



UNIVERSITÀ
DEGLI STUDI
FIRENZE

FLORE

Repository istituzionale dell'Università degli Studi di Firenze

Sleep Disordered Breathing and Arrhythmia Burden in Pacemaker Recipients

Questa è la Versione finale referata (Post print/Accepted manuscript) della seguente pubblicazione:

Original Citation:

Sleep Disordered Breathing and Arrhythmia Burden in Pacemaker Recipients / MARGHERITA PADELETTI;SIMONE VIGNINI;GIUSEPPE RICCIARDI;PAOLO PIERAGNOLI;VALERIO ZACÀ;MICHELE EMDIN;STEFANO FUMAGALLI;SANJA JELIC. - In: PACING AND CLINICAL ELECTROPHYSIOLOGY. - ISSN 0147-8389. - STAMPA. - 33:(2010), pp. 1462-1466. [10.1111/j.1540-8159.2010.02881.x]

Availability:

This version is available at: 2158/771349 since: 2020-05-15T08:24:18Z

Published version:

DOI: 10.1111/j.1540-8159.2010.02881.x

Terms of use:

Open Access

La pubblicazione è resa disponibile sotto le norme e i termini della licenza di deposito, secondo quanto stabilito dalla Policy per l'accesso aperto dell'Università degli Studi di Firenze (<https://www.sba.unifi.it/upload/policy-oa-2016-1.pdf>)

Publisher copyright claim:

(Article begins on next page)

Sleep Disordered Breathing and Arrhythmia Burden in Pacemaker Recipients

MARGHERITA PADELETTI, M.D.,* SIMONE VIGNINI, M.D.,† GIUSEPPE RICCIARDI, M.D.,† PAOLO PIERAGNOLI, M.D.,† VALERIO ZACÀ, M.D.,* MICHELE EMDIN, M.D.,‡ STEFANO FUMAGALLI, M.D.,§ and SANJA JELIC, M.D.¶

From the *Department of Cardiovascular Diseases, University of Siena, Siena, Italy; †Postgraduate School of Cardiology, University of Florence, Florence, Italy; ‡Cardiovascular Medicine Department, G. Monasterio Foundation, CNR, Pisa, Italy; §Department of Critical Care Medicine and Surgery, Unit of Gerontology and Geriatrics, University of Florence, Florence, Italy, and ¶Columbia University College of Physicians and Surgeons, Division of Pulmonary, Allergy, and Critical Care Medicine, New York, New York

Background: Sleep disordered breathing (SDB), a common condition among patients with permanent pacemaker (PM), is associated with greater incidence of cardiac arrhythmias. Scarce availability of sleep laboratories and the high costs of nocturnal-attended polysomnography limit the routine screening of patients with PM for SDB. We investigated whether a novel PM that utilizes variations in transthoracic impedance to record the fluctuations in breathing pattern and minute ventilation could be used to screen patients for SDB.

Methods: Twenty patients who underwent dual-chamber PM implantation were studied. The Talent 3 DR PM (SORIN Group Italy S.r.l., Milan, Italy) calculates apnea-hypopnea index (AHI) by computing minute ventilation signal derived from transthoracic impedance measurements. Within a month after PM implantation, an in-home respiratory monitoring was performed to evaluate the accuracy of PM-derived AHI. Patients were followed for mean \pm standard deviation, 487 ± 166 days. The PM was checked at each follow-up visit to retrieve the information about recurrent arrhythmias.

Results: Eleven patients were diagnosed with SDB by an in-home respiratory monitoring. An AHI derived from an in-home respiratory monitoring was similar to pacemaker-derived AHI (27 ± 14 vs 16 ± 13 events/hour, $P = 0.15$). The cumulative incidence of cardiac arrhythmias, including atrial fibrillation, extrasystolic beats, sustained and nonsustained ventricular tachycardia, and supraventricular tachycardia was similar in patients with and without SDB.

Conclusion: SDB is highly prevalent in patients with permanent pacemaker. Screening for SDB with Talent 3 DR PM may facilitate diagnosis and treatment of SDB. (PACE 2010; 33:1462–1466)

electrophysiologist—clinical, pacing, new technology

Introduction

The majority of patients with implanted permanent pacemaker (PM) suffer from unrecognized sleep disordered breathing (SDB).¹ Untreated obstructive sleep apnea (OSA), the most common sleep disorder that affect patients with permanent PM, is strongly and independently associated with increased risk for coronary artery disease, stroke, heart failure, and increased mortality.² Untreated SDB increases risk for cardiac arrhythmias. Prevalence of atrial fibrillation (AF), nonsustained

ventricular tachycardia, and complex ventricular ectopy (nonsustained ventricular tachycardia, bigeminy, trigeminy, or quadrigeminy) is greater in patients with SDB compared with controls matched for age, gender, adiposity, and cardiovascular comorbidities.³ Repetitive episodes of hypoxia/reoxygenation during transient cessation of breathing followed by hypertensive and sympathetic surges associated with arousals from sleep in SDB may underlie increased risk for arrhythmias and nocturnal sudden cardiac death in patients with untreated SDB.⁴ Treatment of SDB with continuous positive airway pressure (CPAP) is associated with a significant reduction in arrhythmia recurrence.⁵

Nocturnal-attended polysomnography is the gold standard for the diagnosis of SDB.⁶ However, the limited availability of sleep laboratories and the high costs of nocturnal-attended polysomnography render the routine screening of patients with permanent PM for SDB impractical. The challenge of establishing the diagnosis of SDB in the elderly, who comprise the majority of patients with

Sources of funding: none declared.

Conflicts of interest: none declared.

Address for reprints: Margherita Padeletti, M.D., Università degli Studi di Siena, Dipartimento di Cardiologia, Ospedale Le Scotte, Viale Bracci 16, 53100, Siena, Italy. Fax: +39 0577 585331; e-mail: marghepadeletti@yahoo.com

Received April 7, 2010; revised June 8, 2010; accepted June 20, 2010.

doi: 10.1111/j.1540-8159.2010.02881.x

permanent PM, is further compounded by barriers to optimal health care that are specific for this age group and reluctance of healthcare providers to pursue the diagnosis of additional co-morbidity in elderly patients.⁷ More practical alternatives to nocturnal-attended polysomnography, such as in-home cardio-respiratory monitoring, may allow for the diagnosis of SDB in the elderly who cannot easily access formal polysomnography. Simplified in-home cardio-respiratory monitoring devices have been recently approved and validated for the diagnosis of SDB.⁸

Accordingly, we investigated whether a novel PM that utilizes variations in transthoracic impedance to record the fluctuations in breathing pattern and minute ventilation could be used to screen elderly patients for SDB, and whether recurrence of arrhythmias was greater in elderly patients with permanent PM and co-existent SDB than in those free of SDB.

Methods

Study Patients

Twenty patients aged ≥ 65 years who underwent implantation of a Talent 3 DR PM (ELA Medical—SORIN Group, Milan, Italy) were enrolled in the study. The indications for permanent pacing were second and third atrioventricular blockade, sinus node dysfunction, and bradycardia. Exclusion criteria included the presence of heart failure, malignancy, chronic renal and pulmonary diseases, and previously diagnosed SDB. All patients underwent screening for SDB within 1 month after PM implantation. All patients returned for follow-up visit every 3 months. All subjects signed informed consent as approved by the institutional review board.

Pacemaker

The Talent 3 DR PM calculates apnea-hypopnea index (AHI) by computing minute ventilation signal derived from trans-thoracic impedance measurements. Changes in amplitude to period ratio of the respiratory cycle provide basis for measurement of transthoracic impedance. The Talent 3 DR PM discriminates between resting and activity state by comparing minute ventilation (MV) at a single time point with a self-adapted "minute ventilation resting daily threshold." An index of MV is calculated by averaging the ratio of amplitude/period over a number of respiratory cycles. The PM sensor detected a 39% decrease in MV during nocturnal sleep/rest compared with daytime activity.⁹ The PM was interrogated at each follow-up visit to retrieve the information about recurrent arrhythmias. This includes the total number of atrial and ventricular ectopic events

(% of total cardiac cycles), and the presence of nonsustained and sustained atrial and ventricular tachycardia, and episodes of paroxysmal AF. During episodes of paroxysmal AF, the device was programmed to switch from an atrioventricular (AV)-association pacing mode (DDD) to an AV-dissociation mode to prevent prolonged fast-rate ventricular pacing.

Screening for SDB

An in-home respiratory monitoring allows for unattended screening for SDB. Nasal and oral airflow (termistor), chest wall impedance, arterial oxyhemoglobin saturation (SaO₂), snoring, and body position are simultaneously acquired during sleep. The data were analyzed in the morning following the sleep study. Respiratory events (apneas and hypopneas) were scored according to the standard guidelines.¹⁰ An obstructive apnea was defined as a cessation of airflow in association with continued respiratory effort for ≥ 10 seconds. An obstructive hypopnea was defined as a discrete reduction in airflow associated with a decrease in SaO₂ of $\geq 4\%$ for ≥ 10 seconds in the presence of thoracoabdominal ventilatory efforts. Cessation of respiratory effort in association with the absence of airflow was scored as central apnea. AHI was defined as the number of obstructive apnea plus hypopnea episodes per hour of sleep. All study participants had at least 8 ± 1.5 hours of in-home sleep recording. SDB was defined as AHI > 10 events/hour.

Statistical Analysis

Continuous variables are expressed as mean \pm standard deviation (SD). Categorical variables are expressed as percentages. The Student *t*-test and chi-square test with application of the McNemar test were used for data comparisons as appropriate. The relationship between sleep parameters acquired by PM and in-home respiratory monitoring was assessed using the Pearson correlation coefficient. A two-tailed *P* value < 0.05 was considered to indicate a statistically significant difference. Analysis was performed with SPSS for Windows (version 15; SPSS, Inc., Chicago, IL, USA).

Results

Patients' demographic and clinical characteristics are shown in Table I. All patients were in stable clinical conditions at the time of permanent PM implantation. The follow-up data were available for all patients (duration of follow-up was mean \pm SD, 487 ± 166 days). Eleven (55%) patients had SDB diagnosed by in-home respiratory monitoring. Indications for the PM implantations were similar in patients with SDB

Table I.
Demographics of the SDB and non SDB Patients Studied

Patients n = 20	SDB (n = 11)	Non SDB (n = 9)	P
Gender (M)	8	7	0.769
Age (years)	78.8 ± 8.0	77.1 ± 10.5	0.693
BMI (Kg/m ²)	26.8 ± 4.8	24.1 ± 2.8	0.141
Berlin positive	5	4	0.202
Comorbidity			
Hypertension	7	8	0.319
CAD	3	5	0.362
Diabetes Mellitus	2	2	0.769
Indication to PM implantation			
AV blockade (II-III degree)	4	1	
Synus dysfunction (sick sinus syndrome, brady tachy)	2	7	
Other (bradycardia, vasovagal syndrome)	5	1	
Therapy			
ACE-I	5	6	0.406
Beta-blockers	3	3	0.769
Diuretics	3	3	0.769
Ejection fraction ≥50%	11	7	0.189
Sleep parameters diagnosed with in-home respiratory monitoring			
AHI events/hour	27.2 ± 14.1	5.9 ± 2.0	0.001
Obstructive events/hour	8.0 ± 7.1	1.9 ± 1.2	0.018
Central events/hour	0.3 ± 0.4	0.1 ± 0.2	0.326
Mixed apnea events/hour	0.5 ± 0.5	0.2 ± 0.4	0.13
Hypopnea events/hour	18.4 ± 8.2	3.7 ± 2.1	>0.001
Desaturation mean (%)	91.2 ± 0.9	92.8 ± 1.3	0.007

BMI = body mass index; SDB = sleep disordered breathing; CAD = coronary artery disease; ACE-I = Angiotensin converting enzyme inhibitors; AV = atrio-ventricular; AHI = apnea-hypopnea index.

and those free of SDB. Patients with SDB and those free of SDB were similar for age, gender, body mass index (BMI), and comorbidities (Table I). Obstructive events comprised the vast majority of all respiratory events during sleep (Table I).

No difference was found between the in-home respiratory monitoring-derived AHI and the PM-derived AHI (27 ± 14 events/hour vs 16 ± 13 events/hour, P = 0.15). During the follow-up, all runs of tachycardia were paroxysmal and asymptomatic (Table II). The cumulative incidence of AF and the other arrhythmic events (i.e., number of extrasystolic beats, number and length of sustained and nonsustained ventricular and supraventricular tachycardia) was similar in patients with and without SDB (Table II).

Discussion

The present data indicate that a novel PM that utilizes variations in transthoracic impedance to record the fluctuations in breathing pattern can be used to screen elderly patients for SDB, and that recurrence of arrhythmias tends to be similar in elderly patients with permanent PM and untreated SDB and in those free of SDB. In addition, our findings are in agreement with previous reports that SDB is highly prevalent in patients with permanent PM.^{1,2}

Cardiac arrhythmias are more frequent in patients with SDB and severity of arrhythmias correlates with severity of SDB.¹¹ AF is the most commonly sustained cardiac arrhythmia. The growing obesity epidemic combined with

Table II.

Long-term Comparison of Cumulative Incidence of Arrhythmias in Patients with SDB and Patients free of SDB

	SDB patients	Non SDB patients	P
AHI (events/hour)	16 ± 13	15 ± 11	NS
Run SV ≥ 5 seconds (n)	271.3 ± 619.6	408.3 ± 875.9	0.698
Run V ≥ 5 seconds (n)	180.5 ± 327.8	101.7 ± 194.9	0.534
Ventricular couple (n)	7183.7 ± 11903.1	1588 ± 2233.5	0.183
Extrasystolic beats (n)	81241 ± 89994.6	155694.4 ± 256004.2	0.426
Paroxysmal AF (n)	15.5 ± 50.3	7.2 ± 20	0.629
Duration of paroxysmal AF (minutes)	354 ± 1173.1	1253 ± 3760	0.507

SDB = Sleep disordered breathing; AHI = Apnea-Hypopnea Index; V = Ventricular; SV = Supraventricular; AF = Atrial fibrillation.

ageing population and frequently unrecognized and, thus, untreated SDB portends an increased incidence of AF.¹² In a retrospective cohort study of 3,542 adults without history of AF, sleep apnea, in addition to obesity, male gender, and the presence of coronary artery disease, was reported as an independent risk factor for AF in subjects aged 65 years or less but not in those older than 65 years.³ The risk for developing AF correlates with severity of nocturnal oxyhemoglobin desaturations in OSA patients. The risk for recurrence of AF in the first year following direct current cardioversion is reduced by 50% in OSA patients who adhere to CPAP therapy.³ Our patients were older than 65 years and had a relatively low incidence of AF. The frequency and duration of paroxysmal AF was similar in elderly patients with and without SDB. Similarly, the incidence of ventricular arrhythmias, including isolated beats, coupled beats, and runs of five or more beats, was not different in SDB patients compared with patients free of SDB. In addition to age ≥ 65 years, the exclusion of obesity and chronic heart failure may

have contributed to similar incidence of AF and ventricular arrhythmias in our study patients.^{3,11}

The frequency and duration of paroxysmal AF events was similar in patients with and without SDB that is in agreement with previous reports in a larger population of patients with permanent PM.¹³ A low prevalence of overall arrhythmic events similar to that observed in our study has been reported previously in a larger cohort of patients aged >65 years with SDB.¹⁴

Similar to previous studies, the PM AHI did not correlate with the in-home respiratory monitoring AHI, probably because the sensitivity and the specificity of the PM algorithm are high and allow a diagnosis when the condition is severe, with corresponding polysomnographic values of AHIs ≥30 events/hour.⁹

In conclusion, SDB is highly prevalent in patients with permanent PM. Screening for SDB with novel PM may facilitate diagnosis and treatment of SDB in elderly patients. Prompt treatment with CPAP may alleviate cardiovascular complications associated with SDB.

References

- Garrigue S, Pépin JL, Defaye P, Murgatroyd F, Poezevara Y, Clémenty J, Lévy P. High prevalence of sleep apnea syndrome in patients with long-term pacing: The european multicenter polysomnographic study. *Circulation* 2007; 115:1703–1709.
- Somers VK, White DP, Amin R, Abraham WT, Costa F, Culebras A, Daniels S, et al. Sleep Apnea and Cardiovascular Disease. An American Heart Association/American College of Cardiology Foundation Scientific Statement From the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council on Cardiovascular Nursing Council. *Circulation* 2008; 118:1080–1111.
- Mehra R, Benjamin EJ, Shahar E, Gottlieb DJ, Nawabit R, Kirchner HL, Sahadevan J, et al. Association of nocturnal arrhythmias with sleep-disordered breathing: The Sleep Heart Health Study. *Am J Respir Crit Care Med* 2006; 173:910–916.
- Gami AS, Howard DE, Olson EJ, Somers VK. Day-night pattern of sudden death in obstructive sleep apnea. *N Engl J Med* 2005; 352:1206–1214.
- Kanagala R, Murali NS, Friedman PA, Ammash NM, Gersh BJ, Ballman KV, Shamsuzzaman AS, et al. Obstructive sleep apnea and the recurrence of atrial fibrillation. *Circulation* 2003; 107:2589–2594.
- AASM Task Force. Sleep-related breathing disorders in adults: Recommendations for syndrome definition and measurement techniques in clinical research. *Sleep* 1999; 22:667–689.
- Maciejewski ML, Perkins M, Li YF, Chapko M, Fortney JC, Liu CF. Utilization and expenditures of veterans obtaining primary care in community clinics and VA medical centers: An observational cohort study. *BMC Health Serv Res* 2007; 7:56.
- Levendowski D, Steward D, Woodson BT, Olmstead R, Popovic D, Westbrook P. The impact of obstructive sleep apnea variability measured in-lab versus in-home on sample size calculations. *Int Arch Med* 2009; 2:2.
- Defaye P, Pépin JL, Poezevara Y, Mabo P, Murgatroyd F, Lévy P, Garrigue S. Automatic recognition of abnormal respiratory events during sleep by a pacemaker transthoracic impedance sensor. *J Cardiovasc Electrophysiol* 2004; 15:1034–1040.

10. Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Bethesda, MD, National Institutes of Health; 1968, pp. 1–12.
11. Gami AS, Hodge DO, Herges RM, Olson EJ, Nykodym J, Kara T, Somers VK. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. *J Am Coll Cardiol* 2007; 49:565–571.
12. Fuster V, Rydén LE, Cannom DS, American College of Cardiology/American Heart Association Task Force on Practice Guidelines, European Society of Cardiology Committee for Practice Guidelines, European Heart Rhythm Association, Heart Rhythm Society. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): Developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation* 2006; 114:e257–e354.
13. Padeletti L, Gensini GF, Pieragnoli P, Ravazzi P, Diotallevi P, Baldi N, Russo V, et al. The risk profile for obstructive sleep apnea does not affect the recurrence of atrial fibrillation. *Pacing Clin Electrophysiol* 2006; 29:727–732.
14. Monahan K, Storfer-Isser A, Mehra R, Shahar E, Mittleman M, Rottman J, Punjabi N, et al. Triggering of nocturnal arrhythmias by sleep-disordered breathing events. *J Am Coll Cardiol* 2009; 54:1797–1804.