SUPPLEMENTAL MATERIAL

APPENDIX A

Questionnaires

Clinical data and sleep characteristics of the patients were included through questionnaires and direct measurements highlighting: sex, age, specialist who referred the patient, reason for consultation or referral, profession, if they drive for their profession (yes/no), if it is a risky profession or if they operate dangerous machinery (yes/no), weekly kilometers driven, if they experience sleepiness after driving > 1 hour (yes/no), traffic accidents or scares due to excessive sleepiness (yes/no), physical activity (active, moderate, sedentary), toxic habits (alcohol, tobacco), pack year index (PYI), number of cups of coffee per day, comorbidities including cardiovascular risk factors (Hypertension, Diabetes Mellitus, Dyslipidemia; defined as a medical diagnosis associated with the presence of treatment for them) (yes/no); history of cardiovascular diseases (ischemic heart disease, dilated heart disease, hypertensive heart disease, arrhythmia, heart failure), neurological diseases (Cerebrovascular accident, dementia, epilepsy), chronic respiratory diseases (COPD; asthma), neoplastic diseases, depression or anxiety (any diagnosis of disease was defined such as the presence of a medical diagnosis with more than one year of follow-up). Menopause (yes/no). Nasal obstruction (yes/no). ORL surgery. Regular treatment of the patient (highlighting among them those that can potentially interfere with sleep).

In relation to the clinical symptoms suggestive of OSA for the majority of the included symptoms, the participants responded with responses of 0 (never), 1 (sometimes), 2 (frequently), and 3 (always). The questionnaire contained the following variables: snoring, feeling of restorative sleep, asphyxia, nocturia (numerical value of 0-6), witnessed apneas, nocturnal awakenings, morning headache, daytime excessive sleepiness, fatigue, memory or attention disorders, irritability, apathy, depression, as well as other clinical data suggestive of other sleep pathologies such as nocturnal motor activity, paresthesia - dysesthesias in legs, hallucinations, cataplexy, sleepwalking, sleep interrupted by heartburn, teeth grinding during sleep, decreased libido and insomnia (conciliation, maintenance or mixed; when the patient reported frequent difficulty falling asleep, staying sleep or waking up early). Data related to the patient's sleep hygiene included bedtime, time to get up, and napping time (on weekdays and weekends). Likewise, the visual analog scale of subjective perception of the disease was included, and subjective daytime sleepiness was evaluated using the Epworth Sleepiness Scale (ESE) (excessive daytime sleepiness was defined when the ESS was greater than 12).

Physical exam:

Weight (kg), height (cm), body mass index (defining obesity as a BMI ≥30 kg/m2), short neck (yes/no), nasal septum deviation (yes/no), retrognathia (yes/no), micrognathia (yes/no), tonsillar hypertrophy (grade 0-IV), uvular hypertrophy (yes/no), hypertrophy at base of tongue (yes/no), ogival palate (yes/no), Mallampati (I-IV), auscultation of the lung, auscultation of the heart and oxygen saturation were recorded.

Once the clinical history and physical exam were completed, the clinical probability of suffering from sleep apnea syndrome was established, and home respiratory polygraphy was requested in cases of high or intermediate clinical probability or a scheduled admission to perform a complete monitored polysomnography in cases of medium or low clinical probability or associated comorbidity. After the completion of the study, a report was prepared by manually coding the relevant polygraphy and polysomnography data and the diagnostic categorization of the patient and therapeutic decision according to current clinical guidelines.

Sleep studies:

Cardio-respiratory polygraphy:

A portable device (Embletta-ResMed) validated for the diagnosis of OSA was used. This device has measurement variables such as oronasal flow by thermistor and/or nasal cannula, snoring, thoracic and abdominal movements by plethysmographic bands, heart rate and oxygen saturation by pulse oximetry and body position. The recording was carried out in the patients' homes, with the polygraph previously programmed to record at a time determined by the technicians and the patient adequately trained for placement. A study was considered invalid when the recording time of the flow and/or saturation signal was less than 4 hours. The following morning, a manual analysis was performed by the specialized physicians of the unit. The total time of analysis was evaluated based on the questionnaires of the patients on the onset of sleep and wakefulness, and the review of the study was performed by a sleep technician; the time in the upright position was excluded from the analysis. It was assumed that this interval was the total sleep time.

Polysomnography:

A properly validated Grael polysomnograph (Ergometrix) was used for the diagnosis of this disease. In addition to the signals recorded by the polygraph, it allows obtaining electroencephalogram (EEG), electromyogram (EMG) and electrooculogram (EOG) signals to assess the efficiency and structure of sleep, as well as measurement of leg movements and electrocardiogram (ECG). As with polygraphy, the analysis was manual.

Polygraphy and Polysomnography reports:

The respiratory events (in both types of study) were categorized according to the AASM 2017 regulations as apneas when there was a cessation of flow through the oronasal cannula greater than or equal to 10 seconds. Hypopnea was defined as a decrease of 30% of the flow through the oronasal cannula greater than or equal to 10 seconds, associated with a decrease in oxygen saturation greater than 3% in the baseline saturation or a microawakening (arousals) during the polysomnography. The classification of obstructive or central events was defined by the presence or absence of thoraco-abdominal effort recorded by the thoracoabdominal bands of the polygraphy or polysomnography. Oxygen desaturations were defined as a 3% decrease in the absence of artifacts occurring during baseline. The oxygen desaturation index was calculated by dividing the total desaturations by the total number of minutes the patient slept or recording time in the case of polygraphy. As indices of nocturnal oxygen saturation, the mean saturation and the minimum saturation were recorded, during which time the saturation was below 90% (CT90) and 80% (CT 80).

The variables considered for the study objective were apnea-hypopnea index (AHI), mean oxygen saturation, minimum oxygen saturation, oxygen desaturation index, saturation time less than 90%, saturation time less than 80%, percentage of apnea, percentage of obstructive sleep apnea, percentage of central sleep apnea and mean apnea time (measured in seconds).

Comorbidities:

With respect to comorbidities, obesity was defined as a BMI ≥30 kg/m2; hypertension due to a self-reported diagnosis, the use of antihypertensive medication or a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or both, obtained with the conventional measure in consultation [1]; diabetes such as HbA1c ≥6.5% (48 mmol/mol) or fasting plasma glucose ≥7.0 mmol/L (126 mg/dL) or plasma glucose at 2 hours after the oral glucose overload test ≥11.1 mmol/L (≥ 200 mg/dL) or plasma glucose ≥11.1 mmol/L (≥200 mg/dL) in patients with classic symptoms of hyperglycemia or hyperglycemic crisis [2]; Dyslipidemia was defined by the presence of hypertriglyceridemia (≥ 150 mg/dl), low-density lipoprotein-bound cholesterol (HDL-C) (<40 mg/dl in men, <46 mg/dl in women) and low-density lipoprotein cholesterol (LDL-C) ≥ 140 mg/dL [3]; Respiratory disease by performing spirometry that will demonstrate the presence of chronic irreversible airflow obstruction (COPD) [4] or reversible airflow obstruction (asthma), or a methacholine test in cases with normal and clinical spirometry compatible with asthma [5]; Heart disease was defined as the presence of a history of cardiovascular diseases (ischemic heart disease, dilated heart disease, hypertensive heart disease, arrhythmia, heart failure) diagnosed by a cardiologist with more than one year of

follow-up; Neurological disease was defined as the presence of acute stroke, dementia or epilepsy diagnosed by a neurologist with more than one year of follow-up; Anxiety and depression was defined after the diagnosis given by a psychologist or psychiatrist and taking medication for it.

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A-TABLES:

Table A-1. Comparison of the reason for consultation and impact of sleepiness among patients assigned to different clusters *

	Cluster 1 (n=663)	**Cluster 2** (n=203)	**Cluster 3** (n=457)	**Cluster 4** (n=332)	**p**
Reason for consultation					0.001
Pauses in breathing, %	25.7	32.3	26.8	30.3	
Snoring, %	25.3	21.9	24.4	21.1	
Sleepiness, %	18.6	28.4	19.5	24.1	
Fatigue, %	13.7	7.5	14.1	9.0	
Asphyxia, %	4.6	2.0	4.3	2.8	
Insomnia, %	3.1	2.0	2.9	3.7	
Accident rate and impact of sleepiness					
Sleepiness interferes with life, %	45.0	40.8	35.8	32.3	<0.001
Previous occupational accidents, n	0.09 ± 0.39	0.06 ± 0.24	0.03 ± 0.25	0.08 ± 0.40	0.388
Occupational accidents due to sleepiness, %	2.9	3.7	5.6	5.6	0.332
Sleepiness while driving, %	30.9	37.3	20.3	34.1	0.001
Traffic accidents due to sleepiness, %	21.8	26.8	14.9	26.3	0.019
Traffic accidents in 5 years, n	0.08 ± 0.30	0.17 ± 0.42	0.13 ± 0.87	0.29 ± 2.16	0.186

*Values are the mean ± standard deviation or percentage. Comparison between groups by the chi-square test or ANOVA with post hoc comparisons by the Bonferroni test: ‼ p<0.05 vs. Cluster 2.

Table A-2. Comparison of other clinical characteristics, sleep duration and hygiene, physical exam and preclinical probability of SAHS among patients assigned to different clusters*

	Cluster 1 (n=663)	**Cluster 2** (n=203)	**Cluster 3** (n=457)	**Cluster 4** (n=332)	**p**
Other sleep symptoms					
Nocturia, episodes/night	0.86 ± 1.13	1.21 ± 1.30 **#**	1.06 ± 1.16 **#**	1.17 ± 1.21 **#**	<0.001
Nocturnal motor activity, %	34.2	35.3	28.4	29.0	0.106
Paresthesia, %	15.6	15.7	16.0	15.1	0.992
Apathy > 3 months, %	18.3	11.5	17.0	12.8	0.019
Cataplexy, %	1.9	1.0	0.7	0.6	0.210
Hallucinations, %	4.0	5.1	3.4	4.3	0.761
Sleepwalking, %	1.9	1.1	1.2	2.3	0.571
Heartburn, %	18.1	16.1	14.1	15.2	0.328
Teeth grinding, %	24.8	15.3	18.2	18.4	0.009
Decreased libido, %	19.0	4.0	16.9	11.3	0.049
Insomnia, %	9.5	5.4	8.6	5.8	0.085
Visual analog scale disease	6.5 ± 1.9	6.4 ± 1.9	6.2 ± 2.1	6.3 ± 1.9	0.556
Characteristics of sleep					
Workday sleep duration (min)	458 ± 93	456 ± 109	467 ± 82	462 ± 107	0.532
Weekend sleep duration (min)	512 ± 103	519 ± 86	510 ± 86	502 ± 91	0.423
Increased sleep on weekends (min)	56 ± 91	76 ± 95	47 ± 77 **‼**	46 ± 109 **‼**	0.014
Workday nap duration, min	25 ± 40	35 ± 46	33 ± 43	33 ± 40	0.015
Weekend nap duration, min	35 ± 46	44 ± 48	35 ± 43	36 ± 39	0.305
Sleep hygiene					0.003
Poor, %	16.2	14.6	8.9	11.3	
Fair, %	20.2	22.5	18.2	25.9	
Good, %	63.6	62.9	72.9	62.8	
Physical exam					
Retrognathia, %	12.5	15.5	10.7	7.6	0.037
Short neck, %	34.3	62.8	32.2	37.9	<0.001
Tonsillar hypertrophy, %	39.2	38.8	28.4	26.0	0.006
Uvular hypertrophy, %	12.8	17.2	7.5	16.3	0.001
Hypertrophy at base of tongue, %	10.0	19.0	9.9	7.5	0.029
Nasal septum deviation, %	10.7	8.8	6.1	11.3	0.315
Mallampati	2.1 ± 1.0	2.6 ± 1.1 **†**	2.3 ± 1.1 **#$‼**	2.3 ± 1.0 **¶‼**	<0.001
Ogival palate, %	6.3	3.2	1.5	4.1	0.008
Micrognathia, %	11.9	11.4	9.4	5.7	0.029
Clinical probability of SAHS					<0.001
Low, %	18.6	8.4	27.5	18.8	
Mean, %	21.7	18.3	25.2	26.5	
High, %	59.7	73.3	47.3	54.7	

*Values are the mean ± standard deviation or percentage. Comparison between groups by the chi-square test or ANOVA with post hoc comparisons by the Bonferroni test:

Comparison vs. Cluster 1: † p<0.001; ¶ p < 0.01; # p<0.05

Comparison vs. Cluster 2: $ p<0.01; ‼ p<0.05