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Original Article

Accuracy and utility of a pacemaker respiratory monitoring algorithm for the detection of obstructive sleep apnea in patients with atrial fibrillation

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ABSTRACT

Introduction: The usefulness and diagnostic value of new-generation pacemakers (PM) with enhanced monitoring capabilities are not yet clearly established. The aim of this study was to evaluate the diagnostic utility and accuracy of a PM-incorporated respiratory monitoring algorithm and its interaction with atrial fibrillation (AF).

Methods: A single-center prospective study was performed in consecutive patients who underwent PM implantation featuring a respiratory monitoring algorithm. All patients had polysomnography recording. The respiratory disturbance index of the polysomnography and pacemaker (RDI-PM) were recorded on the same night. Occurrence and burden of AF were also recorded. The diagnostic utility of RDI-PM and its interaction with AF were evaluated.

Results: A total of 81 patients were included (age 73 ± 11 years). Obstructive sleep apnea syndrome (OSAS) was diagnosed in 62%. RDI-PM had good diagnostic accuracy for OSAS (area under the curve: 0.767 [95% CI: 0.65–0.88]; $p < 0.001$), with an ideal diagnostic cut-off of 13.3 (sensitivity 78%; specificity 78%) and 90% sensitivity for the diagnosis of moderate-to-severe OSAS. Time to AF first episode and total AF burden were not significantly different between patients with and without OSAS. However, in those whose OSAS diagnosis was based on RDI-PM, there was a significantly greater AF burden in patients with vs without OSAS (cut-off ≥13, 488 vs 83 min, $p = 0.05$). In patients with AF, the RDI-PM cut-off of 13.3 decreased specificity (57%) vs the general population, but in patients without AF the specificity was 100% and sensitivity 77%.

Conclusion: OSAS was prevalent in PM patients. RDI-PM diagnosed OSAS accurately, with high sensitivity for the detection of moderate-to-severe OSAS, making it a suitable screening method. AF, however, significantly decreased the specificity of RDI-PM for OSAS diagnosis.

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a very prevalent condition, affecting approximately 2–5% of the adult population and 20% of the elderly population (>70 years of age) [1]. Recently, the HypnoLaus study showed increasing prevalence, about 49.7% for men and 23.4% for women, regarding moderate-to-severe OSAS [2]. It is characterized by the occurrence of repetitive collapses of the upper airway during sleep, leading to nocturnal apnea and hypopnea. These cause periods of hypoxemia and hypercapnia, with marked variations in intrathoracic impedance, increased sympathetic autonomic nervous system activity, activation of the renin–angiotensin–aldosterone system and other adverse metabolic effects [3]. The consequences are sleep fragmentation,

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occurrence of relevant daytime symptoms (drowsiness and tiredness, excessive daytime sleepiness, headache, memory loss, decreased libido, mood changes) [4] and increased morbidity and mortality, mainly cardiovascular related. Indeed, the relation with multiple cardiovascular comorbidities is well established [1,4,5] (tachyarrhythmia and bradyarrhythmia [6,7], coronary artery disease, heart failure [8], type 2 diabetes mellitus, arterial hypertension [9], pulmonary hypertension, obesity, stroke [3]), and the average life expectancy of a patient with untreated OSAS may be up to 20 years lower than that of the general population.

One of the most frequent comorbidities of OSAS is atrial fibrillation (AF) [10], which shares most of the risk factors associated with OSAS. Approximately 40–50% of patients with AF have concomitant OSAS [11], and there is a fourfold increase in the prevalence of AF in patients with severe OSAS [6]. The presence of OSAS also influences the response to antiarrhythmic therapy [12] and the rate of AF recurrence after ablation [13,14] and electrical cardioversion [15]. There is also an association between OSAS and the occurrence of bradyarrhythmia. It is estimated that approximately 25% of patients with an indication for pacemaker (PM) implantation are diagnosed with OSAS, and the prevalence of OSAS is higher in patients with bradyarrhythmia requiring pacemaker implantation [16].

Despite the high prevalence and clinical importance of OSAS, it is often underdiagnosed (it is estimated that 50–90% of OSAS patients are not diagnosed, with a higher percentage in some developing countries) [1,17]. The gold standard for diagnosis is polysomnography (PSG) [4]. However, owing to its poor accessibility, impracticality, and lengthy evaluation time, new methods of assessment, such as portable monitoring devices, have appeared and are increasingly being studied and used [1,4].

The purpose of this study was to evaluate the diagnostic accuracy of a PM-incorporated respiratory monitoring algorithm by comparing RDI-PM with the RDI obtained with the polysomnography (RDI-PSG), and to determine the sensitivity and specificity of RDI-PM for the diagnosis of OSAS in patients with and without AF, compared to the general population.

2. Methods

This was a single-center prospective study conducted in the Centro Hospitalar Lisboa Norte, in Portugal, with inclusion of consecutive patients during 2015 and 2016, and with the following eligibility criteria: age $\geq$18 years; ability to provide informed consent; indication for a dual-chamber PM implantation; and no previous history of OSAS or AF.

The patients underwent PM implantation, using the standard percutaneous technique, with the following devices: ReplyTM 200, KoraTM 100 and KoraTM 250 (MicroPort®, Clamart, Paris, France).

These devices incorporate a sleep apnea monitoring (SAM) feature that detects, counts, and reports abnormal breathing events during a period of five consecutive hours during the night (programmed by the physician to cover sleeping time, according to patient habits). The SAM works using the minute ventilation signal (MV), which represents the expansion/contraction of the thorax in real time [18]. This signal is determined by measuring variations in transthoracic impedance, with very low pulses of electrical current that pass between the bipolar lead tip and the PM, using Ohm's Law. Static impedance is not taken into account in the transthoracic impedance measurement; any temporary instability (sudden change in static impedance), related, for example, to change in the patient's position, is eliminated via a high-pass filter. In the end, only dynamic impedance is analyzed by the PM, and there is validation/exclusion of each cycle, based on a reliability marker and/or previous cycles. This allows the calculation of apneas (absence of a significant respiratory cycle for >10 s) and hypopneas (reduction during >10 s of the respiratory amplitude by at least 50% compared to the mean minute ventilation of preceding validated respiratory cycles). It does not permit the detection of respiratory effort–related arousals, and it does not distinguish central from obstructive respiratory events. The total number of detected events per hour of the estimated sleep is automatically computed by pacemaker and corresponds to the RDI-PM.

A respiratory disturbance index (RDI) was calculated every night and reported since the last follow-up (up to the last six months). Fig. 1 shows 24-h RDI-PM on-screen together with the time spent in AF.

All patients were followed up at the outpatient clinic with visits at 1, 6, and 12 months after implantation. At each visit, the patient's demographic and anthropometric data, smoking status, cardiovascular symptoms, and symptoms suggesting OSAS, such as snoring, witnessed sleep apnea, restless sleep, and excessive daytime sleepiness, were obtained. Between one and six months of follow-up, all patients underwent nocturnal PSG, regardless of the suspicious OSAS. The PSG included measurements from the electroencephalogram, chin electromyogram, electrocardiogram, electro-oculogram, pulse oximetry, nasal pressure, and thoracic and abdominal movements (measured by respiratory inductance plethysmography). The reading of the PSG was performed by a skilled sleep technician, according to American Academy of Sleep Medicine (AASM) scoring rules [19]. The RDI of the PSG was defined as the number of abnormal respiratory events per hour of sleep, including obstructive apneas and hypopneas (excluding central hypopneas/apneas) and respiratory effort–related arousals. The scoring of hypopneas was made using the criteria of a $\geq$30% drop in the nasal pressure excursion for 10 s or greater associated with $\geq$3% oxygen desaturation or an arousal. Diagnosis of OSAS was based on AASM criteria, requiring an RDI-PSG of $\geq$5 events per hour. Excessive daytime sleepiness was defined by a score of >10 on the Epworth Sleepiness Scale.

By interrogating the device, RDI-PM was determined on the night when PSG was performed. Average RDI-PM in the month prior to PSG was also calculated. The occurrence of episodes of AF was determined by the occurrence of switching mode; its total duration (AF burden) and time from implantation to first AF episode were also determined.

Statistical analysis was performed using SPSS software version 21 (SPSS Inc., Chicago, IL). The descriptive results are presented as absolute and relative frequencies, median and range. The χ^2 and Mann–Whitney *U* test were used to compare groups. The correlation of two continuous variables was assessed using linear regression and expressed by the Pearson correlation coefficient. The receiver operating characteristic (ROC) curve and the analysis of the area under the curve and the C statistic were used to determine the diagnostic value of the RDI-PM and to calculate the threshold value of the RDI-PM diagnostic predictor of OSAS in the different subgroups of patients, including those with and without AF. It was also compared to AF burden between patients with and without OSAS using the different diagnostic criteria. Statistical significance was considered for p values <0.05.

Local ethics committee approved the study protocol, which complied with the principles enunciated in the Declaration of Helsinki. Informed consent was obtained from all subjects enrolled in this study.

3. Results

A total of 81 patients were included in this study, with a mean age of 73 ± 11 years. The indication for PM implantation or replacement was atrioventricular node disease in 58% of cases and

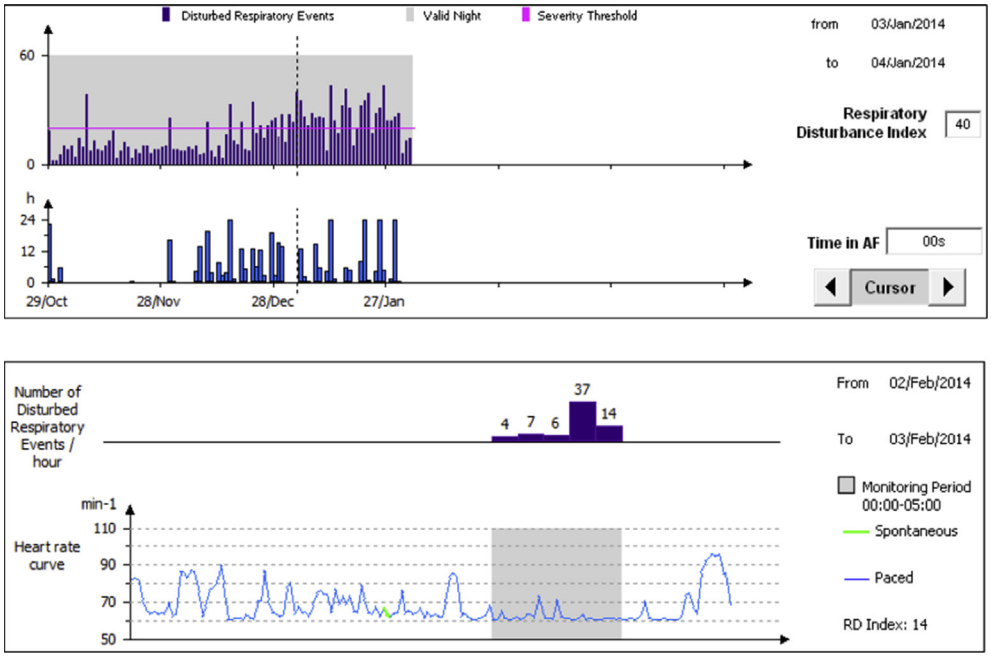

Fig. 1. Representation of the RDI-PM, time in AF, number of respiratory events/hour by the programmer during interrogation of the PM. AF, atrial fibrillation; PM, pacemaker; RDI, respiratory disturbance index.

sinus node disease in the remaining cases. The characteristics of the population are presented in Table 1.

Diagnosis of OSAS based on AASM criteria was established in 62% of patients (40% mild, 30% moderate, and 30% severe). None of the patients showed criteria to diagnose central sleep apnea, since all showed predominance of obstructive respiratory events.

Patients diagnosed with OSAS had significantly higher RDI-PM on the night of PSG, when compared with patients without OSAS (23.75 vs 12.05; $p < 0.001$). The same finding was observed for RDI-PM in the month prior to polysomnography (18.2 vs 11.8; $p = 0.004$) (Fig. 2) There was a significant correlation between RDI-PSG and RDI-PM ($R = 0.34$, $p = 0.004$).

RDI-PM had good diagnostic accuracy for identifying a diagnosis of OSAS (AUC: 0.767 [95% CI: 0.65–0.88]; $p < 0.001$). The ideal diagnostic RDI-PM cut-off was 13.3, which had a sensitivity of 78%, specificity of 78%, positive predictive value (PV) of 85.37%, negative PV of 67.74%, and overall diagnostic accuracy of 78% (comparable to the overall diagnostic precision of 79% with the commonly used cut-off) (Fig. 3). Based on this value, a diagnosis of OSAS was determined in 57% of patients. The same cut-off value of 13.3 showed a sensitivity of 90% for the diagnosis of moderate-to-severe OSAS, with a specificity of 63%, a negative PV of 90%, and a positive PV of 63% (Fig. 3).

The AF burden was evaluated after one year of follow-up, and the sensitivity and specificity of the RDI-PM for the diagnosis of OSAS were determined in the subgroups of patients with and without AF. Unexpectedly, the time to development of AF was not significantly different between patients with the diagnosis of OSAS

Table 1
Characteristics of the study population.

	Total (N = 81) % (n)	OSAS (N = 50) % (nP)	No OSAS (N = 31) % (n)	*p*
Age (mean ± SD)	73 ± 11	74 ± 8.7	71 ± 14	0.18
Sex				
Female	42% (34)	38% (19)	48% (15)	0.36
Male	58% (47)	62% (31)	52% (16)	0.36
Indication for PM implantation				
Sinus node disease	42% (33)	38% (18)	48% (15)	0.34
Atrioventricular node disease	58% (46)	62,5% (30)	52% (16)	0.34
Comorbidities				
Arterial hypertension	74% (31)	82% (41)	60% (19)	0.13
Diabetes mellitus	14% (6)	14% (7)	13% (4)	0.90
Smoking	18% (15)	20% (10)	16% (5)	0.67
Obesity (BMI > 30 kg/m^2)	22% (17)	28% (14)	10% (3)	0.23
Atrial fibrillation during follow-up	44% (36)	42% (21)	48% (15)	0.58
symptoms				
Excessive daytime sleepiness (ESS score >10)	11% (9)	14% (7)	6.5% (2)	0.31
Snoring	58% (47)	68% (34)	42% (13)	0.14
Witnessed sleep apnea	20% (16)	20% (10)	19% (6)	0.45
Restless sleep	30% (24)	28% (14)	32% (10)	0.74

Data are % (n) unless otherwise indicated.
BMI, body mass index; ESS, Epworth Sleepiness Scale; PM, pacemaker; SD, standard deviation; OSAS, obstructive sleep apnea syndrome.

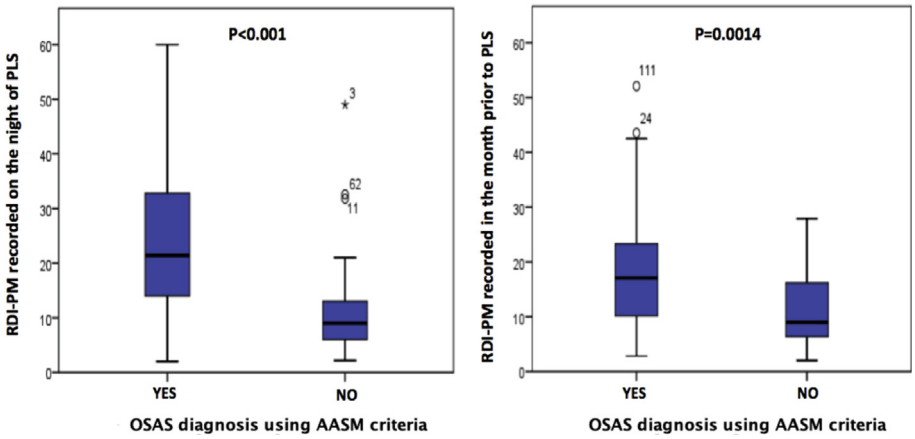

Fig. 2. RDI-PM in patients with (YES) and without (NO) diagnosis of OSAS, according to AASM criteria, on the night of polysomnography (left) and in the preceding month (right). AASM, American Academy of Sleep Medicine; OSAS, obstructive sleep apnea syndrome; PLS, polysomnography; RDI-PM, respiratory distress index determined by pacemaker.

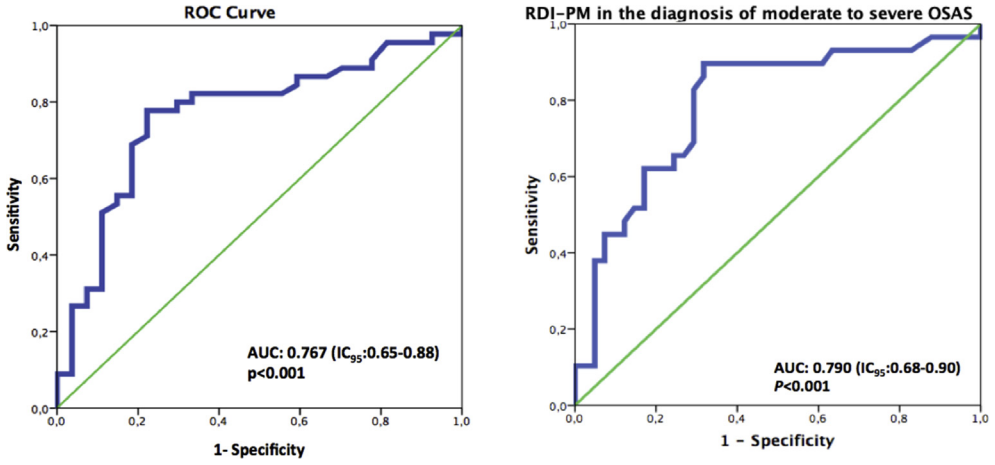

Fig. 3. Receiver operating characteristic (ROC) curve for RDI-PM in the diagnosis of OSAS. The threshold value of 13.3 showed better sensitivity, specificity, and diagnostic accuracy. The same cut-off value of 13.3 showed higher sensitivity in the diagnosis of moderate-to-severe OSAS. OSAS, obstructive sleep apnea syndrome; RDI-PM, respiratory distress index determined by pacemaker.

using AASM criteria and RDI-PM. Furthermore, patients diagnosed with OSAS using the AASM criteria did not present with a significantly higher total AF burden than those without OSAS (219 vs 381 min, $p = 0.447$). However, in those whose OSAS diagnosis was based on RDI-PM (cut-off $\geq$13.3), there was a greater burden of AF (488 vs 83 min, $p = 0.05$) (Table 2). Also, mean monthly RDI-PM, but not RDI-PSG, correlated significantly with time in AF ($\rho = 0.3$, $p = 0.014$).

In patients with AF, the RDI-PM cut-off of 13.3 determined as optimal in the general population for the diagnosis of OSAS had similar sensitivity (79%), but decreased specificity (57%). In patients without AF, the RDI-PM cut-off of 13.3 had a specificity of 100% for the diagnosis of OSAS and a sensitivity that was almost the same as that of the general population (77%) (Fig. 4). Interpreting the results, it becomes clear that the presence of AF decreases the specificity of RDI-PM for the diagnosis of OSAS.

4. Discussion

As previously described, OSAS has a high prevalence in the general population, especially in patients with rhythm disturbances and PM. In fact, in this study, nearly two-thirds of patients included (62%) were diagnosed with OSAS during follow-up. This elevated

Table 2
Presence of AF, total time in AF after 1 year of follow-up and time to development of AF according to the presence (Yes) or absence (No) of a diagnosis of OSAS using AASM criteria and RDI-PM $\geq$13.3.

	Diagnosis of OSAS using AASM criteria				*p*
	Yes			No	
Presence of AF (no. of patients)	21			15	0.580
Total time in AF (min)	219			381	0.447
Time to development of AF (days)	272			244	0.791
	Mild	Moderate	Severe	NO	
Presence of AF	7	6	8	15	0.812
Total time in AF (min)	140	401	281	381	0.425
Time to development of AF (days)	349	187	281	244	0.832
	Diagnosis of OSAS using RDI-PM $\geq$ 13.3				*p*
	Yes			No	
Presence of AF (no. of patients)	21			12	0.344
Total time in AF (min)	488			83	0.050
Time to development of AF (days)	263			308	0.670

AASM, American Academy of Sleep Medicine; AF, atrial fibrillation; OSAS, obstructive sleep apnea syndrome; RDI-PM, respiratory distress index determined by pacemaker.

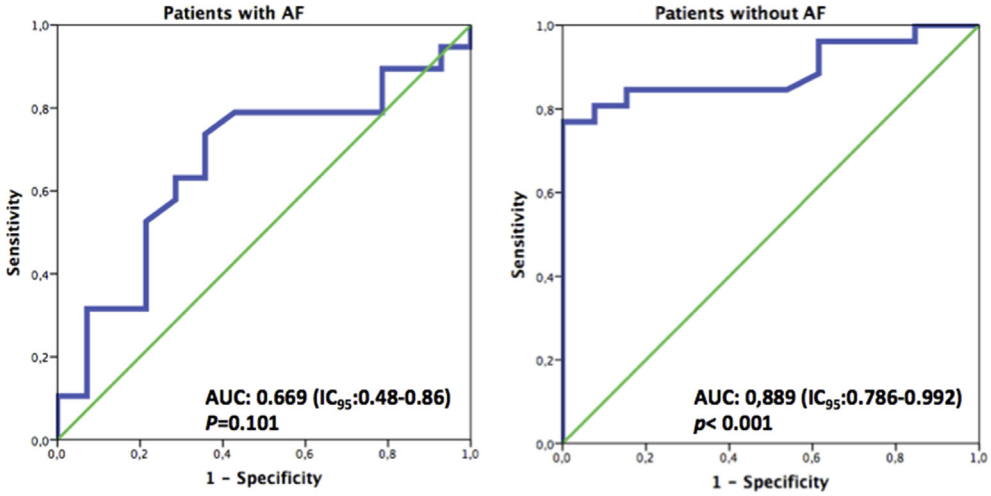

Fig. 4. Receiver operating characteristic (ROC) curve for RDI-PM in the diagnosis of OSAS, using AASM criteria, in patients with AF (left) and in patients without AF (right). The presence of AF decreases the specificity of RDI-PM in the diagnosis of OSAS. AASM, American Academy of Sleep Medicine; AF, atrial fibrillation; OSAS, obstructive sleep apnea syndrome; RDI-PM, respiratory distress index determined by pacemaker.

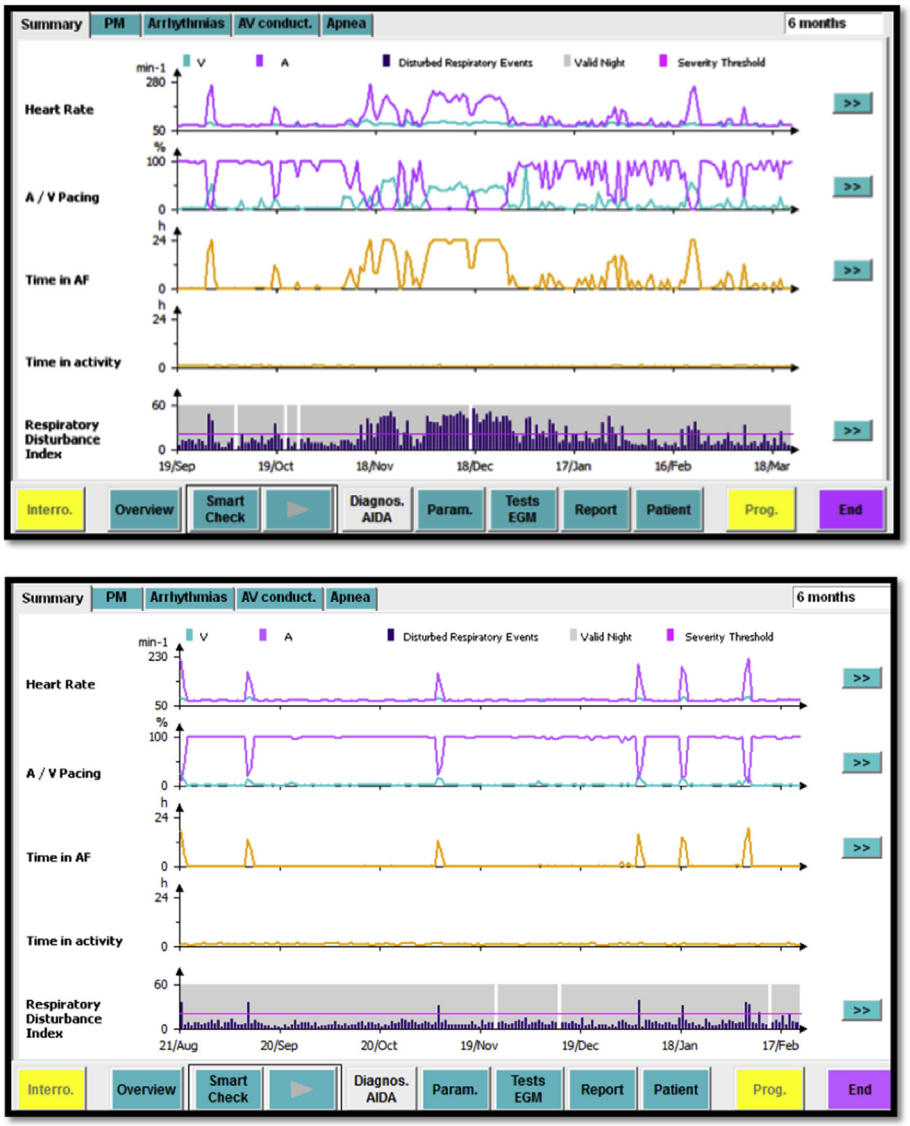

Fig. 5. Two examples of individual patient PM interrogations showing changes in RDI-PM alongside changes in AF occurrence and changes in heart rate. AF, atrial fibrillation; PM, pacemaker; RDI-PM, respiratory distress index determined by pacemaker.

percentage alerts us to the underdiagnosis of this condition, which is mostly related to the undervaluing of its symptoms and to the logistical difficulties of accessing diagnosis with the standard method, polysomnography.

The incorporation of a respiratory monitoring algorithm in pacemakers is especially relevant, considering the high prevalence of this comorbidity. The main advantage seems to be the possibility of prolonged monitoring, allowing an increase in the detection period of respiratory sleep disorders versus polysomnography. The validation of this algorithm was previously performed by the manufacturer in the clinical trial DREAM [20]. This study, like ours, included unselected patients with an indication for pacemaker implantation; RDI obtained with pacemakers correlated with the RDI and apnea hypopnea index obtained with PSG. A total of 40 patients were initially enrolled, but only 31 were included in the final analysis due to patient withdrawal from participation. This study demonstrated that an RDI-PM cut-off of $\geq$20 had good specificity (85%) and sensitivity (89%) for detecting severe sleep apnea. The utility of this algorithm was also demonstrated by Dias et al. [21], from our center, following the same methodology (study population, n = 54 patients), finding a best cut-off value of RDI-PM of 13 for the detection of moderate to severe sleep apnea, with a sensitivity of 100% and a specificity of 70%, affirming its utility as a promising screening tool.

In the present study, new-generation PMs incorporating this respiratory monitoring algorithm demonstrated good diagnostic accuracy for OSAS, enabling its screening and early detection in at-risk patients and thus their referral for definitive diagnosis and adequate therapy. This tool seems to be particularly useful because it is highly sensitive in detecting moderate-to-severe OSAS. Because it is also a test with a high negative predictive value, it allows the exclusion of severe OSAS in patients with lower values in favor of more rigorous follow-up in patients with higher values, pointing them toward expert evaluation for a definite diagnosis using standard criteria.

However, this study also showed something not previously described, which is that the occurrence of AF, a frequent comorbidity in OSAS patients, seems to unfavorably alter the diagnostic value of RDI-PM. Although the total time in AF did not differ between patients with a formal diagnosis of OSAS versus patients without OSAS, it was significantly higher in patients with higher RDI-PM values. Thus, the value of RDI-PM seems to change with the occurrence of AF, regardless of whether or not OSAS is present. In the ROC curve analysis, the presence of AF altered the specificity of RDI-PM in the diagnosis of OSAS, with specificity of 100% in patients without AF, but only 57% in patients with AF.

Indeed, when interrogating the PMs of individual patients, it was possible to detect this interaction, as shown in the two examples presented in Fig. 5. It shows changes in RDI-PM in parallel with changes in AF occurrence and heart rate. The mechanism is unknown, but can occur due to variations in transthoracic impedance signal associated with AF.

Despite being one of the largest studies to assess the performance of new-generation pacemakers for the diagnosis of OSAS and being the first evaluating its interaction with AF, it is a relatively small single-center study, and the results must be interpreted with caution. One of the limitations of this study is the fact that PSG-detected respiratory events were not compared side-by-side with pacemaker-detected respiratory events, but only through RDI comparison. As the respiratory index is not exactly obtained with the same scored method, it may not reflect the same level of respiratory disturbance.

As previously noted, one unexpected finding of our study was the absence of a significant difference in AF burden between patients diagnosed with OSAS (using the AASM criteria) and patients without OSAS; it is possible that the relatively small sample size may be insufficient to demonstrate that association. However, it is clear that the presence of AF altered the specificity of RDI-PM in the diagnosis of OSAS. One possible explanation for this interaction may be a previously hypothesized association between AF and central apneas/hypopneas [22]. Since pacemaker SAM algorithm does not discriminate between obstructive and central apneas (in both situations there is a change in the variation of the transthoracic impedance), an increase in central apneas that may be a consequence or trigger of AF and can modify the value of RDI-PM. It seems essential to clarify this interaction in further studies, so that we can clearly understand this effect and use it in our advantage, maximizing the utility of this promising screening and diagnostic method.

Conflict of interest

The authors have no conflicts of interest to declare.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2019.01.051.

References

[1] Lee W, Nagubadi S, Kryger MH, et al. Epidemiology of obstructive sleep apnea: a population-based perspective. Expert Rev Respir Med 2008;2:349–64.
[2] Heinzer R, Vat S, Marques-Vidal P, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med 2015;3:310–8.
[3] Jun J, Polotsky VY. Sleep disordered breathing and metabolic effects: evidence from animal models. Sleep Med Clin 2007;2:263–77.
[4] Epstein LJ, Kristo D, Strollo Jr PJ, et al. Clinical guideline for evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 2009;5:263–76.
[5] Bradley TD, Floras JS. Obstructive sleep apnea and its cardiovascular consequences. Lancet 2009;373:82–93.
[6] Mehra R, Benjamin EJ, Shahar E, et al. Association of nocturnal arrhythmias with sleep-disordered breathing: the sleep heart health study. Am J Respir Crit Care Med 2006;173:910–6.
[7] Padeletti M, Zacà V, Mondillo S, et al. Sleep-disordered breathing increases the risk of arrhythmias. J Cardiovasc Med (Hagerstown) 2014;15:411–6.
[8] Gottlieb DJ, Yenokyan G, Newman AB, et al. A prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure: the Sleep Heart Health Study. Circulation 2010;122:352–60.
[9] McEvoy RD. Obstructive sleep apnea and hypertension: the ESADA study. Eur Respir J 2014;44:835–8.
[10] Lin GM, Colangelo LA, Lloyd-Jones DM, et al. Association of sleep apnea and snoring with incident atrial fibrillation in the multi-ethnic study of atherosclerosis. Am J Epidemiol 2015;182:49–57.
[11] Hohl M, Linz B, Böhm M, et al. Obstructive sleep apnea and atrial arrhythmogenesis. Curr Cardiol Rev 2014;10:362–8.
[12] Monahan K, Brewster J, Wang L, et al. Relation of the severity of obstructive sleep apnea in response to anti-arrhythmic drugs in patients with atrial fibrillation or atrial flutter. Am J Cardiol 2012;110:369–72.
[13] Naruse Y, Tada H, Satoh M, et al. Concomitant obstructive sleep apnea increases the recurrence of atrial fibrillation following radiofrequency catheter ablation of atrial fibrillation: clinical impact of continuous positive airway pressure therapy. Heart Rhythm 2013;10:331–7.
[14] Ng CY, Liu T, Shehata M, et al. Meta-analysis of obstructive sleep apnea as predictor of atrial fibrillation recurrence after catheter ablation. Am J Cardiol 2011;108:47–51.
[15] Kanagala R, Murali NS, Friedman PA, et al. Obstructive sleep apnea and the recurrence of atrial fibrillation. Circulation 2003;107:2589–94.
[16] Garrigue S, Pépin JL, Defaye P, et al. High prevalence of sleep apnea syndrome in patients with long-term pacing: the European Multicenter Polysomnographic Study. Circulation 2007;115:1703–9.
[17] Sreedharan SE, Agrawal P, Rajith RS, et al. Clinical and polysomnographic predictors of severe obstructive sleep apnea in the South Indian population. Ann Indian Acad Neurol 2016;19:216–20.
[18] Duru F, Cho Y, Wilkoff BL, et al. Rate responsive pacing using transthoracic impedance minute ventilation sensors: a multicenter study on calibration stability. Pacing Clin Electrophysiol 2002;25:1679–84.
[19] Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions task force of the American Academy of sleep medicine. J Clin Sleep Med 2012;8:597–619.

[20] Defaye P, de la Cruz I, Martí-Almor J, et al. A pacemaker transthoracic impedance sensor with an advanced algorithm to identify severe sleep apnea: the DREAM European study. Heart Rhythm 2014;11:842–8.
[21] Dias M, Gonçalves I, Amann B, et al. Utility of new-generation pacemakers in sleep apnea screening. Sleep Med 2017;37:27–31.
[22] Strotmann J, Fox H, Bitter T, et al. Characteristics of sleep-disordered breathing in patients with atrial fibrillation and preserved left ventricular ejection fraction. Clin Res Cardiol 2018;107:120–9.