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Drug-induced sleep endoscopy in elderly patients with obstructive sleep apnea syndrome

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	Polysomnographic data and clinical parameters such as the daytime sleepiness, and body mass index (BMI) were evaluated for both groups of patients. All patients underwent DISE examination with VOTE classification. Results: The AHI value increased with aging whereas elderly patients presented a reduction in daytime sleepiness. Elderly patients showed a higher incidence of total collapse in the velum region compared to younger patients (90.9% vs 70%;); the older patients showed a lower degree of total oropharyngeal lateral wall collapse with respect to younger patients, (20% vs 50%). No difference in tongue base collapse emerged between the two subgroups of patients. Conclusion: Elderly patients showed a higher incidence of total collapse in the velum and a lower incidence in the oropharyngeal lateral wall compared to younger patients.

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Drug-induced sleep endoscopy in elderly patients with obstructive sleep apnea syndrome

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ABSTRACT

Purpose: To evaluate, using drug-induced sleep endoscopy (DISE), sites of upper airway obstruction and pattern of collapse in patients over 65 years old affected by obstructive sleep apnea (OSA). To compare sites and pattern of collapse of elderly patients with a group of patients younger than 65 years.

Methods: A group of 55 patients aged over 65 years old were enrolled in this prospective study.

Fifty patients under 65 years old were collected in the control group.

Polysomnographic data and clinical parameters such as the daytime sleepiness, and body mass index (BMI) were evaluated for both groups of patients.

All patients underwent DISE examination with VOTE classification.

Results: The AHI value increased with aging whereas elderly patients presented a reduction in daytime sleepiness. Elderly patients showed a higher incidence of total collapse in the velum region compared to younger patients (90.9% vs 70%;); the older patients showed a lower degree of total oropharyngeal lateral wall collapse with respect to younger patients, (20% vs 50%). No difference in tongue base collapse emerged between the two subgroups of patients.

Conclusion: Elderly patients showed a higher incidence of total collapse in the velum and a lower incidence in the oropharyngeal lateral wall compared to younger patients.

Keywords: Obstructive Sleep Apnea, OSAS, sleep endoscopy, DISE, elderly

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Informed consent: Informed consent was obtained from all individual participants included in the study.

INTRODUCTION

Obstructive Sleep Apnea (OSA) syndrome is a respiratory sleep disorder characterized by partial or complete recurrent episodes of upper airways collapse, that occurs during the night. OSA manifested with a reduction (hypopnea) or complete cessation (apnea) of airflow in the upper airways, in presence of breathing effort [1-3].

OSA is a frequent and often underestimated pathology affecting between 2% and 5% of middle-aged population [3-5]. However, it has been observed that it may reach a much higher incidence in older people [7-11]. Different studies have estimated OSA incidence rates from 5.6% to 70% in people over 65 [8-13]. Analyzing 427 elderly people over 65, suffering from OSA, Ancoli et al [8], showed that 24% of them had an apnea/hypopnea (AHI) index greater than 5 and that 62% had a respiratory disturbance, with a Respiratory Disorder Index (RDI) ≥ 10. In another study comprising 5615 men and women between 40-98 years of age, sleep apnea was found to be most frequent in subjects aged 60 years or older (approximately 50% had an AHI of 5-14, and approximately 20% had an AHI≥15) [4].

Aging is also associated with changes in OSA related parameters (increase of AHI, reduction of night-time SpO2, reduction of daytime sleepiness etc.) and type of sleep [10-14]. Therefore, is possible that the number of obstruction, sites and collapse pattern may change over time due to changes in pharyngeal anatomy, redistribution of body fat and/or the increased laxity of the oro/ipo-pharyngeal muscular structures, that are known to occur with aging. [15-18]

These findings implicate the importance of assessment and classification of sites and patterns of collapse in elderly OSA patients. Polysomnography (PSG) is the gold standard for the diagnosis of OSA and evaluation of its severity (number of obstructive events per hour, SpO2 etc.), but it cannot provide detailed and accurate data regarding the anatomic localization of the obstructive sites [1,19].

Drug-induced sleep endoscopy (DISE) is a fiber-optic examination of the upper airway under controlled sedation. It is considered the best procedure to determine the site(s) and grade of obstruction(s), and patterns of airways collapse in OSA patients. Moreover, it quantifies, with the use of the DISE, the location and collapse pattern of the upper airway in OSA patients and can be used to customized treatments options and/or improve therapeutic outcomes [20-22].

The DISE examination studies reported in the literature were mainly performed in middle-aged adults [22-26]. To our knowledge, no clinical prospective studies have compared of upper airways DISE examination between elderly and younger OSA patients.

This study was designed to analyze the role of DISE for evaluation of obstructive sites and pattern of collapse in patients over 65 years old affected by OSA. Besides, the sites and pattern of collapse of elderly patients has been compared with a group of patients younger than 65 years that have been evaluated with the same study protocol.

MATERIALS AND METHODS

In accordance with the existing literature, in this study an age over 65 years old was taken to be indicative of elderly patients [8-13]. Patients with age over 65 years old, consecutively admitted to our Department to underwent DISE, were initially enrolled in this prospective study.

All the DISE procedures were performed at the Otolaryngology, Head and Neck and Oral Surgery Unit of the Morgagni Pierantoni Hospital in Forlì, Italy, between January 2016 and June 2018.

Exclusion Criteria: Patients submitted to surgical treatments for OSA or that had performed other head-neck surgical procedures were excluded from the study, in order to evaluate the sites/pattern of collapse without surgical bias. Patients receiving pharmacological treatment for the OSA or drugs with an impact on the cognitive function were also excluded from the study. Patients with ASA 4, or with propofol allergy were also excluded to the study.

As a control group, patients aged under 65 years, who underwent DISE in the same period of time, were prospectively enrolled in the study, following the same exclusion criteria of the study group.

Clinical parameters such as the daytime sleepiness, evaluated through the Epworth Sleepiness Scale (ESS), and body mass index (BMI) were assessed for both groups of patients.

The night before the DISE procedure all patients of the study underwent a polysomnographic (PSG) examination.

The apnea-hypopnea index (AHI), Oxygen Desaturation Index (ODI), and the lowest SpO2 (LOS) were scored by a blinded registered polysomnographic technician using established criteria [1,19]. The PSG data of both subgroups of patients was analyzed and compared.

In accordance with the American Academy of Sleep Medicine (AASM) [27-28], diagnosis and classification of OSA was made on the basis of the Apnea-hypopnea index (AHI) index. Patients were classified into mild OSA (AHI ≥5 and <15), moderate OSA (AHI ≥15 and <30) and severe OSA (AHI ≥30) (18,19). The simple snorers according to PSG results (AHI was <5 / h) were excluded from the study.

DISE protocol and obstructive pattern classification

The standardized protocol was employed in all the procedures, as reported in the European position paper on DISE [20,29]. All the DISE procedures were performed by two of the co-authors of this study (R.G. and G.I).

All DISE procedures were executed in the operating room with an anesthesiologist.

Propofol represented the sedative agent applied during all the DISE procedures and the Target Control Infusion system (TCI) was adopted [29,30]. No decongestion or topical anesthesia was employed.

The bispectral index (BIS) was employed to monitor the depth of sedation during DISE [29-32].

At least two or more cycles (snoring, collapse) for each segment of the upper airway were observed.

The VOTE system proposed by Kezirian et al. [33] was applied to classify all DISE procedures (Tab. 1).

Patients were observed firstly in standard supine primary position and after in lateral decubitus, for assessing significant modification of the upper airways during the latter position, in order to identify the positional OSA (POSA) [20,29,34,35]. Finally, the efficacy of mandibular advancement (pull-up manoeuver) was tested in each patient during the DISE.

Statistical analysis

The $\chi 2$ test was employed to evaluate the differences between the two groups of patients. The Student t-test was used to compare the analyzed factors. A p value of <0.05 was taken as the threshold of statistical significance. Linear regression was used to correlate AHI and ESS with aging.

This research study was performed in accordance with the principles of the Declaration of Helsinki and approved by the local Ethics Committee. Informed consent was obtained from all individual participants included in the study.

RESULTS

Fifty-five patients with OSA diagnosis and age ≥ 65 years old were enrolled in the study. Fifty patients with age <65 years old, were enrolled in a control group of younger patients.

Patients characteristics (Age, BMI and ESS) and PSG data (AHI, ODI and LOS) are summarized in Table 2.

The mean age of patients over 65 years was 68.6 years (range 65-80), whereas the mean age of the control group was 50.7 (range 21-62) years-old (p=0.0001). The average BMI of the study group was 28.5 while the average ESS was 7.3. The mean BMI of elderly patients was found to be greater that younger patients (mean BMI 27.2) with a significative statistical difference (p = 0.02). The average ESS of elderly patients was lower than those of younger patients (p 0.0001). Regression analysis showed ESS reduction with aging (p=0.0001) (Fig.1).

Regarding the severity of OSA, a mean AHI of 37.7 and 31.7 emerged in elderly and young patients respectively. Comparing these two mean values, no statistical difference emerged (p=0.07). Similarly, no differences emerged in a comparison of the AHI classes of elderly and young patients (p>0.05 for each class of OSA severity) (Tab. 3). However, in the entire group of patients studied (both above and below 65 years of age) regression analysis showed an increase in AHI as patients' age increased (p=0.03) (Fig.2).

A statistical difference (p=0.001) was present between the average LOS value of elderly patients (70.8) and that of younger patients (72.5).

No differences in the method of DISE execution were found among elderly and young patients. This is confirmed by the similar average values of BIS and propofol that emerged in both sub-groups of patients (Tab. 4).

During the DISE procedure, interesting data regarding different sites of obstruction and pattern of collapse emerged in elderly and young patients. The data regarding DISE in elderly and younger patients is summarized in Table 5.

Velum (V) collapse was present in 100% of elderly patients (90.9% grade 2 and 9.1% grade 1); elderly patients showed a higher incidence of total collapse in the velum region compared to younger patients (90.9% vs 70%;); this difference was statistically significant ($p = 0.01$). No differences in the pattern of velum collapse were found between the two sub-group of patients ($p>0.05$ in each case).

Oropharynx lateral wall (O) collapse was present in 45.4% of elderly patients. The lateral wall collapse was differently represented in the two groups of patients ($p=0.02$). Elderly patients showed a lower incidence of total oropharyngeal lateral wall collapse respect to younger patients, with an incidence of 20% and 50% in the two groups of patients respectively ($p = 0.002$).

A total collapse of the tongue base (T) was present in 45.4% of elderly patients and 50% of young patients ($p = 0.7$). No difference in this type of collapse emerged between the two subgroups of patients.

Epiglottis collapse was present in 49.1% of elderly patients. This subgroup of patients would seem to present most frequently a partial epiglottis collapse, compared to young patients ($p=0.0006$).

Finally, during the DISE procedure, elderly patients showed a lower LOS in comparison to young patients (72.5 vs 78.9, $p=0.001$), whereas similar values in terms of POSA and positive mandibular pull-up emerged between the two sub-groups of patients (Tab. 6).

DISCUSSION

Aging substantially increases the risk of obstructive sleep apnea. Besides, elderly patients may present differences in polysomnographic parameters (AHI, oxygen desaturation index; LOS) with respect to young patients. Despite the fact that the AHI value increases with aging, elderly patients have a reduction in daytime sleepiness [7-14]. George et al. [36] reported higher duration of apnea/hypopnea events, longer hypoxemia, as well as lower oxygen saturation in elderly patients than in their younger counterparts, whereas, Morrell et al [10], studying 1281 patients affected sleep disordered breathing, found a significative reverse correlation ($p=0.04$) between age and ESS.

Evaluation of AHI and ESS in this study seems to confirm these aspects. Regression analysis showed greater AHI values as patient age increased ($p=0.03$). The elderly patients in our study had a lower average ESS compared with the younger ones with a positive inverse correlation (p=0.0001), confirming the daytime sleepiness reduction in patients> 65 years-old.

The mechanisms underlying the tendency of elderly patients to have a greater incidence/severity of OSA syndrome still remain unclear [11,17]. Probably, as reported by some authors, the number, site and pattern of upper airway obstructions could change over time due to changes in pharyngeal anatomy and biomechanics, or deterioration in the function of pharyngeal dilator muscles [12-17].

Given the high incidence and severity of the OSA syndrome in the elderly population and considering the increase in the average age of the world population, is important to understand if there are there are changes in the pharyngeal anatomy and sites/pattern of obstruction in people over 65 years [8-12].

Imaging studies have demonstrated that, compared to middle-aged subjects, older adults present changes in bony structure and fat deposits in the pharyngeal walls, which result in a greater upper airways collapsibility[16-18,37]. Malhotra et al [17], demonstrated a significant increase in the size of the pharyngeal fat pads with aging, independently from BMI and also suggested that soft tissue volume is a risk factor for OSA in older people. Also, Carlisle et al. [15] reported that older males compared with younger patients, had a greater pharyngeal caliber measured using acoustic reflection, a greater combined retro-palatal and retro-glossal pharyngeal length, larger and longer soft palate and increased para-pharyngeal fat measured using MRI. Besides, as reported by some authors, increasing age is related to both velopharyngeal collapsibility ($p < 0.01$) and an increase in pharyngeal resistance during sleep ($p < 0.01$), independently from body mass index (BMI) and gender [13-18].

However, these studies were based on an analysis of an awake patient population which only allows only a static assessment of upper airways, whereas upper airway obstruction in OSA patients is a dynamic process. This is the main reason why we decided to carry out the upper airway assessment during the DISE procedure, which allows a more effective dynamic analysis of the upper airways in terms of site, pattern and grade of collapse during drug-induced sleep.

In this study, using the DISE, we analyzed the sites and pattern of upper airways collapse present in elderly patients and evaluated the differences that emerged with patients younger than 65 years old.

Our results showed that velum collapse was present in 100% of elderly patients with a statistical difference in the incidence of total collapse compared to younger patients (p = 0.01). This finding could be explained by the greater velopharyngeal collapsibility and increase in the length of the soft palate and uvula, observed in elderly patients [13-18].

Collapse of the oropharynx lateral walls (O) during DISE was present in 45.4% of elderly patients of our study. These patients also showed a lower incidence of total oropharyngeal lateral wall collapse respect to younger patients, (20% vs 50%, p=0.002). The atrophy of the lateral pharyngeal muscle that generally occurs with age could contribute to the reduction of the lateral wall collapse observed in older patients [14-17,38].

Similar incidences for total or partial tongue base collapse were observed. This finding could be related to the absence of age-related effects on pathogenetic factors causing tongue base collapse.

In OSA patients the different grade of AHI could influence the different sites and collapse patterns observed during the DISE procedure. In this study the regression analysis showed an increase of the AHI value with aging. However, the average AHI, as well as the incidence of the different sub-classes of OSA severity of the two sub-groups of patients, did not present a statistical difference (p>0.05 in each cases). This would suggest that the AHI values found in the two patient sub-groups are not to be considered as potential biases of the study. Besides, no differences between propofol concentrations and BIS values in the two groups of patients emerged. This could mean that there is no bias in the DISE execution that have could have interfered with the different results obtained in elderly and young patients.

The limitation of this study is that the pathophysiological mechanisms of pharyngeal collapse (pharyngeal critical pressure, oral breathing and negative pressure reflex, etc.) were not evaluated and analyzed. However, this may be considered as a preliminary observational study. Further studies are under way to confirm these data and to relate the sites and pattern of upper airways collapse in elderly patients with the pathophysiological mechanisms of OSA syndrome.

Another limiting factor of this study is the different mean BMI which emerged between the two groups of patients. Usually BMI increases with aging. However, it should be considered that the role of BMI variation in the incidence and severity of OSA in the elderly population has not yet been clarified by the published studies [13-17].

CONCLUSION

DISE is an effective and safe method that allows the evaluation of sites and collapse pattern in elderly people. Elderly patients showed a higher incidence of total collapse in the velum and a lower incidence of total oropharyngeal lateral wall collapse respect to young patients.

An accurate knowledge of the sites and pattern of collapse of elderly patients with OSA is potentially useful for customizing treatment options and/or for improving therapeutic outcomes [39].

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LEGEND

Figure 1: Regression plot between ESS and age; regression analysis showed ESS reduction with aging (p=0.0001).

Figure 2: Regression plot between AHI and age; regression analysis showed an increase in AHI as patients' age increased (p=0.03).

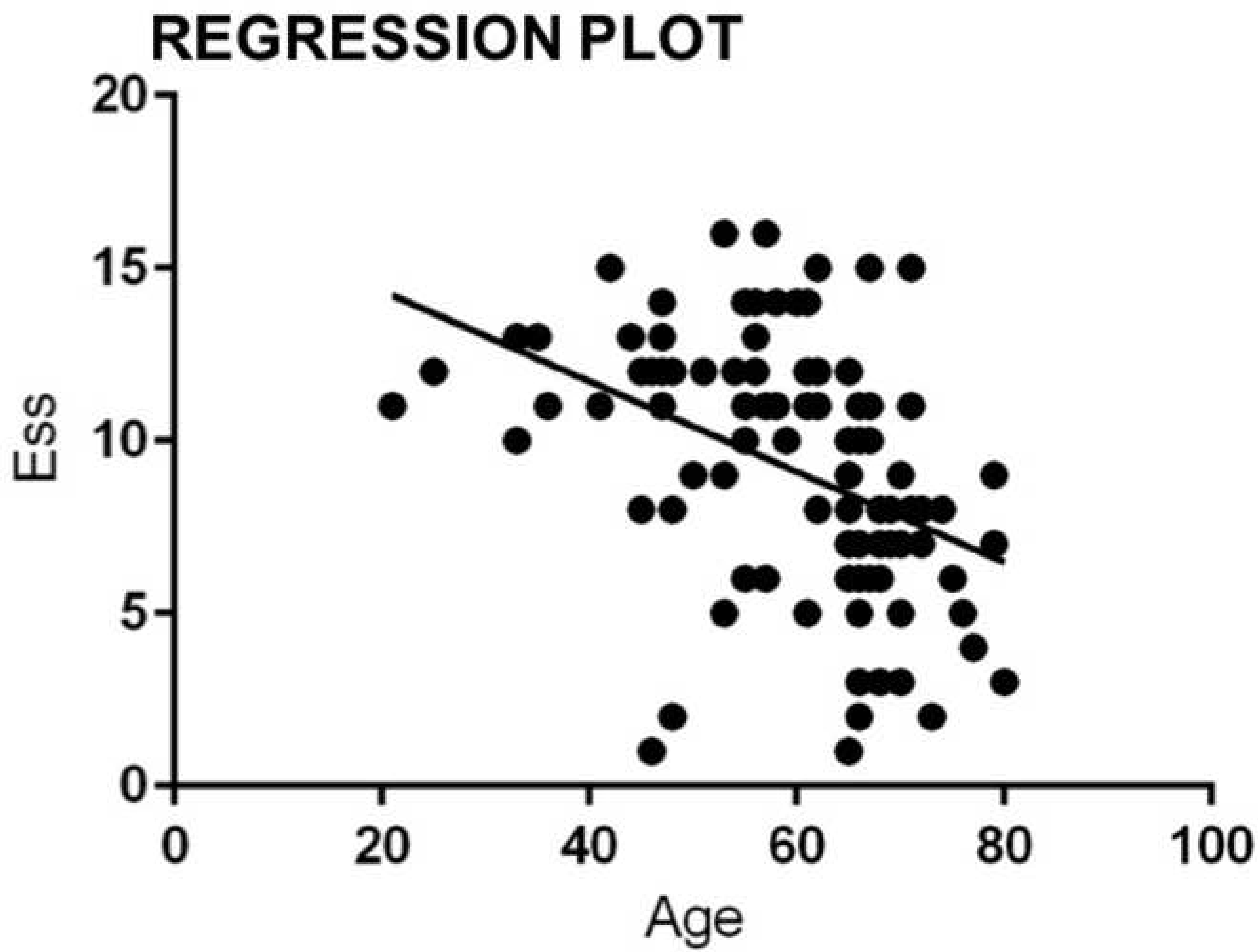
REGRESSION PLOT
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Figure 2

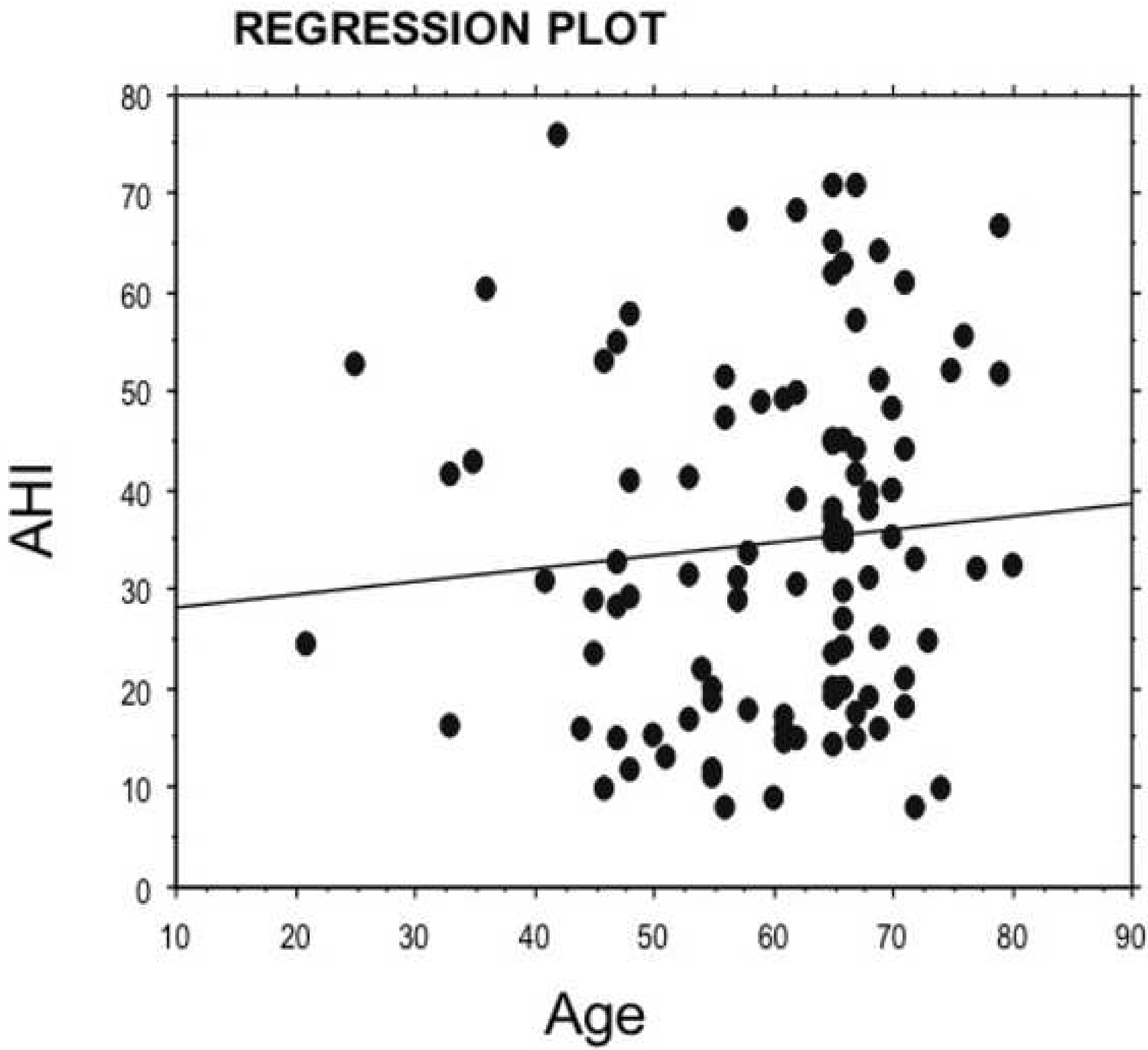
REGRESSION PLOT
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Table

Table 1; VOTE classification as proposed by Kezirian et al. [33]

STRUCTURE	DEGREE OF OBSTRUCTION*	CONFIGURATION**		
		A-P	LATERAL	CONCENTRIC
Velum				
Oropharynx lateral walls				
Tongue Base				
Epiglottis				

*Degree of obstruction has one number for each structure: 0, No obstruction (no vibration); 1, Partial obstruction (vibration); 2, Complete obstruction (collapse); X, Not visualized
**Configuration noted for structures with degree of obstruction greater than 0

[33] Kezirian EJ, Hohenhorst W, de Vries N. (2011) Drug-induced sleep endoscopy: the VOTE classification. Eur Arch Otorhinolaryngol. 268:1233-1236

Table 2 patient's characteristics and PSG data in elderly and young patients

	> 65 years 55 patients (39 MALE 16 FEMALE)			<65 years 50 patients (27 MALE 13 FEMALE)			P (t-student test)
	Mean value	**Standard Deviation**	**Median value**	**Mean value**	**Standard Deviation**	**Median value**	
AGE	68.6 (Hi = 80.0 Low = 65.0)	4.02	67.0	50.7 (Hi = 62.0 Low = 21.0)	9.7	53.0	**0.0001**
BMI	28.5 (Hi = 34.8 Low = 21.4)	2.9	28.4	27.2 (Hi = 35.6 Low = 19.5)	3.3	26.9	**0.02**
ESS	7.3 (Hi = 15.0 Low = 1.00)	2.9	7.00	11.0 (Hi = 16.0 Low = 1.00)	3.2	12	**0.0001**
AHI	37.7 (Hi = 70.9 Low = 7.90)	16.4	36	31.7 (Hi = 76.0 Low = 2.00)	18.1	29.1	0.07
ODI	36.7 (Hi = 71.6 Low = 10.0)	17.3	35	31.4 (Hi = 75.2 Low = 7.40)	18.5	27	0.1

LOS	70.8 (Hi = 91.0 Low = 46.0)	9.08	73.0	72.5(Hi = 93.0 Low = 62.0)	6.09	80.0	**0.001**

Table 3; apnea/hypopnea index (AHI) sub-classes in elderly and young patients

	> 65 years 55 patients	**<65 years 50 patients**	**P chi square test**
Mild	3	8	**0.1**
Moderate	16	18	**0.5**
Severe	36	24	**0.08**

Table 4; differences in bispectral index (BIS) mean value and plasmatic levels of Propofol between elderly and young patients

	> 65 years 55 patients	**<65 years 50 patients**	**p chi square test**
PROPOFOL µg/ml (Average value)	3.3	3.47	**0.1**
BIS (Average value)	63.6	62.9	**0.9**

Table 5; Sites of obstruction, pattern and grade of collapse in according to the VOTE classification proposed by Kezirian et al.[33]

		> 65 years 55 patients		<65 years 50 patients		p Chi square test
Site of collapse	**Grade of collapse according to the VOTE classification**	**Number of patients**	**Percentage**	**Number of patients**	**Percentage**	
VELUM	**0** (No Obstruction)	0	-	6	12%	**0.009**
	1 (Partial obstruction)	5	9.1%	9	18%	0.2
	2 (Complete obstruction)	50	90.9%	35	70%	**0.01**
	Concentric	28/55	50.9%	26/42*	61.9%	0.3
	A-P	23/55	41.8%	16/42*	38%	0.8
	Lateral	4/55	7.2%	0	-	0.7
OROPHARYNX LATERAL WALLS[b]	**0** (No Obstruction)	29	52.7%	14	28%	**0.02**
	1 (Partial obstruction)	14	25.4%	11	22%	0.8
	2 (Complete obstruction)	11	20%	25	50%	**0.002**
TONGUE BASE	**0** (No Obstruction)	8	14.5%	7	14%	1
	1 (Partial obstruction)	22	40%	18	36%	0.6
	2 (Complete obstruction)	25	45.5%	25	50%	0.7
EPIGLOTTIS	**0** (No Obstruction)	28	50.9%	36	72%	**0.02**
	1 (Partial obstruction)	16	29.1%	2	4%	**0.0006**
	2 (Complete obstruction)	11	20%	12	24%	0.6
	A-P	24/27**	88.8%	11/14***	78.5%	0.3
	Lateral	3/27**	11.2%	3/14***	21.5%	0.3

*42 patients showed total or partial collapse

*27 patients showed epiglottis collapse

*14 patients showed epiglottis collapse

Tab.6. DISE; lowest oxygen saturation (LOS), positional obstructive sleep apnea (POSA) and positive mandibular pull-up in elderly and young patients

	>65 years 55 patients		**<65 years 50 patients**		**p**
LOS (Average value of SpO2)	72.5		78.9		**0.0001 (t-student test)**
POSA	24/55	43.6%	23/50	46%	**0.8 (chi square test)**
POSITIVE PULL-UP	36/55	65.4%	27/50	54%	**0.2 (chi square test)**