon (CC) and the same team anesthetist. Subjects were placed in a supine position on the operating room table with lights dimmed, wearing their usual pillow and night closes, in order to better simulate home sleeping conditions. An intravenous infusion, administrated by target-controlled infusion (TCI) pump, of propofol was used as the sole sedative agent to achieve the target depth of anesthesia: loss of arousal to verbal stimulation. The depth of anesthesia during the procedure was supported by a Bispectral Index (BIS) monitor, aiming values between 50 and 70, which was valuable to stop excessive deepening.[18,19] Additional patients monitoring comprised cardiac and respiratory parameters, including oxygen saturation rate.

With the onset of unconscious sedation, a flexible fiberoptic examination was performed. DISE findings were characterized using the Velum, Oropharyngeal Lateral Walls, Tongue and Epiglottis (VOTE) Classification.[20] This classification system evaluates the structures (Velum, Oropharyngeal Lateral Walls, Tongue, and Epiglottis) that most commonly play a role in pharyngeal airway obstruction in OSA. The severity of structure-related obstruction is graded on a 3-point scale: 0, no obstruction; 1, partial obstruction; or 2, complete obstruction. Although the pattern of the obstruction (anteroposterior, lateral, or concentric) is also graded, this information was not used in this study. For the purposes of this study only the supine position values were used. Table 1 illustrates the VOTE classification scheme used routinely and the one used in this study (darker).

Computed Tomography with Lateral Cephalometry (CTLC)

Computed tomography with lateral cephalometry (CTLC) of the pharynx was taken at the Radiology Service of Hospital CUF Tejo, using GE lightspeed VCT 64 slices or GE Revolution 256 slices. Patients were awake in a standard supine position and were told not to move or swallow. The measurements included those cited in the sleep surgery literature for upper airway evaluation, and others related to head posture and pharyngeal airway dimensions.[21–24] Three lengths were con-

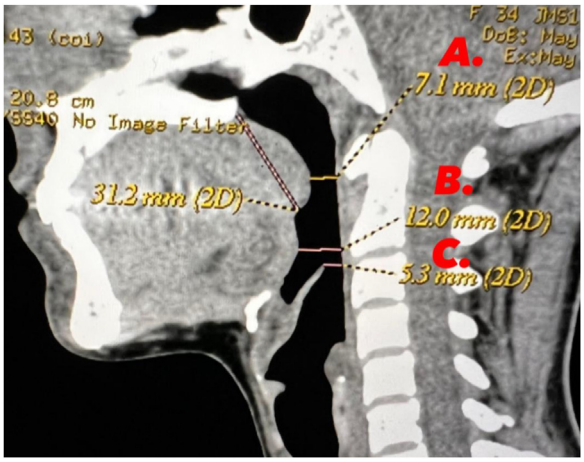

Figure 1 Example of computed tomography with lateral cephalometry. (A) Velum-pharynx space; (B) Posterior tongue base-pharynx space; (C) Epiglottis-pharynx space).

sidered in this study: the velum-pharynx space (from the posterior edge of the velum to the anterior border of the posterior pharynx wall), posterior tongue base space (from the posterior end of the tongue base to the anterior border of the posterior pharynx wall) and epiglottis-pharynx space (from the free edge of the epiglottis to the posterior pharynx wall). All cephalometric measurements were analyzed as continuous measures (in mm) and in a dichotomous fashion (normal vs. reduced). All cephalometric measurements were performed by one radiologist blinded to patient history and DISE findings (SC). Fig. 1 illustrates the measurements used in this study and Table 2 specifies their normal range.

Statistical analysis

Data were analyzed using IBM SPSS software (version 25.0) and subjected to descriptive statistical analysis techniques (mean), dispersion and variability measures (standard deviation). Parametric tests, namely, test t-Student was computed to compare means between groups when the variables had a normal distribution and homogeneity of variances, otherwise Mann-whitney test was used. Pearson chi-square test (or Fisher test) was used to assess differences between groups. Pearson correlation was computed for the variables age, gender and BMI. P values less than 0.05 were considered statistically significant. For comparison of DISE and cephalometric findings, the VOTE structures were evaluated separately. Only complete (degree 2 on VOTE classification) obstruction was considered to reflect obstruction.

Table 2 Normal range of the measures considered in this study.

Structure	Reference value	Reduced space
Velum-pharynx space (VPS)	13 mm ± 5	<8 mm
Posterior tongue base space (PTBS)	11 mm ± 1	<10 mm
Epiglottis-pharynx space (EPS)	9 mm ± 3	<6 mm

Results

Seventy-one (n = 71) patients were included in the study. Collected data is shown in Table 3.

We studied the correlation between AHI and BMI and AHI and age. Only the association between AHI and BMI was statistically significant (p = 0,006), as higher AHI was associated with increased BMI. We found no statistically significant differences between men and women's AHI (p = 0,056).

DISE results according to VOTE classification are shown in Table 4.

Regarding the CTLC, the mean velum-pharynx-space (VPS) was 6.30 mm with a standard deviation (SD) of 2,53 mm (min 2,00mm-max 13,00), the mean tongue base-pharynx space (TBPS) was 12,36 mm (SD 3,79) (min 5,20-max 23,00) and the mean epiglottis-pharynx space (EPS) was 7,57 mm (SD 2,36) (min 2.00-max 14.00). The most commonly reduced space was TBPS (59 patients / 83,1% of the

Table 3 Study population collected data.

DATA	Frequency	%	Mean	Standard	Minimum	Maximum
Male	52	73				
Female	19	27				
Age			46,56	10,92	18	62
BMI			26,54	3,57	19,00	36,50
Normal weight	24	33,8				
Overweight	34	47,9				
Class I obesity	12	16,9				
Class II obesity	1	1,4				
AHI			16,09	12,01	0,3	78,7
LOS			83,25	9,60	50	93
No OSA	7	9,9				
Mild OSA	36	50,7				
Moderate OSA	19	26,8				
Severe OSA	9	12,7				

BMI, body mass index; AHI, apnea-hypopnea index; LOS, lowest oxygen saturation.

Table 4 DISE results according to VOTE classification.

		Frequency	%
V - Velum	0 - No obstruction	16	22,5
	1- Partial obstruction	24	33,8
	2- Complete obstruction	31	43,7
O - Oropharynx lateral walls	0 - No obstruction	51	71,8
	1 - Partial obstruction	14	19,7
	2 - Complete obstruction	6	8,5
T - Tongue Base	0 - No obstruction	38	53,5
	1 - Partial obstruction	17	23,9
	2 - Complete obstruction	16	22,5
E - Epiglottis	0 - No obstruction	32	45,1
	1 - Partial obstruction	19	26,8
	2 - Complete obstruction	20	28,2
Single Level obstruction		21	29,6
Two Level obstruction		26	36,6
Three Level obstruction		15	21,1
Four Level obstruction		8	11,3

subjects), followed by VPS (50/70,4%) and EPS (16/28,2%). Only 7/9,9% of individuals had no space reduction and most of them (45/63,3%) had several spaces reduced. One-space reduction was found in 19/26,8%, two-space reduction in 29/40,8%, and three-space reduction in 16/26,5% of individuals.

Potential associations between places of complete obstruction in DISE and diminished spaces in CTLC in the same anatomical location were evaluated. Specifically, velum collapse in DISE and velum-pharynx space reduction in CTLC, epiglottis collapse in DISE and epiglottis-pharynx space reduction in CTLC, tongue base collapse and tongue base-pharynx reduced space. Only one statistically significant association was identified: patients with reduction of the EPS space on CTLC had also complete obstruction at epiglottis level on the VOTE classification of DISE ($p = 0,027$). Reduction of VPS or TBPS were not related to complete obstruction of the velum ($P = 0,623$) or the tongue base ($p = 0,594$) found in DISE. Although not statically significant, those patients with two or more space reductions on LCCT tended to have also multilevel obstruction seen in DISE ($p = 0.089$).

Discussion

AHI, gender and age

We studied several associations in patients who underwent DISE and CTLC. Firstly, we found that higher AHI was associated with higher BMI. This relationship is well established in the literature, especially in obese (BMI>30 kg/m^2) patients.[1–3] We found no associations between AHI and age or gender, although OSA is more frequent in males and tends to increase with advancing age. This might be due to our sample characteristics, with the presence of only 27% of women in our sample with a mean age of 45 years, as it is also known that gender differences in OSA tend to fade in post-menopausal women.[2]

DISE results

The most prevalent site of obstruction was the velum, with 77,5% individuals showing some kind of obstruction, followed by the epiglottis (55%). Multiple sites of obstruction (multilevel) were found in 70,4%. The velum and multilevel are common patterns of obstruction observed in DISE, but the incidence of epiglottis related obstruction is usually lower.[25] In recent studies, though, the importance of epiglottis-related obstruction in OSA is being stressed out, especially in non-obese patients, which was the case of 81,7% of our population.[26–29]

CTLC results

The analysis of CTLC measurements in the same pharynx levels showed different patterns of obstruction than those observed in DISE. In this exam, the more common obstruction site (presented as the most frequently observed reduced space) was the tongue base, as 83,1% of patients had reduction of the TBPS. The VPS was reduced in 70,4% of individuals. Epiglottis seemed to have little implication in obstruction, as only 28,2% of patients had a reduction of the EPS. Tongue and soft palate dimensions and their relation to OSA have been demonstrated by cephalometry studies,[21,22,24] yet epiglottis or EPS importance is seldom reported. Reduction in several spaces was seen in 67,3% of individuals, similarly to DISE (70,4%), which is in accordance with the literature in both exams.[30–33]

DISE and CTLC results associations

Despite a wide array of statistical testing, we only found one statistically significant association: patients with reduction

of epiglottis-pharynx space on CTLC had also an obstruction at epiglottis level on the VOTE classification of DISE (p = 0,027). Interestingly, albeit the prevalence of epiglottis-related obstruction is quite different in the two exams, as we discussed previously, it seems that the reduction of the EPS on CTLC is rather specific for an obstruction at epiglottis level observed in DISE. Although interesting from a scientific point of view, we think that, on it's own, this finding is of little use in daily practice, as only if all measures were significantly related one could postulate that CTLC could eventually replace DISE in selected patients. Moreover, epiglottic collapse can be primary (due to a floppy or underdeveloped epiglottis) or secondary to an anteroposterior collapse of the tongue base.[29] These phenomena are difficult to observe in a static image of an awake patient and therefore CTLC doesn't provide information about the etiology of the problem.

Although we couldnt́ determine a statistically significant difference, it appears that patients with multiple space reduction in CTLC tend to have multilevel obstruction in DISE (p = 0.089), which is not surprising, once the frequent involvement of several anatomic structures in the pathophysiology of OSA is being increasingly accepted.[30–33]

There are very few studies comparing DISE and CTLC results, but our results are consistent with a similar study by George et al. comparing DISE and lateral cephalometric head film analysis that concluded that they were not interchangeable in OSA patientś evaluation.[34] Beyond the obvious fact that these exams provide very different information (as the first is a dynamic three-dimension evaluation, whereas the second is a static bidimensional image), the complexity of OSA pathophysiology may not be simply explained by upper airway morphology, shown in DISE findings and/or CTLC results. The development of OSA is multifactorial and not just anatomically driven. Non-anatomic traits, including genioglossus muscle responsiveness, arousal threshold and respiratory control stability, must be taken into account and may vary substantially in an awake versus a sleeping patient.[35,36]

Nevertheless, imaging modalities have proven useful in OSA patientś evaluation in the past and in this study, CTLC appears to be an interesting alternative to evaluate epiglottis and multi-level related obstruction, able to provide findings that entail earlier referral of selected cases for further assessment.

Conclusions

In this study we tried to understand if CTLC could substitute DISE in selected OSA patient's assessment, by comparing obstruction sites found in DISE with reduction of pharyngeal spaces in the same anatomic levels or structures shown in CTLC.

We found a significant correlation between reduction of epiglottis-pharynx space on CTLC and complete obstruction at epiglottis level on the VOTE classification of DISE. However, the results of other structures evaluated by these exams, namely the velum and the tongue base were not related, suggesting the distinct and complementary character of these techniques. We therefore conclude that when evaluating the obstruction level(s) of an OSA patient, efforts should be made to perform drug-induced sleep endoscopy, which cannot be replaced by CTLC.

Author contributions

Ana Campos: substantial contributions to the conception, design of the work; to the acquisition, analysis, and interpretation of data for the work; drafting the work and revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Pedro Cebola: substantial contributions to the conception, design of the work; to the acquisition, analysis, and interpretation of data for the work; drafting the work and revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Sara Simões Dias: substantial contributions to the conception, design of the work; to the acquisition, analysis, and interpretation of data for the work; drafting the work and revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; José Pais: substantial contributions to the acquisition, analysis, and interpretation of data for the work; revising the work critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Susana Teixeira: substantial contributions to the acquisition, analysis, and interpretation of data for the work; revising the work critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Sergio Cardoso: substantial contributions to the acquisition, analysis, and interpretation of data for the work; revising the work critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; João Paço: substantial contributions to the acquisition, analysis, and interpretation of data for the work; revising the work critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Cristina Caroça: substantial contributions to the conception, design of the work; to the acquisition, analysis, and interpretation of data for the work; drafting the work and revising it critically for important intellectual content; final approval of the version to be published; agreement to

be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of interests

None.

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