'REM-related OSA': a forgotten diagnostic? Possible path to under-diagnosing sleep apnea

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Introduction. Restrictive criteria are proposed to define the disorder 'REM-related OSA' disorder, and questions remain about its nosological transcendence and clinical management.

Aim. To evaluate the criteria proposed to define 'REM-related OSA', its relationship with cardio-metabolic comorbidity, and aspects related to it diagnostic.

Patients and methods. Retrospective observational study of clinical and polysomnographic data from outpatients. 525 patients over 18 years old who had an Apnea Hypopnea Index (AHI) ≥ 5 (total, or partial, in REM and/or NREM) were included.

Results. 'Phase-dependent' subgroups were formed using a criterion based on the 'ratio ≥ 2' and another 'strict' criterion based on a partial AHI ≥ 5 compared to another partial AHI <5 (in REM or in NREM). In the 'strict REM-related OSA' subgroup, half of the patients showed an overall AHI < 5, with less severity in the respiratory parameters, but with lower comorbidity percentages. With the current diagnostic criteria, these patients would be excluded from the sleep apnea diagnosis.

Conclusions. The application of the strict criterion to detect 'REM-related OSA' makes it possible to filter milder forms of sleep apnea associated with percentages of cardiovascular and/or metabolic comorbidity that are not significantly different from other more severe forms of sleep apnea. To avoid under-diagnosis, it would be advisable to review the sleep apnea diagnostic criteria and the indications of the reduced sleep apnea diagnostic techniques.

Key words. Comorbidity. Obstructive sleep apnea. Phase-dependent OSA. Polysomnography. REM-related OSA. Under-diagnosis.

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Accepted:
03.05.16.

How to cite this paper:
Benetó A, Soler-Algarra S, Salavert V. 'REM-related OSA': a forgotten diagnostic? Possible path to under-diagnosing sleep apnea. Rev Neurol 2016; 63: 481-7.

Versión española disponible en www.neurologia.com

Introduction

The obstructive sleep apnea-hypopnea syndrome (OSA) is a prevalent disorder characterized by a recurrent partial or total obstruction of the upper airway (UA) that is related to severe cardiovascular and metabolic consequences. The diagnostic criteria and the different severity levels are based on the Apnea-Hypopnea Index per hour of sleep (AHI), compared to the total amount of sleep during the night, including both REM and NREM sleep [1].

During REM sleep there is a retraction of the noradrenergic and serotoninergic stimuli toward the motor neurons of the UA, which reduces the muscular activity of the pharynx and significantly increases the probability of UA collapse [2]. Consequently, during the phases of REM sleep, it is common to observe an increase in the frequency, duration and desaturation of the apneas and hypopneas in patients with OSA. The term 'REM-related OSA' is used to define those cases where the apneas and hypopneas mainly or exclusively occur during REM sleep [3].

In the bibliography on 'REM-related OSA', variability can be observed in the criteria used to define it, and there is no uniformity when describing its clinical traits. One criterion has been widely used with diverse nuances, a ratio criterion, where the REM AHI has to be at least twice the NREM AHI [4-8]. However, this criterion has been criticized because it does not exclude the 'portion of the disorder' that corresponds to NREM sleep. To avoid this limitation, various more restrictive criteria have been proposed [9-14] until arriving at a very strict one that requires a REM AHI ≥ 5 + NREM AHI < 5 and a total REM sleep time ≥ 30 minutes [3].

The 'REM-related OSA' phenomenon poses a series of relevant questions that justify the insistence on its clinical description, such as: What is the best criterion to define it?; Does it make sense to apply the strictest criterion?; Does it have the same consequences as the overall OSA with regard to somnolence and cognitive and cardiovascular-metabolic impact? Even when the overall AHI is irrelevant or very mild, if the AHI REM is high, should it be treated with CPAP? [3,15,16].

The purpose of this retrospective observational study is to evaluate patients with 'REM-related OSA' extracted from the polysomnographic studies (PSG) carried out in our Sleep Disorder Unit in the period between 2011 and 2014, The aim is to assess the defining criteria used to select the patients, describe their clinical characteristics and PSG, evaluate the presence of cardio-metabolic comorbidity, and, finally, propose the possible need to review the current diagnostic criteria for OSA, which only consider the overall AHI values for all sleep and not the phase-dependent partials.

Patients and methods

A review was carried out of the PSG studies conducted during the period from November 2011 to November 2014 with patients over 18 years old who had been referred to the Sleep Unit of the Milennium-Sanitas Medical Center in Valencia to confirm or rule out the *de novo* objective diagnosis of OSA. Retrospective analysis of the clinical data and PSG was approved by the Ethical Committee of Milennium-Sanitas.

All the patients underwent a complete and supervised nighttime PSG with a standard clinical set-up to measure OSA severity. All the PSG data were collected and stored using Xltek Systems equipment with the Sleep Works application (Natus Medical Incorporated, USA). The staging of the sleep phases, the arousals, and the respiratory events were analyzed according to the 2007 American Academy of Sleep Medicine criteria [17]. Hypopneas were considered when there was a reduction in the airflow signal of at least 30% for a minimum of 10 seconds, accompanied by drops in the SaO_2 ≥ 3% measured through transcutaneous pulse oximetry, and/or an arousal [18].

Patients were included who did have any AHI ≥ 5 (total or partial in REM and/or NREM). To establish phase-dependent OSA groups, two types of criteria were used: one that we will call the 'ratio' criterion, and another 'strict' criterion, based on the Mokhlesi and Punjabi proposal [3]. Thus, five subgroups of patients were established:

A. *Strict REM-related OSA:* REM AHI ≥ 5 + NREM AHI < 5 + at least 30 minutes of REM sleep, divided, in turn, into two subgroups depending on whether the overall AHI was ≥ 5, or not.
B. *REM-OSA ratio:* REM AHI ≥ 2 NREM AHI + overall AHI ≥ 5.
C. *Non phase-dependent OSA:* overall AHI ≥ 5, without meeting either of the two criteria.
D. *Strict NREM-related OSA:* REM AHI < 5 + NREM AHI ≥ 5 + at least 30 minutes of REM sleep.
E. *NREM-OSA ratio:* NREM AHI ≥ 2 REM AHI + overall AHI ≥ 5.

The patients filled out a questionnaire that includes demographic data, sleep history, the Epworth scale [19], and information about comorbidities. Consideration was given to subjective complaints of insomnia, depression, physical fatigue, estimated sleep duration < 6 hours/night, impaired cognitive performance (memory and attention), and symptoms compatible with restless leg syndrome, as well as the smoking habit and references to accidents/incidents with driving vehicles. In addition, evaluations were performed of the body mass index (BMI), antecedents of arterial hypertension (AHT), type-2 diabetes mellitus, and dyslipidemia in treatment. Comorbidity was also considered to include any abnormal laboratory results for glycaemia, cholesterol, and its fractions in patients who were still not receiving specific treatment for them.

Statistical analysis

Statistical analysis was performed using the SPSS 22.0 program. Initially, a descriptive analysis was carried out of the study parameters for the whole sample and for the subgroups established. Continuous variables are presented as mean ± SD, and categorical variables as *n* (%).

Then, a comparative study was conducted of the different groups described in the previous section. To do so, the normality of the samples compared was first analyzed. In the case of continuous variables with normal distribution, a *t*-test for paired samples was performed. In addition, in the case of variables with a non normal distribution, the statistical analysis carried out was the Wilcoxon test. In the case of categorical variables, a Pearson Chi-squared or Fisher exact test was obtained through contingency table analysis.

Results

The sample is composed of 525 patients (Figure), 285 (54.3%) non phase dependent and 240 (45.7%) phase dependent. In the case of REM sleep, there are 187 patients (35.6%), of whom 82 (15.6% of the entire sample) meet the strict criterion (A), and 146 (27.8% of the entire sample) meet the ratio criterion (B). In the case of NREM sleep, there are 53 patients (10.1%), of whom 26 (4.9% of the entire sam-

ple) meet the strict criterion (D), and 45 (8.6% of the entire sample) meet the ratio criterion (E). In subgroup A, 41 patients (50 %) had a overall AHI < 5, whereas in subgroup D only 3 patients (11.3%) had an overall AHI < 5.

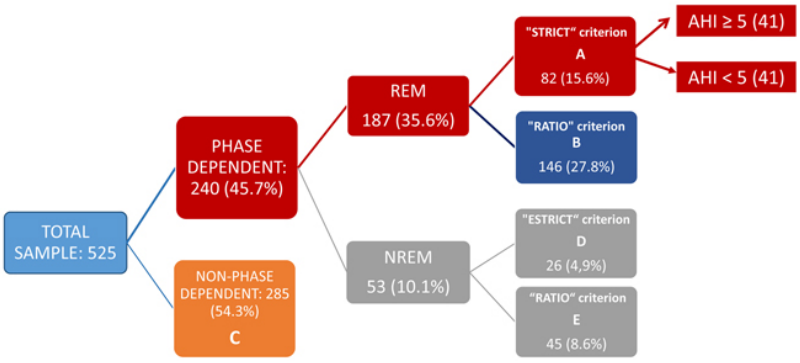
Table I shows the results and statistical significance of the demographic, morphological, comorbidity, and respiratory parameters evaluated in the total sample and in the subgroups of patients. The non phase-dependent OSA are slightly older, and the REM-OSA groups contain is a higher percentage of women. In the latter, the total sleep time and efficiency are higher, as occurs with the percentage of REM sleep, which is practically 20% of the total sleep time (TST) in the 'strict' group. The comparative analysis shows significant differences in the amount and quality of sleep, which are greater in the REM-OSA subgroups than in the other subgroups. In addition, there is a significant difference in BMI between the REM-OSA and non phase-dependent OSA subgroups, but there are no differences in subjective complaints, cardiovascular/metabolic comorbidity, or the percentage of obese patients with a BMI > 30.

The respiratory parameters show a less negative impact in the REM-OSA subgroups compared to the non phase-dependent OSA subgroups. There is a noteworthy pattern for the overall AHI and the NREM AHI in all the subgroups: higher values are registered in the non phase-dependent OSA and lower values in the REM-OSA subgroups. The non phase-dependent OSA is the most severe form, followed by the NREM groups, and finally the REM, especially the 'strict' criterion REM-OSA group. The percentage of positional OSA is significantly lower in the strict REM-OSA and non phase-dependent OSA groups, compared to the other groups, which did not show any significant differences between them.

When comparing the two REM-OSA groups, 'ratio' criterion versus 'strict' criterion, there are no significant differences in the demographic, clinical, or comorbidity data. However, there are differences on all the apnea-hypopnea indices expressing the number of respiratory events, their duration, and the minimum oxyhemoglobin saturation (SaO_2) in REM and NREM sleep.

In the 'strict' REM-OSA subgroup, half of the patients show a overall AHI < 5, which makes it possible to create two subgroups based on this trait. When comparing them (Table II), there are no statistically significant differences in the demographic, morphological, or comorbidity data, except BMI and the percentage of dyslipidemia, which are higher in the AHI < 5 subgroup. There are also significant differences in all the AHI, overall and partial, the minimum SaO_2 in REM, and the maximum and minimum duration of the apneas, with lower values in the subgroup whose overall AHI is < 5.

Figure. Distribution of the sample in the different subgroups.



The analysis of the correlation between the different parameters in all the subgroups showed an association between 'usually sleep < 6 hours/night' and insomnia complaints in all the groups. In the 'strict' REM-OSA group, the patients with subjective usual duration of sleep < 6 hours also showed percentages of antecedents of AHT that were significantly different from those who usually sleep more than 6 hours, but this did not occur in the rest of the subgroups.

Discussion

A recent study established a prevalence of 'REM-related OSA' in a range between 13.5% and 36.7%, depending on whether the ratio criterion of AHI REM ≥ 2 AHI NREM is applied or a strict criterion that minimizes the NREM AHI, with values < 8. It is more prevalent in women and young people, and no statistically significant clinical differences are found between patients selected with these two criteria [13]. The prevalence and the traits of our two REM-OSA subgroups (A and B) agree with the published series [4-6,9,10,12-14]. They are younger patients, with a greater presence of women and less severity than the non phase-dependent OSA subgroup, both on the respiratory parameters and on the amount and quality of sleep. However, there are no differences in the percentages of obesity (BMI > 30),

Table I. Demographic, morphological, comorbidity and respiratory data.

	Total sample	Strict REM-OSA (A)	REM-OSA ratio (B)	OSA non-phase dependent (C)	Strict NREM-OSA (D)	NREM-OSA ratio (E)
Patients	525	82	146	285	26	45
Age (years old)	51 ± 12.4	46.3 ± 11.9	49.6 ± 11.8	52.8 ± 12.4	45.9 ± 11.4	48 ± 11.6
Men (%)	71.5	53.7	60	80	77	84
Sleep efficiency (%)	82.7 ± 12.6	86 ± 9.6 (C [c], D [b])	83.5 ± 12.1 (E [a])	82.5 ± 12.9	79.6 ± 14	80.7 ± 12.6
TST (min)	371.5 ± 180.9	381.7 ± 56 (C [a], D [b])	365 ± 64.4 (E [a])	377 ± 237	349 ± 60.3 (C [a])	358 ± 59.9
REM (min)	60.1 ± 28.9	76.5 ± 24.3	70.4 ± 27.9 (C a)	53.9 ± 27.9	65.3 ± 22.6	56.7 ± 28.4
REM (% TTS)	16.1 ± 6.7	19.9 ± 5	18.8 ± 5.96	14.3 ± 6.6	18.6 ± 5.1	15.6 ± 6.87
III-IV NREM (% TTS)	18.4 ± 10.6	24 ± 8.1	22.8 ± 8.8	15.6 ± 10.9	19.4 ± 8.23	16.4 ± 9.71
Epworth Scale score	9.7 ± 5	9.7 ± 5.5	10.1 ± 5.04	9.57 ± 4.7	8.29 ± 5.48	8.95 ± 5
BMI (kg/m^2)	29 ± 5.1	26.9 ± 5.3 (C [c])	28 ± 5.46 (C [a])	29.7 ± 4.94	26 ± 3.46	28.5 ± 4.5
Obesity (BMI > 30) (%)	33	15	31	43	16	32
AHT (%)	33	21	27 (C [a])	38	40	34
Diabetes mellitus (%)	24	13	21	27	20	35
Dyslipidemia (%)	39	25	33	46	20	32
AHT and/or diabetes and/or dyslipidemia (%)	44	34	39	51	42.3	38
AHI	33.8 ± 26.2	5.6 ± 3.4 (B, C, D [c])	16.2 ± 9.2 (C [c])	47.1 ± 25.3	16 ± 14	35.4 ± 22.2
REM AHI	38.1 ± 25.3	19.3 ± 13.9 (B, C, D [c])	39.1 ± 18.2 (C [a], E [c])	46.2 ± 25.7 (D [c])	2.09 ± 1.51 (E [c])	10.3 ± 9.6
NREM AHI	32.4 ± 27.7	2.2 ± 1.4 (B, C, D [c])	11 ± 8.59 (C, E [c])	46.8 ± 26	19 ± 16.7	39.5 ± 23.9
$MinO_2$ REM (%)	81.8 ± 12.8	87 ± 6.9 (B [b], C, D [c])	84.2 ± 7.48 (C [c], E [b])	78.2 ± 14.9 (D, E [c])	91.9 ± 3.97	88.3 ± 9.02
$MinO_2$ NREM (%)	84.1 ± 8.5	90 ± 4.9 (D [a], B [b], C [c])	87 ± 6.92 (E [b], C [c])	81.5 ± 8.93 (E [a], D [c])	88.6 ± 4.27	84.5 ± 7
A D REM (s)	38.4 ± 19.4	17.8 ± 5.2 (C [c])	19.2 ± 5.2 (C [c])	41.7 ± 20.7	15.5 ± 4.8	19.4 ± 8.9
A D NREM (s)	42.1 ± 18.5	16.7 ± 3.7 (C [c])	17.8 ± 3.7 (C [c])	49.6 ± 18.4	18.2 ± 6.2	20.1 ± 5.7
Positional OSA (%)		39 (B [a], D [b])	56 (C [c])	34 (D, E [c])	69	62

TST: total sleep time; AHT: arterial hypertension; AHI: Apnea-Hypopnea Index per hour of sleep; REM AHI: Apnea-Hypopnea Index per hour of REM sleep; NREM AHI: Apnea-Hypopnea Index per hour of NREM sleep; $MinO_2$ REM: minimum oxygen saturation during REM sleep; $MinO_2$ NREM: minimum oxygen saturation during NREM sleep; A D REM: average duration of the apneas in the REM sleep phase; A D NREM: average duration of the apneas in the NREM sleep phase. Statistical significance of the comparisons of the groups: [a] $p < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$.

the Epworth scale, metabolic and cardiovascular comorbidity (except the AHT in the ratio REM-OSA subgroup), or the other parameters evaluated.

Regarding the criteria used to define 'REM-related OSA', when comparing the REM-OSA A and B subgroups, significant differences are only found on

the respiratory parameters, with greater severity in group B (ratio). On the degree of severity, the ratio REM-OSA subgroup appears as a milder form of OSA, and the strict REM-OSA subgroup would be much milder.

We could speculate that the OSA linked to REM sleep is the first stage of the disease, as the REMA-HI alone has 'little weight' in the overall AHI value of these patients, compared to what occurs in OSA linked to NREM sleep, where the overall AHI has much higher, statistically significant values. Even the AHI of the non phase-dependent OSA is not statistically different from the AHI of the two 'NREM-OSA' subgroups, probably due to the longer duration of NREM sleep throughout the night, as suggested in studies that emphasize the role of apneas in NREM sleep in the severity of the OSA [8]. A ratio of 3:1 is calculated for the contribution of NREM AHI and REM AHI, respectively, to the overall AHI for the whole night [20].

The lower presence of positional OSA in the non phase-dependent OSA subgroup and the strict REM-OSA subgroup suggests less influence of the positional factor during sleep in the most severe forms. Its role is relativized by the presence of other pathogenic factors, and in milder forms of OSA by the greater pathogenic impact of respiratory control during REM sleep.

The strict REM-OSA subgroup is made up of two types of patients: 50% with an overall AHI ≥ 5 and 50% with AHI < 5, with a milder respiratory profile in the latter. However, this subgroup shows significantly higher figures for BMI and dyslipidemia, which means that their cardiovascular and metabolic risk does not differ from the subgroup with AHI ≥ 5 and can even be greater. However, objectively, with the current OSA diagnostic criteria, this subgroup would be excluded from a positive diagnosis and, therefore, from treatment. A recent study that formulates the hypothesis of the association between REM-OSA and hypertension showed this same result, highlighting that up to 70% of PSG studies with REM AHI ≥ 15 can be classified as non-OSA (AHI < 5) or mild OSA (AHI: 5-14.9) [21].

The greater percentage of AHT and insomnia in patients who usually sleep less than 6 hours/night in the strict REM-OSA subgroup coincides with other studies [22-26] and supports the previously mentioned possibility [27] of an interaction between OSA and severe chronic insomnia, where hyperactivity of the hypothalamic-pituitary-adrenal axis plays a relevant role [27-31]. The recent description of the insomnia phenotype with reduction in the total amount of sleep [28] reinforces this hypothesis.

Table II. Demographic, polysomnographic, comorbidity and respiratory data of the patients in the two 'strict' criterion REM related subgroups with AHI < 5 vs AHI ≥ 5.

	AHI < 5	AHI ≥ 5	*p*
Patients	41	41	
Age (years-old)	46.3 ± 12	46.9 ± 11.6	NS
Men (%)	54	53	NS
Sleep efficiency (%)	84.9 ± 10.7	86.9 ± 8.3	NS
TST (min)	373.8 ± 58.7	388.6 ± 53	NS
REM (min)	71.7 ± 25	81.1 ± 23.2	NS
REM (% TST)	19.0 ± 5.1	20.7 ± 4.8	NS
III-IV NREM sleep (% TST)	23.6 ± 8	24.4 ± 8.3	NS
Epworth Scale score	9.5 ± 6.1	9.9 ± 4.9	NS
BMI (kg/m^2)	27.5 ± 4.9	26.4 ± 5.7	Significative
Obesity (BMI > 30) (%)	18	18	NS
AHT (%)	21	27	NS
Diabetes mellitus (%)	13	13	NS
Dyslipidemia (%)	25	22	Significative
AHT and/or diabetes and/or dyslipidemia (%)	34	38	NS
AHI	3 ± 1.2	8.2 ± 3	0
REM AHI	10 ± 4.8	29.2 ± 13.5	0
NREM AHI	1.4 ± 1.1	2.9 ± 1.3	0
$MinO_2$ REM (%)	89.2 ± 5.2	84.7 ± 7.6	0
$MinO_2$ NREM (%)	90.6 ± 4.2	89.3 ± 5.6	NS
D A REM (s)	15.7 ± 3.3	19.2 ± 5.8	NS
D A NREM (s)	14.8 ± 2.9	18 ± 3.6	NS

TST: total sleep time; AHT: arterial hypertension; AHI: Apnea-Hypopnea Index per hour of sleep; REM AHI: Apnea-Hypopnea Index per hour of REM sleep; NREM AHI: Apnea-Hypopnea Index per hour of NREM sleep; $MinO_2$ REM: minimum oxygen saturation during REM sleep; $MinO_2$ NREM: minimum oxygen saturation during NREM sleep; A D REM: average duration of the apneas in the REM sleep phase; A D NREM: average duration of the apneas in the NREM sleep phase; NS: non significative.

The transcendence of these ideas is that cardiovascular and metabolic comorbidity in 'strict' REM-related OSA shows a lower percentage than in non

phase-dependent OSA, but the difference is not statistically significant, and it does not differ substantially between the subgroups with AHI ≥ 5 and AHI < 5. For these reasons, it seems appropriate to systematically apply the strict criterion for 'REM-related OSA' [3] to rigorously filter patients with very mild OSA, who are associated with cardiovascular and metabolic comorbidity in percentages that are far from negligible.

Our study has limitations inherent to observational studies. We cannot infer epidemiological causalities among the variables studied, so that the analytical results must be viewed from an exploratory perspective. However, the results of our study are consistent with other data published in the literature that support the need to revise the therapeutic and diagnostic attitude toward patients with milder forms of OSA [3,15,16,21].

The association with cardiovascular and/or metabolic diseases is a determinant in making decisions, including the application of CPAP in mild and moderate forms of OSA [32]. In the specific case of patients with strict REM-OSA with an overall AHI < 5 and the association of cardiovascular and/or metabolic comorbidity, the positive diagnosis of OSA should not merely be ruled out; at least an evolutionary control should be carried out, even proposing the opportunity for active treatment for an OSA that is significant at least part of the night, exactly 19.9 % of the TST in our series.

The diagnostic criteria for OSA, as well as the severity levels, are based on the overall AHI throughout the night [1], and it is likely that they contribute to under-diagnosing very mild forms related to REM sleep. The REM AHI values can be high, even when the overall AHI is low, and even below 5. In other words, during a fraction of the night the patient presents a significant OSA, although when considering the whole night, it does not reach minimum diagnostic values. In this case, the patients are excluded from a positive diagnosis. In contrast to the concept of OSA linked to the whole night, it might be useful to propose the concept of 'partial' OSA during the part of the night that corresponds to REM sleep. Thus, 'REM-related OSA', regardless of whether it is considered a specific entity or a mild preliminary stage of OSA [3], would receive the appropriate attention. It might be advisable to modify the current diagnostic criteria and consider the existence of an OSA not only when the overall AHI is ≥ 5, but also when any of the partial AHIs, REM and/or NREM, is ≥ 5 and accompanied by symptomatology, insomnia complaints with short sleep duration, and/or cardiovascular and/or metabolic comorbidity.

Up to 80% of hypothetical OSA patients are not diagnosed, which makes it necessary to establish strategies to facilitate their diagnosis and treatment [33,34]. When elaborating the OSA diagnostic protocol, it is important to consider these mild-moderate forms of OSA linked to REM sleep. The indiscriminate rise in reduced techniques, given that they do not evaluate sleep and are inoperative for diagnosing REM-related OSA, can be a source of underdiagnosis in patients whose association with comorbidity factors is far from negligible.

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Síndrome de apnea/hipopnea obstructiva ligado al sueño REM: ¿un diagnóstico olvidado? Posible vía de infradiagnóstico del síndrome de apnea/hipopnea obstructiva del sueño

Introducción. Recientemente se han propugnado criterios restrictivos para definir el síndrome de apnea/hipopnea obstructiva ligado al sueño REM y persisten interrogantes sobre su trascendencia nosológica y manejo clínico.

Objetivo. Evaluar los criterios definitorios de la apnea del sueño REM, su relación con la comorbilidad cardiometabólica y los aspectos relacionados con su diagnóstico.

Pacientes y métodos. Estudio observacional retrospectivo sobre datos clínicos y polisomnográficos de pacientes ambulatorios. Se incluyó a 525 pacientes mayores de 18 años que tenían un índice apnea/hipopnea (IAH) por hora de sueño ≥ 5 (total, o parcial en REM o no REM).

Resultados. Se han configurado subgrupos 'dependientes de la fase' utilizando un criterio basado en la 'proporción ≥ 2' y otro 'estricto' basado en uno de los IAH parciales ≥ 5 frente al otro IAH < 5 (en REM o en no REM). En el subgrupo 'apnea del sueño REM estricto', la mitad de los pacientes muestra un IAH global < 5 y menos gravedad en los parámetros respiratorios, pero sin menores porcentajes de comorbilidad. Con los criterios diagnósticos actuales quedarían excluidos del diagnóstico de síndrome de apnea/hipopnea obstructiva del sueño (SAHOS).

Conclusiones. Aplicar un criterio estricto para detectar apnea del sueño REM permite filtrar formas muy leves de SAHOS asociadas a comorbilidad cardiometabólica en porcentajes no diferentes significativamente de otras formas más graves. Para evitar el infradiagnóstico del SAHOS sería oportuno revisar los criterios diagnósticos actuales y las indicaciones de las técnicas reducidas.

Palabras clave. Apnea del sueño REM. Apnea obstructiva del sueño. Comorbilidad. Infradiagnóstico. Polisomnografía. SAHOS dependiente de la fase.