Cardiac Arrhythmias in Obstructive Sleep Apnea

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Summary: Obstructive sleep apnea syndrome (OSA) is associated with different types of cardiac arrhythmias. The original studies, concentrated mostly on nocturnal brady- and tachyarrhythmias. More recent studies documented high prevalence of atrial fibrillation (AF) and its association with obesity and other risk factors for AF. In addition, continuous positive airway pressure (CPAP) prevents recurrence of AF after cardioversion. In, OSA the highest risk for sudden death is at night in comparison to general population most of who die suddenly between six and noon. This observation suggests that hypoxia or other nocturnal abnormality, trigger sudden death. An important recent finding is the beneficial effect of CPAP on sudden death. The role of pacing in OSA remains controversial. In general, pacemaker therapy is not indicated in patients with nocturnal bradyarrhythmias. However, some authors recommend pacing in those with severe nocturnal bradyarrhythmias not tolerating or not responding to CPAP. According to a recent study, 59% of patients with permanent pacemaker have OSA.

Key words: obstructive sleep apnea syndrome – cardiac arrhythmias – atrial fibrillation – obesity – continuous positive airway pressure – nocturnal bradyarrhythmias

Srdeční arytmie při obstruktivní spánkové apnoe

Souhrn: Syndrom obstruktivní spánkové apnoe (OSA) je spojen s různými typy srdečních arytmií. Původní studie se většinou zaměřovaly na noční bradyarytmii a tachyarytmii. Novější studie dokumentují vysokou prevalenci atriální fibrilace (AF) a její souvislost s obezitou a dalšími rizikovými faktory AF. Kontinuální pozitivní přetlak v dýchacích cestách (CPAP) navíc zabraňuje recidivě AF po kardioverzi. Nejvyšší míra rizika náhlého úmrtí při OSA je v noci, na rozdíl od obecné populace, u které většina náhlých úmrtí nastává mezi šestou hodinou a polednem. Z tohoto zjištění lze usuzovat, že hypoxie a další noční abnormality mohou vyprovokovat náhlé úmrtí. Důležitým zjištěním z poslední doby je příznivý účinek, který má na náhlé úmrtí CPAP. Názory na roli kardiostimulace při OSA se nadále různí. Obecně vzato není kardiostimulace indikována u pacientů s noční bradyarytmií. Někteří autoři však doporučují kardiostimulaci u těch pacientů, kteří trpí závažnou noční bradyarytmií a netolerují nebo nereagují na CPAP. Podle studie z nedávné doby je u 59 % pacientů s permanentním kardiostimulátorem přítomna OSA.

Klíčová slova: syndrom obstruktivní spánkové apnoe – srdeční arytmie – atriální fibrilace – obezita – kontinuální pozitivní přetlak v dýchacích cestách – noční bradyarytmie

Introduction

Obstructive sleep apnea syndrome is a common clinical problem. In, middle aged overweight or obese patients its prevalence is 20% [1]. The relationship between OSA and cardiac arrhythmias is complex. Sleep apnea syndrome is frequently associated cardiovascular abnormalities, some of which could contribute to arrhythmias in OSA. On the other hand, prevention of arrhythmias with CPAP supports an association between OSA and cardiac arrhythmias [2,3]. The aim of this article is to review the incidence, and types of cardiac arrhythmias in OSA.

In 1983 Guilleminault et al [4] reported the prevalence of nocturnal cardiac arrhythmias. Subsequent studies [3,5–8] not only confirmed this original observation but also documented higher incidence of AF, sudden death and day time arrhythmias. An important and still controversial question is the role of pacing in bradyarrhythmias. Despite beneficial effect of CPAP, some authors nonetheless recommend pacing in patients with severe bradyarrhythmia not responding or not tolerating CPAP [9–12]. Among main pathophysiological mechanisms playing role in the pathogenesis of arrhythmias are hypoxia, hypercapnia, fluctuation of intrathoracis pressure, reoxygenation and arousal [2].

Nocturnal bradyarrhythmias

Sinus node suppression, different degrees of AV blocks and asystole occur in 5–10% of patients during apnea and hypopnea [3,9]. The main risk factors for nocturnal bradyarrhythmias are increased body mass index (BMI), average number of hypopnea and apnea per hour of sleep (AHI), degree of hypoxia and REM sleep [10]. Increased vagal tone and hypoxia, rather than structural abnormalities are the main triggers of nocturnal bradyarrhythmias [12]. The most effective therapy for nocturnal bradyarrhythmias is CPAP [11,12,14].

Nocturnal tachyarrhythmias

OSA is also associated with ventricular arrhythmias. Mehra et al [15] found that patients with AHI > 30/H have higher prevalence of ventricular premature beats and non-sustained ventricular tachycardia at night. According to

Koshino et al [16] sixty per cent of patients with ventricular arrhythmias and preserved left ventricular function have OSA. In addition, there was no difference in the frequency of ventricular arrhythmias during day and night. Fichter et al [17] evaluated the prevalence of sleep breathing disorder in 38 patients with internal cardioverter-defibrillator and impaired left ventricular function. Sixteen patients (42%) had sleep apnea syndrome with an AHI > 10/H. Central and obstructive sleep apnea syndrome were present in eight patients each. Patients with sleep breathing disorder had higher incidence of ventricular couplets and short runs of ventricular tachycardia mostly at night. Main limitations of these studies [15–17] are lack of comparison between day and nigh [15], few patients [16,17] and no comparison with controls [16,17]. The results of MADIT II sub-study is another indirect evidence of higher incidence of nocturnal life threatening ventricular arrhythmias [18]. Pietrasik et al [18] found that, obesity (BMI > 30%) was an independent risk for ventricular arrhythmias and that the first ICD appropriate therapy occurred at night [19]. Because of high prevalence of OSA in obese subjects, Arias and Sanchez [20] suggested sleep apnea syndrome as a possible cause of nocturnal ventricular arrhythmias.

Atrial fibrillation and OSA

AF is the most common sustained arrhythmias. The relation between OSA and AF is complex. The prevalence of nocturnal AF is 3–5% in OSA [4] and 20% in those with mild congestive heart failure and OSA [2]. Gami et al [2] studied the prevalence of OSA in 151 patients undergoing electric cardioversion and 463 patients seen in general cardiovascular practice. OSA was more frequent in patients with AF than in those in general practice (49 vs 33%). This assumption, however, was not confirmed by Porthan et al [22] in a case control study of 59 patients with lone AF. According to these authors, the prevalence of OSA was similar to gender, age, body mass index, waist and neck circumference matched controls (32 vs 29%).

Obesity is an important risk factor for OSA and AF. This finding prompted Wang et al [23] and Gami and coworkers [7] to evaluate the role of obesity on the prevalence of new onset AF. In the Framingham Heart Study [23] obesity was an independent clinical risk factor for new onset of AF. However, after adjusting for left atrial size by echocardiography, obesity was no longer an independent variable. Gami et al [7] evaluated the risk of obesity and OSA for new-onset AF in 3,542 patients with sleep apnea syndrome. During, follow up of 4.7 years the incidence of new onset AF was 14%. Independent risks for new onset of AF were OSA, degree of nocturnal hypoxia and obesity. Another question is the role of CPAP in prevention of recurrence of AF after cardioversion. According to Kanagala et al [24] patients treated with CPAP had lower recurrence rate of AF after restoration of sinus rhythm in comparison to control group or those not using CPAP.

As discussed, OSA is an important contributing factor for new onset AF. This finding suggests that patients with new onset AF and risk factors for OSA are candidates for sleep study. In, patients with confirmed sleep apnea syndrome the management of AF should include CPAP.

Sudden death and OSA

As discussed, OSA is associated with higher prevalence of complex ventricular ectopy and non-sustained ventricular tachycardia [16], both known risk factors for increased cardiac mortality and sudden cardiac death. In addition, obese patients have higher incidence of first appropriate shock at night, some of whom could have OSA [19]. Doherty et al [25] followed 168 patients with polysomnographic confirmed OSA and AHI > 15/H for a mean of 7.5 years. One hundred seven patients were treated with CPAP, while the remaining sixty one either refused or did not tolerate CPAP. The only difference between these two groups was higher AHI in the treated group ($p = 0.02$). Most patients using CPAP died of non-cardiac causes (6 out of 8 patients), while untreated patients died either suddenly (4 patients) or from other cardiac causes (2 patients). Marin et al [26] showed higher cardiac mortality in untreated patients with OSA in comparison to healthy men, simple snorers and those using CPAP. The incidence of sudden death, however, was not part of their study.

An interesting observation is different timing of sudden death in OSA and general population. The highest incidence of sudden cardiac death in general population is between 6 and noon [8,27], while patients with sleep apnea syndrome died more likely at night [8]. This observation suggests that some nocturnal abnormalities could trigger sudden death in OSA.

Pacing in OSA?

Is there a role of pacing in patients with nocturnal bradyarrhythmias. According to Becker et al [10], pacing should be reserved for patients not responding or those refusing CPAP therapy. Grim et al [11] reported the management of 29 patients with severe bradyarrhythmias. CPAP prevented nocturnal bradyarrhythmias in 21 patients (72%). Because of the recommendation of the primary physicians rather than the authors of the study, permanent pacemakers were implanted in twelve patients. Eight patients with VDI mode pacing used the pacemaker less than one per cent, three patients with DDD mode and lower rate limit of 40–50 were paced < 10% and in one patient with DDD mode and lower rate limit of 60 beats per minute was paced more than 10 per cent. The outcome was similar regardless of pacing. Stegman and coworkers [12] canceled

pacemaker implantation in seven patients with sleep related bradyarrhythmias all of whom did well with CPAP.

Recently, Garrigue et al [28] reported the prevalence of sleep apnea syndrome in 98 patients with permanent pacemakers, implanted at least for one month. Indications for pacing were sinus node disease, AV block, congestive heart failure (biventricular pacemakers) and documented nocturnal heart rate < 50 bpm. Excluded from the study were patients with documented sleep apnea syndrome before pacemaker implantation. All patients underwent polysomnography. The prevalence of sleep breathing disorder was 50% in patients with heart failure (AHI 11/H), 58% in those with sinus node disease (AHI 19/H), while the highest prevalence of sleeping apnea syndrome was in patients with AV block (68% and mean AHI 24/H). There was no correlation between the severity of sleep apnea syndrome, patient's age or BMI.

The reason for pacing in patients with sleep breathing disorder is not clear. The first unlikely possibility is nocturnal bradyarrhythmia. As discussed above, nocturnal bradyarrhythmias are usually seen in severe sleep apnea syndrome, which were not present in these patients [28]. As emphasized by the authors, most patients had only mild forms of sleep apnea syndrome (hypopnea) without classical risk factors. Second, possibility is higher incidence of day time bradyarrhythmias. Allonso-Fernandez and coworkers [29] reported higher prevalence of day time sinus bradycardia, sinus pauses and supraventricular premature beats and tachycardias. Using the Berlin questionnaire, Daccarett et al [30] found sleep apnea syndrome in 57.8% patients with day time bradycardia in comparison to 21.3% in the control group. The main limitation of this study was a few patients (19 patients), its retrospective character and the use of Berlin questionnaire rather than polysomnography for the diagnosis of OSA. The higher incidence of OSA in paced patients requires further study.

Conclusions

Patients with sleep breathing disorders are prone to different cardiac arrhythmias. In, addition to nocturnal brady– and tachyarrhythmias, OSA plays an important role in new onset of AF and CPAP prevents recurrence of AF after cardioversion. Similarly there is also an association between OSA and sudden death and its prevention with CPAP. The highest prevalence of sudden cardiac death in OSA is during the night instead between 6 and noon as seen in other victims of sudden cardiac death. The different timing of death suggests that some nocturnal abnormalities trigger these fatal events. Indications for pacing in OSA remain controversial. In general, pacing is rarely if at all indicated in sleep apnea syndrome because nocturnal bradyarrhythmias are well managed with CPAP. An unanswered question is the high incidence of OSA in patients with permanent pacemakers.

Literature

1. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: A population health perspective. Am J Respir Crit Care Med 2002; 165: 1217–1239.

2. Gami AS, Somers VK. Sleep apnea and cardiovascular disease. In: Libby P, Bonow RO, Mann DL et al (eds). Braunwald's Heart Disease: A textbook of Cardiovascular medicine. 8th ed. Philadelphia: Saunders 2007: 1915–1921.

3. Shamsuzzaman ASM, Gersh BJ, Somers VR. Obstructive sleep apnea. Implication for cardiac and vascular disease. JAMA 2003; 290: 1906–1914.

4. Guilleminault C, Conolly SJ, Winkle RA. Cardiac arrhythmias and conduction disturbances during sleep in 400 patients with sleep apnea syndrome. Am J Cardiol 1983; 52: 490–494.

5. Arias MA, Sanchez AM. Obstructive sleep apnea and its relationship to cardiac arrhythmias. J Cardiovasc Electrophysiol 2007; 18: 1006–1014.

6. Szaboova E, Donic V, Tomori Z et al. Obstructive sleep apnea syndrome as a cause of dysrhythmia in sudden cardiac death. Bratisl Lek Listy 1997; 98: 448–453.

7. Gami AS, Hodge DO, Herges RM et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. J Am Coll Cardiol 2007; 49: 565–571.

8. Gami AS, Howard DE, Olson EJ et al. Day-night pattern of sudden death in obstructive sleep apnea. N Engl J Med 2005; 352: 1206–1214.

9. Koehler U, Becker HF, Grimm W et al. Relations among hypoxemia, sleep stage, and bradyarrhythmias during obstructive sleep apnea. Am Heart J 2000; 139: 142–148.

10. Becker HF, Koehler U, Stamnitz A et al. Heart block in patients with sleep apnea. Thorax 1998; 53 (Suppl 3): S29–S32.

11. Grim W, Koehler U, Fus E et al. Outcome of patients with sleep apnea-associated severe bradyarrhythmias after continuous positive airway pressure therapy. Am J Cardiol 2000; 86: 688–692.

12. Stegman SS, Burroughs JM, Henthorn RW. Asymptomatic bradyarrhythmias as a marker for sleep apnea. Appropriate recognition and treatment may reduce the need for pacemaker therapy. Pace 1996; 19: 899–904.

13. Grimm W, Hoffman J, Menz V et al. Electrophysiologic evaluation of sinus node function and atrioventricular conduction in patients with prolonged ventricular asystole during obstructive sleep apnea. Am J Cardiol 1996; 77: 1310–1314.

14. Harbison J, O'Reilly P, McNicholas WT. Cardiac rhythm disturbances in the obstructive sleep apnea syndrome: Effects of nasal continuous positive airway pressure therapy. Chest 2000; 118: 591–595.

15. Mehra R, Benjamin EJ, Shahar E et al. Association of nocturnal arrhythmias with sleep-disordered breathing. Am J Respir Crit Care Med 2006; 173: 910–916.

16. Koshino Y, Satoh M, Katayose Y et al. Association of sleep-disordered breathing and ventricular arrhythmias in patients without heart failure. Am J Cardiol 2008; 101: 882–886.

17. Fichter J, Bauer D, Arampatzis S et al. Sleep-related breathing disorders are associated with ventricular arrhythmias in patients with an implantable cardioverter-defibrillator. Chest 2002; 122: 558–561.

18. Pietrasik G, Goldenberg I, McNitt S et al. Obesity as a risk factor for sustained ventricular tachyarrhythmias in MADIT II patients. J Cardiovasc Electrophysiol 2007; 18: 181–184.

19. Pietrasik G, Zareba W. Day-night pattern of defibrillator therapies among obese and nonobese patients in Maditt II trial. J Cardiovasc Electrophysiol 2007; 18: E20.

20. Arias MA, Sanchez AM. Obesity and the risk of appropriate defibrillator therapies in Madit II trial. J Cardiovasc Electrophysiol 2007; 18: E19.

21. Gami AS, Pressman G, Caples SM et al. Association of atrial fibrillation and obstructive sleep apnea. Circulation 2004; 110: 364–367.
22. Porthan KM, Melin JH, Kupila JP et al. Prevalence of sleep apnea syndrome in lone atrial fibrillation. A case-controlled study. Chest 2004; 125: 879–885.
23. Wang TJ, Parise H, Levy D et al. Obesity and the risk of new-onset atrial fibrillation. JAMA 2004; 292: 2471–2477.
24. Kanagala R, Murali NS, Friedman PA et al. Obstructive sleep apnea and recurrence of atrial fibrillation. Circulation 2003; 107: 2589–2594.
25. Doherty LS, Kiely JL, Swan V et al. Long-term effects of nasal continuous positive airway pressure therapy on cardiovascular outcomes in sleep apnea syndrome. Chest 2005; 127: 2076–2084.
26. Marin JM, Carrizo SJ, Vincente E et al. Long term cardiovascular outcomes in men with obstructive sleep-apnoe-hypopnoe with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005; 365: 1046–1053.
27. Cohen MC, Rohtla KM, Lavery CE et al. Meta-analysis of the morning excess of acute myocardial infarction and sudden cardiac death. Am J Cardiol 1997; 79: 1512–1516.
28. Gami AS, Howard DE, Olson EJ et al. Day-night pattern of sudden death in obstructive sleep apnea. N Eng J Med 2005; 352: 1206–1214.
29. Garrigue S, Pepin 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: 1703–1709.
30. Alonso-Fernandez A, Garcia-Rio F, Racionanero MA et al. Cardiac rhythm disturbances and ST segment depression episodes in patients with obstructive sleep apnea-hypopnea syndrome and its mechanism. Chest 2005; 127: 15–22.
31. Daccarett M, Segerson NM, Hamdan AL et al. Relation of daytime bradyarrhythmias with high risk features of sleep apnea. Am J Cardiol 20008; 101: 1147–1150.

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