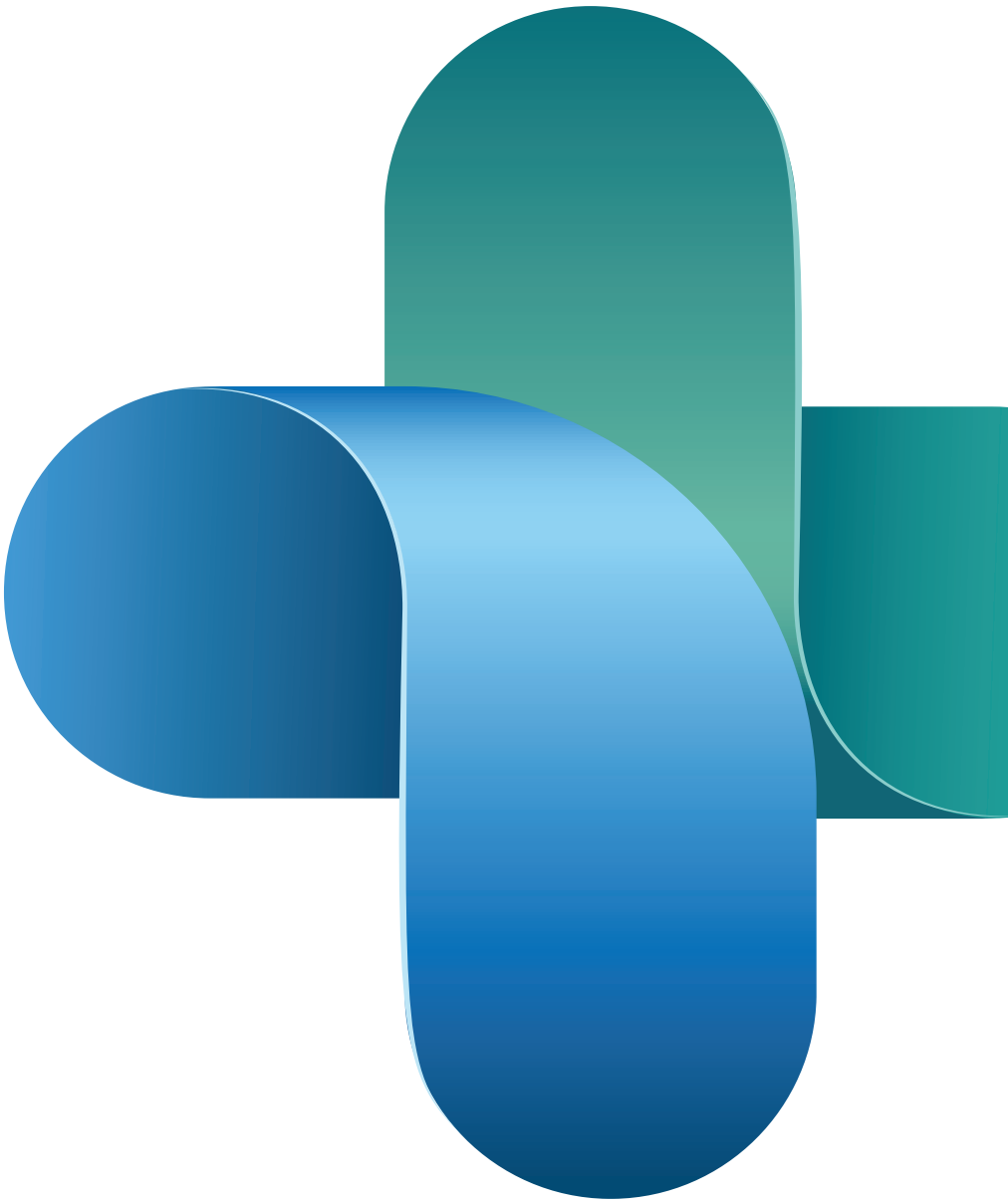
WatchPAT™

Sleep Apnea in Cardiac Diseases

Cardiology Clinical Compendium



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Introduction

Sleep Apnea as cardiovascular comorbidity has been known for over 2 decades. The prevalence of sleep apnea in cardiac patients is estimated to be over 50% and includes Drug-Resistant Hypertension, Coronary Artery Disease, Heart Failure, Diabetes, Atrial Fibrillation and other Arrhythmias, Sudden Cardiac Death, Stroke and even Depression. In recent years, a growing body of evidence has been published on the impact of sleep apnea treatment of CVD outcomes and the results are significant.

This newly available data is changing the landscape of cardiovascular research and clinical practice. For example, in the last 10 years, the annual number of publications of sleep impact on CVD in major cardiology journals like AHA and JACC are almost tripled and reached more than 200. In September 2016, The American Heart Association (AHA) released a scientific statement on sleep duration and quality which stated that moderate and severe sleep apnea were associated with a substantially higher risk of cardiovascular disease. At the same time, the European Society of Cardiology (ESC) published revised guidelines for the management of Atrial Fibrillation including a clear call that “Interrogation for clinical signs of Obstructive Sleep Apnea should be considered in all AF patients. Obstructive sleep apnea treatment should be optimized to reduce AF recurrences and improve AF treatment results”. Joining the trend, the ACC came out in March 2017 with a special editorial “Sleep Apnea: Types, Mechanisms and Clinical Cardiovascular Consequences” calling all cardiologists to consider sleep apnea as modifiable cardiovascular risk factor.

We are delighted to introduce this cardiology clinical compendium featured with **Sleep Apnea in Cardiac Diseases**. In this compendium you will find summaries of various clinical studies which address various cardiology subspecialties such as General Cardiology, Interventional Cardiology and Electrophysiology.

Content

Atrial Substrate and Triggers of Paroxysmal Atrial Fibrillation in Patients With Obstructive Sleep Apnea

Anter et al. Circulation: Arrhythmia and Electrophysiology. 10(11):e005407, NOV 2017

Objective

- Obstructive sleep apnea (OSA) is associated with atrial remodeling, atrial fibrillation (AF) and increased arrhythmia recurrence post pulmonary vein (PV) isolation. This study aims to map the atrial substrate, including identification of AF triggers in patients with paroxysmal AF (PAF) and OSA.

Methods

- 86 patients with PAF (43 with ≥moderate OSA [apnea–hypopnea index ≥15] and 43 without OSA [apnea–hypopnea index <5]), right atrial and left atrial voltage distribution, conduction velocities and electrogram characteristics were analyzed during atrial pacing.
- 2 control patient groups with a normal sleep study and with ≥moderate OSA who underwent PVI alone without mapping and ablation of extra-PV triggers were identified prospectively.
- All 4 groups underwent full substrate evaluation with 3D mapping and ablation.
- AF triggers were examined before and after PV isolation and targeted for ablation.
- Patients with OSA had lower atrial voltage amplitude (right atrial, P=0.0005; left atrial, P=0.0001), slower conduction velocities (right atrial, P=0.02; left atrial, P=0.0002) and higher prevalence of electrogram fractionation (P=0.0001).
- The areas of atrial abnormality were consistent among patients, most commonly involving the left atrial septum (32/43; 74.4%).

Results

- The PVs were the most frequent triggers for AF in both groups; however, after PV isolation patients with OSA had increased incidence of additional extra-PV triggers (41.8% versus 11.6%; P=0.003).
- The 1-year arrhythmia-free survival was similar between patients with and without OSA (83.7% and 81.4%, respectively; P=0.59) that undergo both PVI and Non-PV Trigger ablation.
- Control patients with PAF and OSA who underwent PV isolation alone without ablation on extra-PV triggers had increased risk of arrhythmia recurrence (83.7% versus 64.0%; P=0.003).

Conclusion

- OSA is associated with structural and functional atrial remodeling and increased incidence of extra-PV triggers.
- Elimination of these triggers resulted in improved arrhythmia-free survival.

Key Takeaways

- OSA is associated with structural and functional atrial remodeling.
- More non-PV trigger elimination improves ablation outcome.
- Sleep studies before ablation may help to define the ablation strategy.

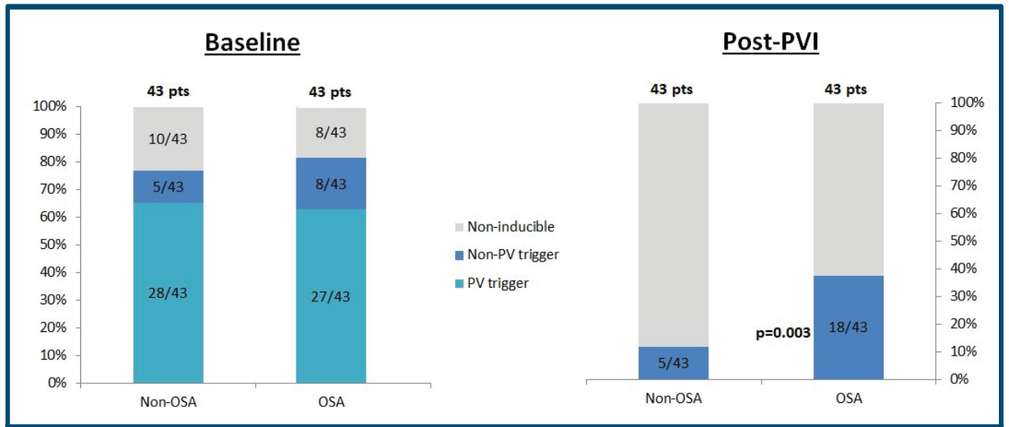


Figure 1. Distribution of atrial fibrillation (AF) triggers in patients with and without obstructive sleep apnea (OSA). PVI indicates pulmonary vein isolation.

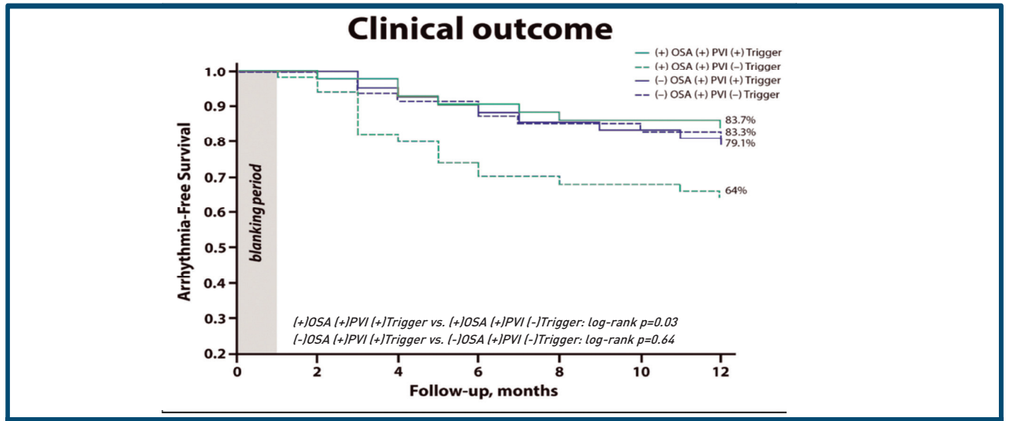


Figure 2. Kaplan–Meier survival curves according to treatment groups.
OSA indicates obstructive sleep apnea; and PVI, pulmonary vein isolation.

Obstructive Sleep Apnea is Associated with Increased Rotor Burden in Patients Undergoing Focal Impulse and Rotor Modification Guided Atrial Fibrillation Ablation

D.J Friedman et al. Europace (2017) 0, 1-6

Objective

- To assess whether obstructive sleep apnea was associated with increased rotor burden among atrial fibrillation patients.

Methods

- The study included 33 consecutive patients who were scheduled for focal impulse and rotor modulation (FIRM) ablation to describe the mapping, ablation, and outcomes, among patients with and without OSA.
- Patients underwent biatrial FIRM mapping in AF with ablation of stable rotors in addition to conventional ablation lesion sets.
- Differences between groups were tested with student's t-tests and Fisher's exact tests, as appropriate.
- Survival analyses were performed using the Kaplan–Meier method.

Results

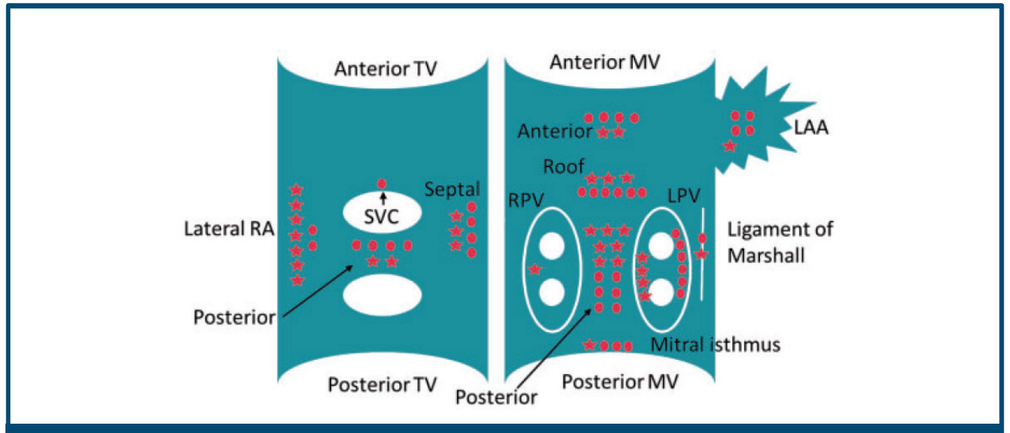
- Focal impulse and rotor modulation mapping demonstrated increased rotor burden in the OSA patients (2.6 ± 0.9 vs. 2.0 ± 1.0, P =0.03).
- The increased rotor burden was more evident in the right atrium (RA) (1.0 ± 0.7 vs. 0.5 ± 0.7, P =0.04 compared with the left atrium (1.7 ± 0.8 vs.1.4 ± 0.7, P = 0.15).
- There was no correlation between BMI and total number of rotors (r = 0.0961, P = 0.59).
- Among the population of patients with OSA, CPAP therapy was associated with a lower number of RA rotors (0.8 ± 0.7 vs. 1.5 ± 0.6, P = 0.05) but no significant difference in overall rotors (P = 0.33).

Conclusion

- Obstructive sleep apnea patients demonstrate increased rotor prevalence, driven predominantly by an increase in RA rotors.
- CPAP therapy was associated with fewer RA rotors.
- OSA patients were less likely to experience an acute intraprocedural endpoint with FIRM (AF cycle length slowing, AF organization, or AF termination) and were more likely to experience an atrial arrhythmia recurrence.

Key Takeaways

- OSA patients demonstrate increased rotor prevalence and increased RA rotors, compared to non-OSA patients. These findings suggest that an alternative RA ablation might lead to improved outcomes in patients with OSA.
- Patients who were already diagnosed with OSA and treated with CPAP demonstrated fewer RA rotors, compared to patients who were not treated.
- Therefore, early diagnosis of OSA, as well as CPAP treatment, might provide a better treatment and outcome for patients having both OSA and AF.



Schematic diagram of the atria depicting rotor locations among OSA patients (stars) and non-OSA patients (circles).

Effect of Sleep Apnea and Continuous Positive Airway Pressure on Cardiac Structure and Recurrence of Atrial Fibrillation

Neilan et al. Journal of the American Heart Association 2013;2:e000421

Objective

- To determine the effect of sleep apnea (SA) on cardiac structure in patients with atrial fibrillation (AF).
- To discuss whether therapy for SA was associated with beneficial cardiac structural remodeling.
- To evaluate whether beneficial cardiac structural remodeling translated into a reduced risk of recurrence of AF after pulmonary venous isolation (PVI).

Methods

- A consecutive group of 720 patients underwent a cardiac magnetic resonance study before PVI.
- The presence or absence of SA was prospectively determined before PVI with the use of a standardized questionnaire administered to all patients.
- All patients diagnosed with SA had undergone formal sleep studies. The diagnosis of SA was established in accordance with the sleep study criteria recommended by the American Academy of Sleep Medicine.
- Patients with SA were separated into 2 groups based on the median time of treatment with CPAP. Treated SA was defined as duration of continuous positive airway pressure therapy of >4 hours per night. Non-treated SA was defined as CPAP duration of less than duration of therapy of 4 hours.

Results

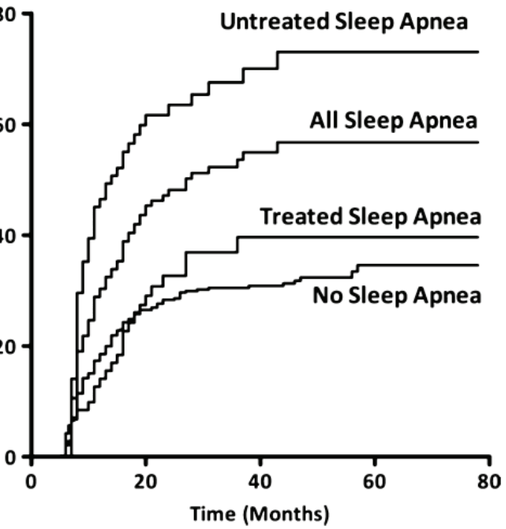
- Patients with SA (n=142, 20%) were more likely to be male, diabetic and hypertensive and have an increased pulmonary artery pressure, right ventricular volume, atrial dimensions and left ventricular mass.
- Treated SA patients (n=71, 50%) were more likely to have paroxysmal AF, a lower blood pressure, lower ventricular mass, and smaller left atrium.
- During a follow-up of 42 months, AF recurred in 245 patients.
- The cumulative incidence of AF recurrence was 51% in patients with SA, 30% in patients without SA, 68% in patients with untreated SA, and 35% in patients with treated SA.
- In a multivariable model, the presence of SA (hazard ratio 2.79, CI 1.97 to 3.94, P<0.0001) and untreated SA (hazard ratio 1.61, CI 1.35 to 1.92, P<0.0001) were highly associated with AF recurrence.

Conclusion

- Patients with SA have an increased blood pressure, pulmonary artery pressure, right ventricular volume, left atrial size and left ventricular mass.
- Therapy with continuous positive airway pressure is associated with lower blood pressure, atrial size, and ventricular mass, and a lower risk of AF recurrence after PVI.

Key Takeaways

- Early diagnosis and treatment of OSA may attenuate the cardiac structural changes among patients with SA.
- Early diagnosis and treatment of OSA may also reduce the incidence of AF recurrence among patients with SA.



The probability of AF recurrence according to the both presence and absence of SA and according to the SA treatment group.

Effect of Obstructive Sleep Apnea Treatment on Atrial Fibrillation Recurrence – A Meta-Analysis

Shulka, Chinitz et al. JACC: Clinical Electrophysiology, 2015. Vol. 1, No. 1-2

Objective

- To evaluate the cumulative effect of treatment of obstructive sleep apnea (OSA) with continuous positive airway pressure (CPAP) on atrial fibrillation (AF) recurrence.

Methods

- Relevant studies were searched for using MEDLINE, EMBASE, CINAHL, Google Scholar, Cochrane Database of Systematic Reviews, and Cochrane Trials Register.
- Seven prospective cohort studies with a total of 1,087 patients who met the inclusion criteria and were used for the meta- analysis.
- The primary outcome has been defined as an evaluation of AF recurrence in CPAP users and nonusers in patients with OSA.
- The secondary outcome has been defined as an evaluation of AF recurrence in CPAP users and nonusers after pulmonary vein isolation (PVI).

Results

- Across all patient groups, the use of CPAP was associated with a significant reduction in AF recurrence (relative risk: 0.58, 95% confidence interval: 0.51 to 0.67; heterogeneity chi-square p = 0.91, I^2= 0%).
- The beneficial effect of CPAP use was statistically significant in both groups of patients: those who underwent catheter ablation with PVI and those who did not undergo ablation and were managed medically.
- No other study covariates had any significant association with these outcomes of AF reduction.

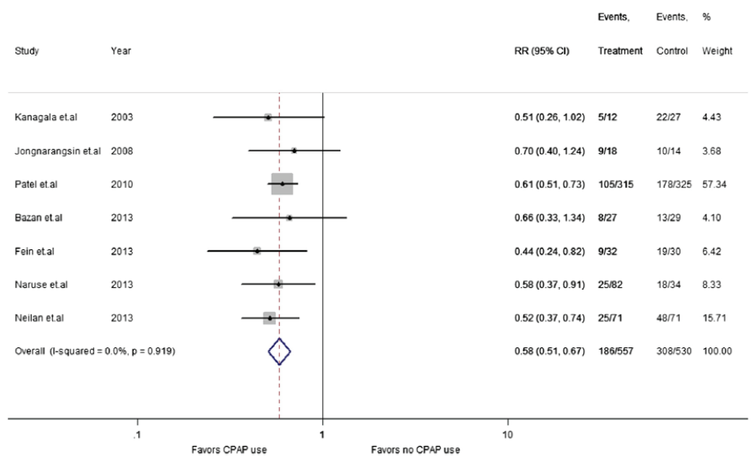
Conclusion

- The use of CPAP is associated with significant reduction in recurrence of AF in patients with OSA. This effect remains consistent and similar across patient populations irrespective of whether they undergo PVI.

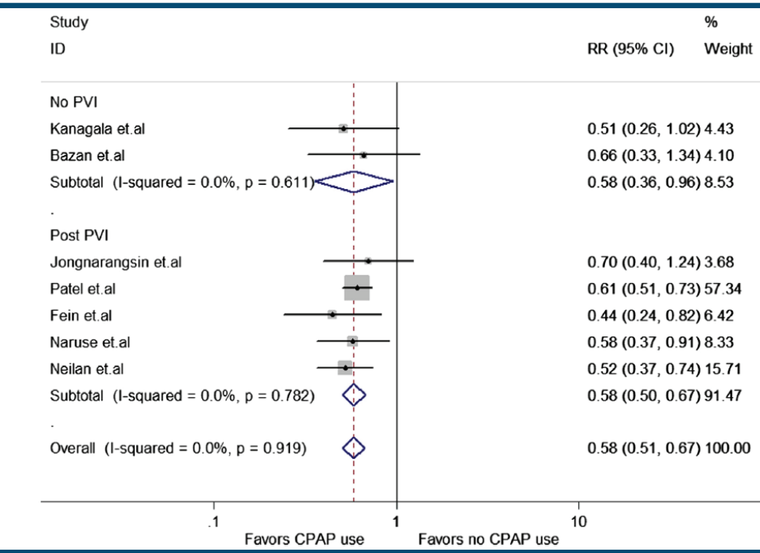
Key Takeaways

- Early diagnosis and CPAP treatment in OSA patients may significantly reduce the recurrence rate of AF.
- The effectiveness of CPAP treatment in OSA patients is relevant for both patients who had undergone catheter ablation with PVI and patients who had been managed with medical treatment only.

Forest Plot to Compare AF Recurrence in Users vs Nonusers of CPAP In Patients With OSA



The forest plot exhibits effect size of each included study (solid box) with 95% confidence interval (CI) (black lines through solid squares). The diamond (and broken vertical line) at the bottom represents pooled summary estimate with its CI given by its width.



AF Recurrence in Users vs Nonusers of CPAP in 2 Groups of Patients With OSA: PVI and Non-PVI Groups
PVI = pulmonary vein isolation

Obstructive Sleep Apnea and Risk of Cardiovascular Disease and All-Cause Mortality: A Meta-Analysis of Prospective Cohort Studies

X. Wang et al. / International Journal of Cardiology 169 (2013) 207–214

Objective

- To evaluate the association between obstructive sleep apnea (OSA) and risk of cardiovascular disease (CVD) and all-cause mortality by performing a meta-analysis of prospective cohort studies.

Methods

- Twelve prospective cohort studies involving 25,760 participants were included in the meta-analysis.
- Generalized least squares regression models were used to estimate the dose–response relationship. Heterogeneity, subgroup, and sensitivity analyses and publication bias were performed.

Results

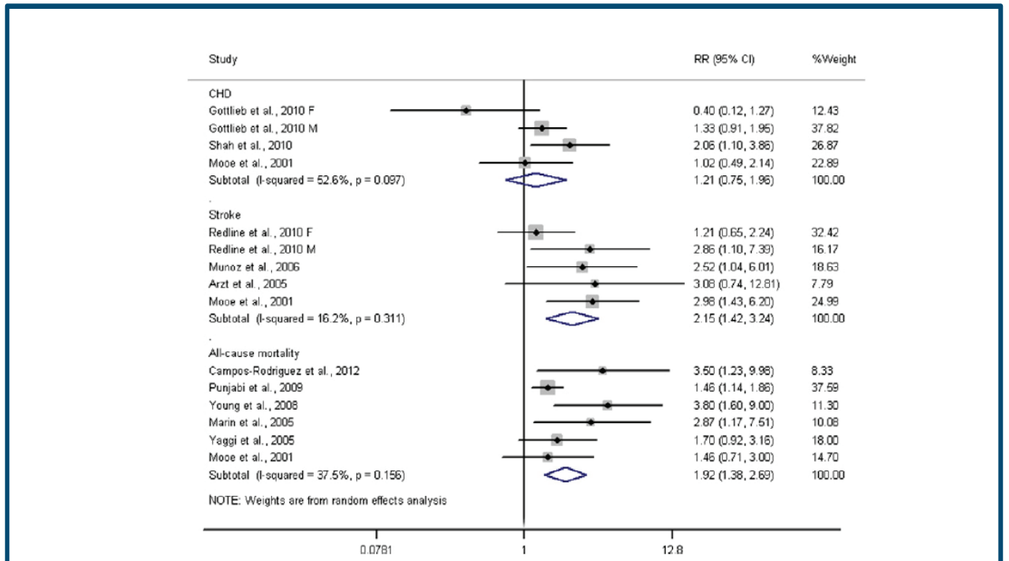
- The overall combined relative risks for individuals with severe OSA compared with individuals with an AHI of <5 were 1.79 (95% confidence interval [CI]: 1.47 to 2.18) for CVD, 1.21 (95% CI: 0.75 to 1.96) for incident fatal and non-fatal coronary heart disease, 2.15 (95% CI: 1.42 to 3.24) for incident fatal and non-fatal stroke, and 1.92 (95% CI: 1.38 to 2.69) for deaths from all-causes.
- A positive association with CVD was observed for moderate OSA but not for mild OSA.
- The results of the dose–response relationship indicated that per 10-unit increase in the apnea–hypopnea index was associated with a 17% greater risk of CVD in the general population.

Conclusion

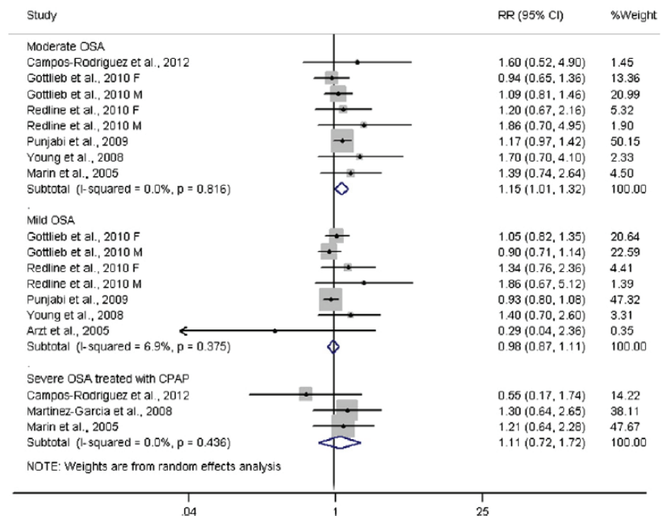
- This meta-analysis of prospective cohort studies suggests that severe OSA significantly increases CVD risk, stroke and all-cause mortality.
- A positive association with CVD was observed for moderate OSA but not for mild OSA.
- CPAP treatment among patients with severe OSA was associated with a decreased in CVD risk.

Key Takeaways

- Evaluation of OSA severity has an important role in order to assess increased risk for CVD, stroke and all-cause mortality.
- The fact that increased severity of OSA is associated with an incremental increase in the risk of CVD in the general population might demonstrate the importance of early evaluation of OSA in patients, when the OSA severity is still mild to moderate.
- The decreased CVD risk among patients with severe OSA who were treated with CPAP emphasizes the importance of diagnosis and an appropriate treatment of OSA.



Severe OSA and risk of CHD, stroke, and all-cause mortality. Forest plots show associations between severe OSA and risk of CHD, stroke, and all-cause mortality.



Moderate, mild OSA, and severe OSA treated with CPAP and risk of CVD. Forest plot shows association between moderate,mild OSA, and severe OSA treated with CPAP and risk of CVD.

Heart Failure and Sleep Disorders

Parati et al. Cardiology Nature Reviews Cardiology volume 13, 389–403 (2016)

Objective

- Sleep-disordered breathing, short sleep time and low sleep quality are frequently reported by patients with heart failure (HF).
- Obstructive sleep apnea (OSA) and central sleep apnea (CSA), are common in patients with HF and have been suggested to increase the morbidity and mortality in these patients.
- The review addresses the complex interactions between HF and sleep alterations, in particular with sleep-disordered breathing and describes the pathophysiology, diagnosis and management of these sleep disorders on the background of increasing evidence from clinical studies.
- An important purpose of the review is to raise the awareness among clinicians of issues related to sleep-disordered breathing in HF and their management.

Methods

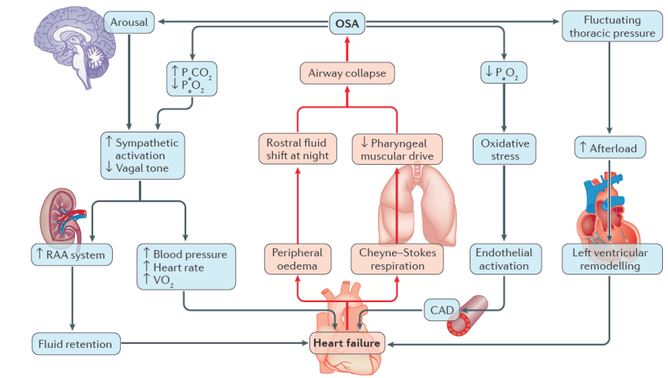
- The review describes the interactions between heart failure and sleep disorders, mainly OSA and CSA. It discusses many aspects: epidemiology, pathophysiology, diagnosis, clinical features and treatment, all based on a wide variety of studies performed in the recent years and regarding the relevant fields.

Conclusion

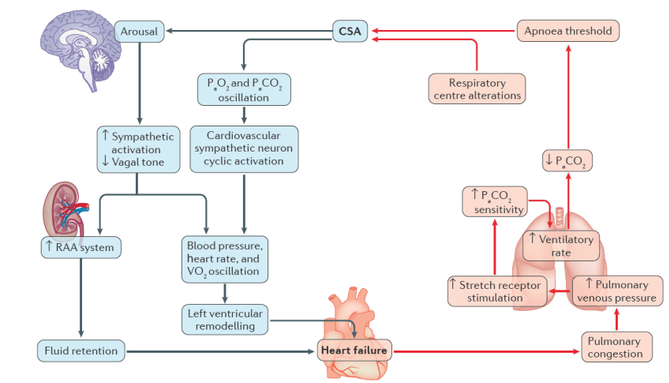
- Patients with heart failure (HF) are characterized by relevant problems during sleep, including short sleep time, low sleep quality and sleep-disordered breathing.
- Sleep deprivation and poor sleep quality have been identified as barriers to self-care and treatment adherence in patients with HF.
- Observational studies have showed that CPAP treatment lowers mortality and improves hospitalization-free survival in patients with HF, particularly in more compliant patients whose average nightly usage of CPAP was high.

Key Takeaways

- Sleep-disordered breathing is highly prevalent in patients with HF, both central and obstructive sleep apneas are frequently observed in these patients and were shown to have an important added prognostic value.
- Continuous positive airway pressure (CPAP) has a beneficial effect on left ventricular ejection fraction and is currently the best treatment option for obstructive sleep apneas in patients with HF.
- The diagnosis of OSA in patients with HF and moreover – the treatment of OSA in those patients, is highly important.



Relationship between obstructive sleep apnea (OSA) and heart failure. Schematic representation of the mutual interactions between OSA and heart failure. CAD, coronary artery disease; PaCO2, arterial partial pressure of CO2; PaO2, arterial partial pressure of O2; RAA, renin–angiotensin–aldosterone; VO2, oxygen consumption rate.



Relationship between central sleep apnea (CSA) and heart failure: Schematic representation of the mutual interaction between CSA and heart failure. PaCO2, arterial partial pressure of CO2; PaO2, arterial pressure partial of O2; RAA, renin–angiotensin–aldosterone; VO2, oxygen consumption rate.

Association Between Treated and Untreated Obstructive Sleep Apnea and Risk of Hypertension

Marin et al. JAMA, May 23/30, 2012—Vol 307, No. 20

Objective

- Systemic hypertension is prevalent among patients with obstructive sleep apnea (OSA). Short-term studies indicate that continuous positive airway pressure (CPAP) therapy reduces blood pressure in patients with hypertension and OSA.
- The objective of the study was to determine whether CPAP therapy for patients with OSA is associated with a lower risk of incident hypertension.

Methods

- A prospective cohort study of 1889 participants without hypertension who were referred to a sleep center in Zaragoza, Spain, for nocturnal polysomnography between the years 1994-2000.
- Patients with apnea-hypopnea index (AHI) of less than 5 events per hour of sleep served as controls (patients without OSA), whereas those patients with an AHI of 5 or more were diagnosed with OSA.
- Incident hypertension was documented at annual follow-up visits up to the year 2011.
- Multivariable models adjusted for confounding factors were used to calculate hazard ratios (HRs) of incident hypertension in participants without OSA, with untreated OSA, and in those treated with CPAP therapy according to national guidelines.
- Change in body mass index from baseline to censored time was considered as a main confounding factor and was highly referred.
- The main outcome measure was the incidence of new-onset hypertension.

Results

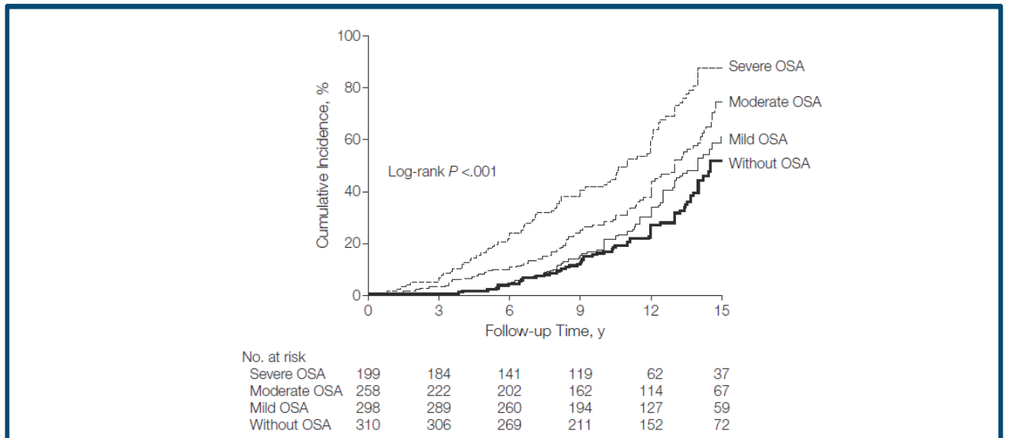
- During 21,003 person-years of follow-up (median 12.2 years), 705 cases (37.3%) of incident hypertension were observed.
- The crude incidence of hypertension per 100 person-years was 2.19 (95% CI, 1.71-2.67) in controls, 3.34 (95% CI,2.85-3.82) in patients with OSA ineligible for CPAP therapy, 5.84 (95% CI, 4.82-6.86) in patients with OSA who declined CPAP therapy, 5.12 (95% CI, 3.76-6.47) in patients with OSA non adherent to CPAP therapy, and 3.06 (95% CI, 2.70-3.41) in patients with OSA and treated with CPAP therapy.
- Compared with controls, the adjusted HRs for incident hypertension were greater among patients with OSA ineligible for CPAP therapy (1.33; 95% CI, 1.01-1.75), among those who declined CPAP therapy (1.96; 95% CI, 1.44-2.66), and among those non adherent to CPAP therapy (1.78; 95% CI, 1.23-2.58), whereas the HR was lower in patients with OSA who were treated with CPAP therapy (0.71; 95% CI, 0.53-0.94).

Conclusion

- Compared with participants without OSA, the presence of OSA was associated with increased adjusted risk of incident hypertension.
- Treatment with CPAP therapy was associated with a lower risk of hypertension.
- Weight gain over a decade does not appear to diminish a protective association of CPAP therapy against development of new-onset hypertension in OSA.

Key Takeaways

- Regarding the high prevalence of OSA in the western population, early recognition and moreover – early treatment, have a significant importance in reducing the risk of incident hypertension among patients.
- Considering the high prevalence of unsuspected OSA among obese patients, the vascular risk that is commonly attributed to obesity may in part be related to OSA.
- The lower risk for new-onset hypertension associated with effective therapy for OSA strengthens the rationale for screening and prompt treatment of OSA in patients who are overweight and obese.



Cumulative Incidence of Hypertension in Participants without OSA and Untreated Patients with OSA

OSA indicates obstructive sleep apnea. Severity of OSA was defined by the apnea-hypopnea index (AHI) as mild OSA (AHI, 5.0-14.9), moderate OSA (AHI, 15.0-29.9), and severe OSA (AHI, _30.0). P value reflects an overall log-rank x2/3 test, providing an overall survival difference among the 4 study groups.

Impact of Sleep-Disordered Breathing on Long-Term Outcomes in Patients With Acute Coronary Syndrome Who Have Undergone Primary Percutaneous Coronary Intervention

Mazaki et al. J Am Heart Assoc. 2016;5:e003270 doi: 10.1161

Objective

- To evaluate the impact of Sleep-Disordered Breathing (SDB) on long-term outcomes in patients with acute coronary syndrome.

Methods

- An overnight sleep study was performed under hospitalization on 241 patients with acute coronary syndrome who were successfully treated with primary percutaneous coronary intervention between the years 2005-2008, using a portable cardiorespiratory monitoring device that was equipped with a pressure sensor for monitoring airflow and snoring and a finger pulse oximeter for determining arterial oxyhemoglobin saturation (SaO2).
- The presence of SDB was defined as apnea–hypopnea index (AHI) ⩾5 events per hour.
- Patients were followed for a median period of 5.6 years.
- The end point was incidence of major adverse cardiocerebrovascular events, defined as a composite of all-cause death, recurrence of acute coronary syndrome, nonfatal stroke, and hospital admission for congestive heart failure.

Results

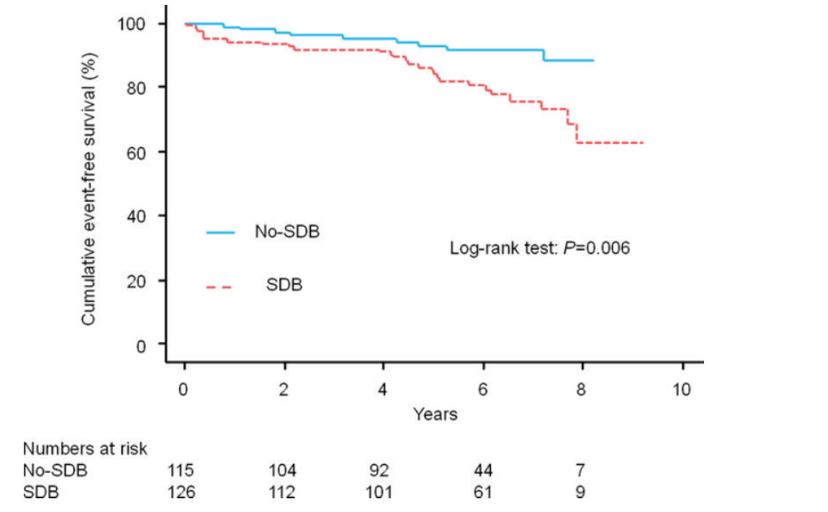
- Among 241 patients, comorbidity of SDB with acute coronary syndrome was found in 126 patients (52.3%).
- The cumulative incidence of major adverse cardiocerebrovascular events was significantly higher in patients with SDB than in those without SDB (21.4% versus 7.8%, P=0.006).
- Multivariable analysis revealed that the presence of SDB was a significant predictor of major adverse cardiocerebrovascular events (hazard ratio 2.28, 95% CI 1.06–4.92; P=0.035).

Conclusion

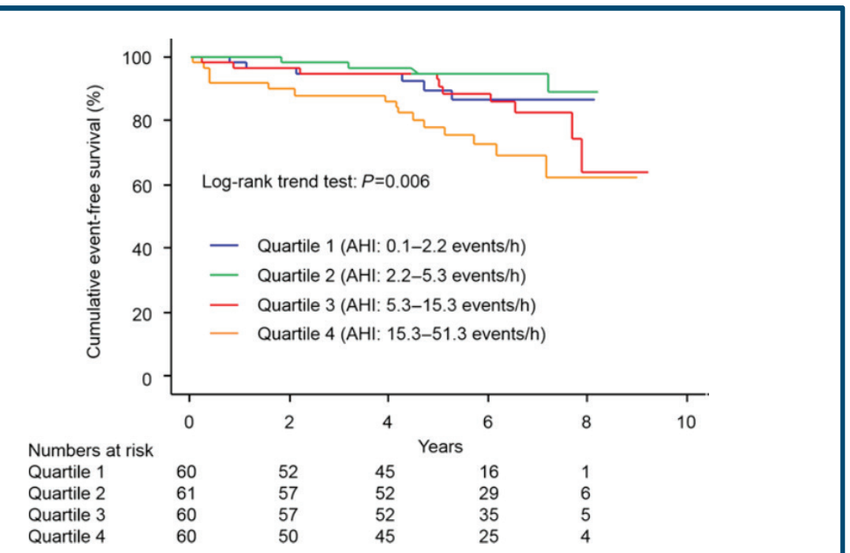
- The presence of SDB among patients with acute coronary syndrome following primary percutaneous coronary intervention is associated with a higher incidence of major adverse cardiocerebrovascular events during long-term follow-up.
- These results are consistent with previous reports regarding exclusively stable coronary heart disease (CAD) patients.
- These results are consistent with previous reports regarding short-term outcomes in patients.

Key Takeaways

- Study findings provide insights into the clinical significance of SDB and perhaps its role in the treatment of ACS patients following primary PCI.
- The AHI evaluated by an overnight sleep study may be a predictor for long-term clinical outcomes.
- The detection of SDB is suggested to be included into the routine clinical care of hospitalized patients following ACS events and primary PCI.



Cumulative event-free survival curves in the entire study group. Patients with SDB had a significantly lower cumulative event-free survival than that in those without SDB.



Cumulative event-free survival curves according to the AHI quartiles in the entire study group. There was a significant trend of worse cumulative event-free survival as quartile increased.

Obstructive Sleep Apnea Affects the Clinical Outcomes of Patients Undergoing Percutaneous Coronary Intervention

Zhang et al Patient Prefer Adherence. 2016; 10: 871–878.

Objective

- To investigate whether OSA affects the clinical outcomes of patients undergoing PCI.

Methods

- All enrolled individuals treated with PCI were evaluated for OSA by polysomnography.
- Overnight sleep studies included nasal airflow, thoracoabdominal movements, arterial oxygen saturation, snoring episodes, limb movement, electrocardiogram, and body position.
- The primary measurement of the sleep study was the apnea–hypopnea index (AHI), which was used to stratify patients into the OSA (AHI ⩾15) and non-OSA groups (AHI <15).
- The primary end point was defined as major adverse cardiac events (MACEs) at 2 years, including cardiac death, myocardial infraction (MI), and/or target vessel revascularization.

Results

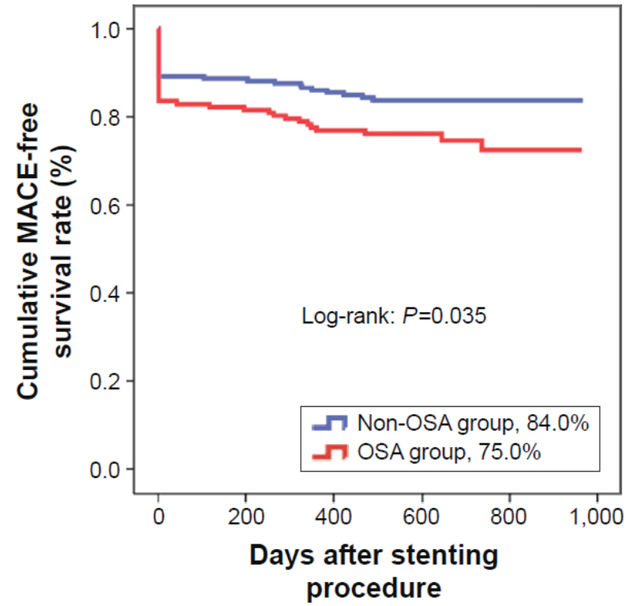
- A total of 340 consecutive patients undergoing PCI were assigned to the OSA (n=152, apnea–hypopnea index ⩾15) and non-OSA (n=188, apnea–hypopnea index <15) groups.
- The incidence of OSA in patients with coronary artery disease undergoing PCI was 44.7%.
- Patients in the OSA group had more three-vessel disease (34.9%), increased number of total implanted stents (3.3±2.0), and longer total stent length (83.8±53.1 mm) when compared to the non-OSA group (23.4%, P=0.020; 2.8±1.9, P=0.007; 68.7±48.4, P=0.010).
- After a median follow-up of 2 years, the incidence of MACEs was significantly higher in patients with OSA (25.0% vs 16.0%, P=0.038), mainly driven by the increased peri-procedural MI (19.2% vs 11.2%, P=0.038) in the OSA group.
- By Cox regression multivariable analysis, the independent predictor of MACEs was OSA (hazard ratio: 1.962, 95% confidence interval: 1.036–3.717, P=0.039).

Conclusion

- There was a high prevalence of moderate-to-severe OSA in patients undergoing PCI.
- Compared to patients without OSA, patients with OSA were more likely to undergo multi-vessel PCI and have an increased number of DESs implanted during PCI.
- OSA was associated with significantly increased MACE rate, mainly due to the increase in peri-procedural MI rate.

Key Takeaways

- OSA has been associated with an increased risk of adverse cardiac events in the general population and patients with ACS.
- Regarding the effect of OSA over the clinical outcomes of patients undergoing PCI, detection of OSA may have a greater significance in evaluation of the risk of future major adverse cardiac events in those patients.



MACE-free survival rate at 2 years.

Treatment of Obstructive Sleep Apnea Is Associated With Decreased Cardiac Death After Percutaneous Coronary Intervention

Cassar et al. JACC Vol. 50, No. 14, 2007 October 2, 2007:1310–4

Objective

- To compare outcomes of patients treated for obstructive sleep apnea (OSA) versus patients with untreated OSA, all of whom had undergone percutaneous coronary intervention (PCI).

Methods

- In a retrospective cohort study, a group of patients with OSA who subsequently underwent a PCI (n = 371), were stratified according to whether they were treated for OSA (n = 175) or not (n = 196).
- The patients were diagnosed with OSA between the years 1992-2004, using polysomnography (defining OSA as apnea-hypopnea index ⩾15).
- Patients who were treated for OSA were mostly treated with CPAP.
- Main outcome measures were cardiac death, general mortality, major adverse cardiac events (MACE) – including severe angina, myocardial infarction, PCI, coronary artery bypass grafting, or death, and major adverse cardiac or cerebrovascular events (MACCE).

Results

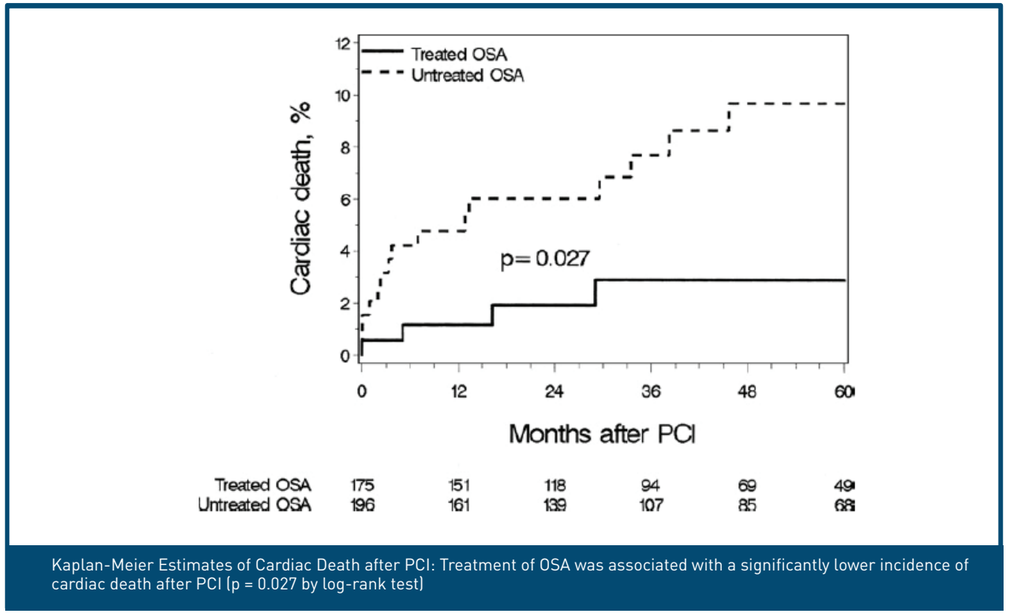
- Patients treated for OSA had a statistically significant decreased number of cardiac deaths on follow-up when compared with untreated OSA patients (3% [95% confidence interval (CI) 0% to 6%] vs. 10% [95% CI 5% to 14%] after 5 years, p = 0.027), as well as a trend toward decreased all-cause mortality (p = 0.058).
- There was no difference in the number of MACE or MACCE between the 2 groups (p = 0.91 and 0.96, respectively).

Conclusion

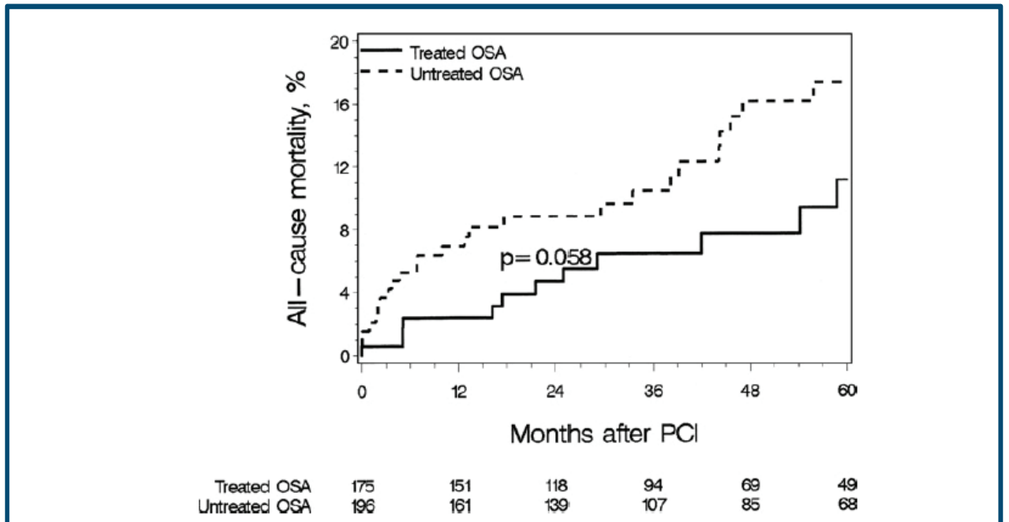
- Treatment of OSA is associated with a reduction in the number of cardiac deaths after PCI.
- However, treatment of OSA is not associated with a reduction in the number of MACE or MACCE after PCI.

Key Takeaways

- Obstructive sleep apnea has been associated with increases in fatal and nonfatal cardiovascular events in general, and when regarding patients after PCI.
- Screening and treating of OSA in patients with coronary artery disease, who may undergo PCI, may result in decreased cardiac death.



Kaplan-Meier Estimates of Cardiac Death after PCI: Treatment of OSA was associated with a significantly lower incidence of cardiac death after PCI (p = 0.027 by log-rank test)



Kaplan-Meier Estimates of All-Cause Mortality after PCI: A lower incidence of death after PCI in those treated for OSA was nearly statistically significant (p = 0.058 by log-rank test)

Patent Foramen Ovale in Severe Obstructive Sleep Apnea

Shaikh et al. Chest Journal Jan 2013 Volume 143, Issue 1, Pages 56–63

Objective

- Patent foramen ovale (PFO) may contribute to nocturnal desaturation in patients with obstructive sleep apnea (OSA), and the effect of PFO closure in OSA is unknown.
- This study tested three hypotheses:
- Patients with severe OSA have a higher prevalence of PFO compared with healthy control subjects.
- Patients with severe OSA with clinically significant PFO experience more nocturnal desaturation than those without.
- PFO closure reduces nocturnal desaturation.

Methods

- Patients with severe OSA and healthy control subjects underwent contrast transthoracic echocardiography and transcranial doppler to detect PFO and determine shunt size.
- A subgroup of patients with OSA with large shunts, underwent percutaneous PFO closure. Polysomnography was performed at baseline and 1, 6, and 12 months post closure.

Results

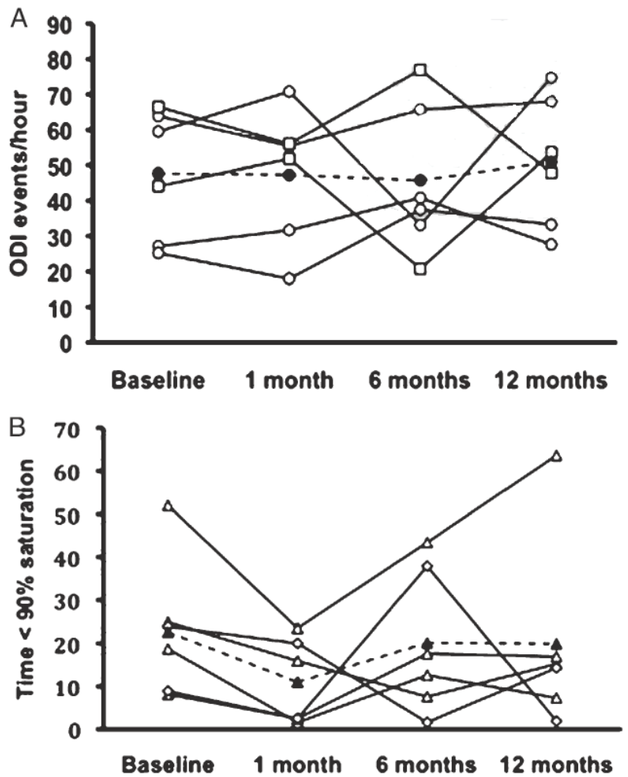
- One hundred patients with OSA and 50 control subjects were studied.
- PFO prevalence was 43% in patients with OSA and 30% in control subjects (P = 0.16).
- Large shunts were detected in 18% of patients with OSA and 6% of control subjects (P = 0.049).
- Patients with OSA with clinically significant shunts had higher oxygen-desaturation index (ODI)/AHI ratios than patients without (mean [SD]; ratio 1.05 [0.27] vs 0.86 [0.26], P = 0.004).
- Six patients with OSA underwent PFO closure, which was not associated with a reduction in ODI (baseline, 48 [18]; 12 months, 51 [19] events/h; P = 0.92) or percentage of the night with arterial oxygen saturation, 90% (Baseline, 23% [16%]; 12 months, 20% [22%]; P = 0.35).

Conclusion

- Patients with severe OSA have a higher prevalence of PFO with large shunts compared to control subjects.
- Overall PFO prevalence was not different from that in the general population.
- Patients with OSA with clinically significant shunts desaturated more for a given respiratory disturbance (had an increased ODI/AHI ratio) than those without clinically significant shunts.
- PFO closure did not reduce nocturnal desaturation, nor did it improve subjective sleepiness or quality of life.

Key Takeaways

- In OSA, PFO may exacerbate the apnea-induced hypoxemia through right-to-left shunting, therefore increasing the cardiovascular morbidity and mortality.
- Considering the fact that PFO is a congenital cardiac defect present in approximately 25% of healthy adults, the prevalence of patients having both OSA and PFO might be relatively high.
- Regarding those above, detection and diagnosis of OSA might have a great importance in patients having a PFO.
- PFO closure is not recommended for treating intermittent hypoxia in OSA. This might suggest other treatment options, such as CPAP, should be considered for the hypoxia in those patients.



ODI at baseline and 1, 6, and 12 months following PFO closure. ○= individual values for patients with sealed PFO; □= individual values for patients with residual large shunts; ● = mean value. B, The percentage of overnight time spent with arterial oxygen saturation , 90% was recorded at baseline and 1, 6 and 12 months later. = individual values for patients with sealed PFO; ◊ = individual value for patients with residual large shunts; ▲= mean value. ODI = oxygen-desaturation index.

Sleep Apnea in Patients with and without a Right-to-Left Shunt

MK Mojadidi, PI Bokhoor, R Gevorgyan et al. Journal of Clinical Sleep Medicine, Vol. 11, No. 11, 2015

Objective

- To assess the presence of right-to-left shunting (RLS) in patients with obstructive sleep apnea (OSA).
- To compare clinical characteristics and parameters of the sleep studies of patients with and without RLS.

Methods

- Patients with an abnormal polysomnogram seen at UCLA-Santa Monica Sleep Medicine Clinic were enrolled.
- A diagnosis of RLS was made using a transcranial Doppler (TCD) bubble study.
- Gender and age-matched controls were drawn from patients referred for cardiac catheterization who underwent a TCD.
- The frequency of RLS in OSA patients and the controls were evaluated.
- Clinical characteristics and polysomnogram parameters were compared between OSA patients with and without a RLS.

Results

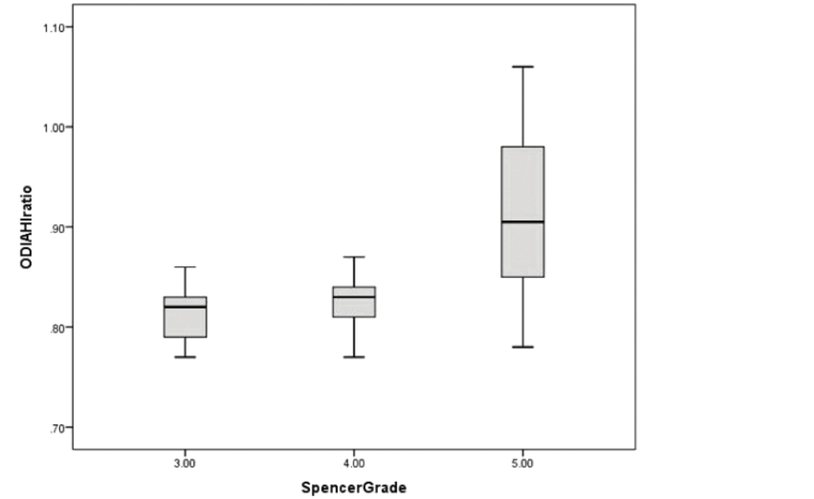
- A total of 100 OSA patients and 200 controls participated in the study.
- The prevalence of RLS was higher in patients with OSA compared to the control group (42% versus 19%; $p < 0.0001$).
- Patients with OSA and a RLS had a lower apnea-hypopnea index (AHI), less obstructive apnea, and fewer hypopnea episodes than patients with OSA without a RLS.
- The baseline and nadir SpO2 were similar in both groups and did not correlate with the level of RLS assessed by TCD.
- The degree of desaturation for a given respiratory disturbance, as measured by oxygen desaturation index (ODI)/AHI ratio, was higher in OSA patients with RLS versus OSA patients without RLS (0.85 ± 0.07 versus 0.68 ± 0.04; $p < 0.0001$).

Conclusion

- RLS, most commonly due to a PFO, occurs 2.2 times more frequently in OSA patients compared to a control population that was matched for age and gender.
- The severity of sleep apnea is not greater in OSA patients who have a PFO.
- However, patients with OSA and a PFO are more likely to become symptomatic at a younger age with an equivalent decrease in nocturnal SpO2, and have greater arterial desaturation in proportion to the frequency of respiratory disturbances.

Key Takeaways

- The most common cause of RLS is due to intermittent flow through a patent foramen ovale (PFO). PFO occurs more frequently in patients with OSA and may be involved in the exacerbation of OSA.
- It is hypothesized that patients with OSA who have a PFO with RLS are more likely to become symptomatic earlier compared with a person with OSA who does not have a RLS.
- Patients with sleep apnea and RLS, even without the high frequency of expected risk factors (high BMI, large neck circumference, high AHI), may still have hypoxemia and significant frequency of arousals. This suggests that the RLS contributes to producing hypoxemia and symptoms at a lower level of obstruction to airflow resulting in presentation of OSA at a younger age.
- These patients emphasize the need for a reliable OSA diagnosis test, which can also report arousals and hypoxemia states.
- It has been demonstrated that treatment with CPAP can reverse shunting in these patients, a fact which even emphasizes more the importance of detection and treatment of OSA for those patients.



Comparison of ODI/AHI in patients with OSA and PFO stratified by Spencer Grade:
Spencer grade is used to assess degree of shunting. Increase in grade correlates with more severe shunting. This illustration depicts that more severe shunting correlated with higher ODI/AHI ratio. AHI, apneahypopnea index; ODI, oxygen desaturation index.

Obstructive Sleep Apnea in Acute Stroke

Ifergane et al Stroke. 2016;47:1207-1212

Objective

- To prospectively evaluate clinical characteristics and laboratory markers of inflammation and coagulability, associated with OSA severity during the acute post stroke period.

Methods

- Consecutive patients admitted to the department of Neurology after an acute ischemic stroke were evaluated during the first 48 hours of symptom onset using WatchPAT.
- Morning blood samples of the patient were tested for tumor necrosis factor, interleukin-6, and plasminogen activator inhibitor-1 levels.
- Primary outcomes of the analysis were the prevalence of sleep apnea among patients with stroke and levels of proinflammatory cytokines during acute stroke period.
- Secondary outcomes included NIHSS at admission and discharge and hospitalization length, compared between the groups of patients with and without OSA.

Results

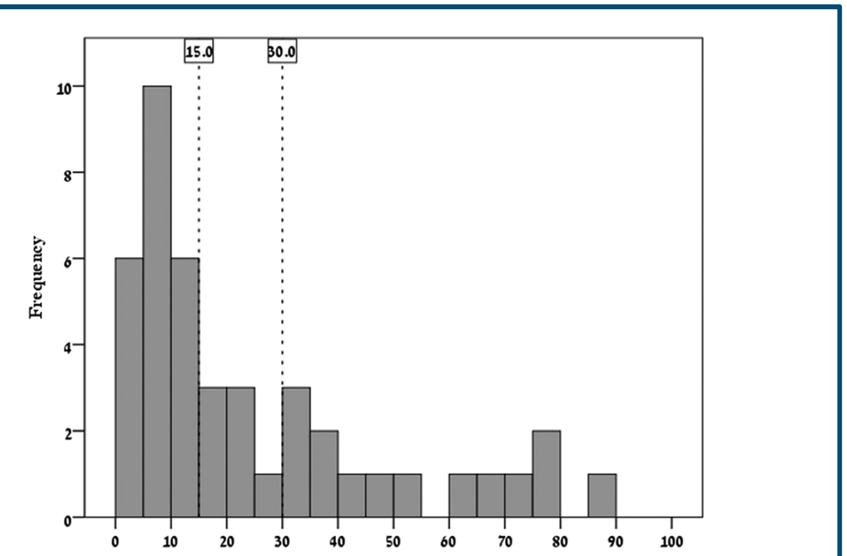
- OA total of 43 patients with acute stroke were admitted during the study period.
- 22 (51%) of which have been found to have moderate sleep apnea (apnea hypopnea index [AHI]≥15), AHI≥5 was found in 86% of the patients, and severe OSA (AHI≥30) in 32.5%
- Patients with OSA (AHI≥15) did not differ from the rest in stroke severity or symptoms, yet they had higher prevalence of recurrent stroke and atrial fibrillation.
- All 3 biomarker levels were higher among patients with AHI≥15: Tumor necrosis factor (6.39 vs 3.57 pg/mL), interleukin-6 (6.64 vs 3.14 pg/mL), and plasminogen activator inhibitor-1 (176.64 vs 98.48 pg/mL).
- After the stratification of AHI into 3 groups (AHI<5, 5–14, and ≥15), the analysis showed that only the highest AHI group differed from the other 2 groups in biomarker levels.

Conclusion

- Use of bed-side somnography technology (WatchPAT) revealed that in an unselected sample of patients with acute ischemic stroke, almost 90% had sleep-disordered breathing, with a third having a severe form of the disorder.
- Sleep disordered breathing was associated with significantly increased levels of inflammatory biomarkers, providing possible pathophysiological explanation of OSA-associated stroke risk.
- These results warrant prospective screening of patients with stroke for the presence of sleep-disordered breathing and lay the rationale for an interventional trial.

Key Takeaways

- The diagnosis of OSA has a major role, regarding patients after an acute ischemic stroke.
- The validity of the diagnosis of OSA was already studied in the past, and the WatchPAT was found to be a reliable alternative to polysomnography (PSG) for confirmation of clinically suspected sleep apnea.
- The use of WatchPAT technology is convenient and enables rapid diagnosis and therapeutic recommendations as part of a secondary prevention program.



Distribution of apnoea hypopnea index in patient population. AHI indicates Apnoea hypopnea index

Variables	AHI<15, n=22	AHI≥15, n=21	*P* Value
Stroke severity			
NIHSS on admission, median (IQR)	4 (2–5)	4 (2–5)	0.79
mRS baseline	0 (0–0)	0 (0–1)	0.25
Stroke symptoms			
Dysarthria	3 (14.3%)	6 (30.0%)	0.27
Dysphagia	1 (4.5%)	0 (0.0%)	1.0
Aphasia	7 (31.8%)	6 (30.0%)	1.0
Motor	18 (81.8%)	14 (70.0%)	0.47
Sensor	8 (36.4%)	3 (15.0%)	0.11
Visual fields	0 (0.0%)	2 (10.0%)	0.22
Ataxia	3 (13.6%)	1 (5.0%)	0.6

Stroke Symptoms and Severity Characteristics

Effect of Obstructive Sleep Apnea on Frequency of Stroke in Patients with Atrial Fibrillation

Yaranov et al. The Journal of American Cardiology, 2015, Volume 115, Issue 4, Pages 461–465

Objective

- Obstructive sleep apnea (OSA) is an independent risk factor for ischemic stroke that is not included in the usual cardioembolic risk assessments for patients with atrial fibrillation (AF).
- The objective of this study was to investigate the impact of OSA on stroke rate in patients with AF.

Methods

- Patients with AF and new diagnoses of OSA were identified from retrospective chart review.
- Patients with histories of stroke at the time of the sleep study were excluded.
- Diagnosis of OSA was made by performing overnight polysomnographic studies.
- The primary outcome was the incidence of stroke, determined by a physician investigator blinded to the results of polysomnography.
- Subgroup analysis was performed among different CHADS2 and CHA2DS2-VASc scores.

Results

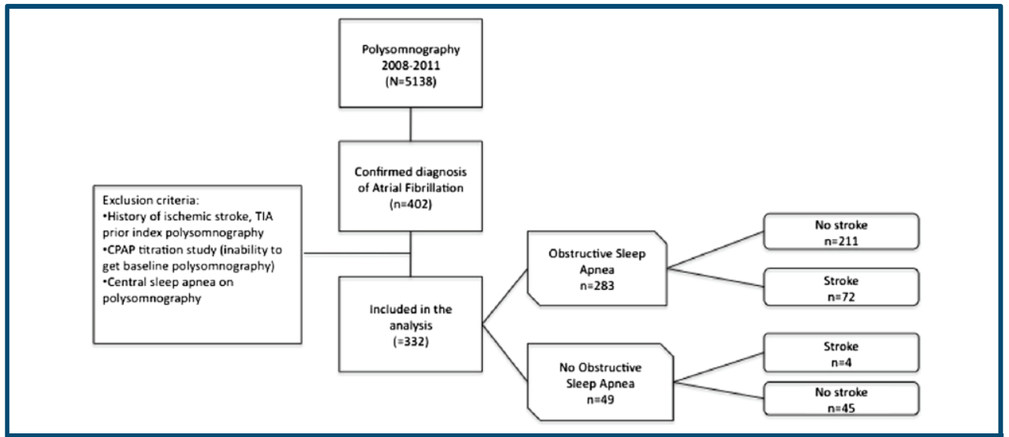
- Out of 5,138 patients screened for OSA, 402 (7.7%) had AF and 332 (6.4%) met the inclusion criteria.
- Among the study population, the occurrence of first-time stroke was 22.9%.
- Ischemic stroke was more common in patients with OSA compared with patients without (25.4% vs 8.2% respectively, p = 0.006).
- After controlling for age, male gender, and coronary artery disease, the association between OSA and stroke remained statistically significant, with an adjusted odds ratio of 3.65 (95% confidence interval 1.252 to 10.623).
- A positive dose effect of the apnea-hypopnea index on the rate of stroke was observed (p = 0.0045).
- Subgroup analysis showed significantly higher rates of stroke in patients with CHADS2 scores of 0 and CHA2DS2-VASc scores of 0 and 1 and co-morbid OSA.

Conclusion

- AF patients with OSA are 3.6 times more likely to have a first-time stroke than those without.
- OSA in patients with AF is an independent predictor of stroke.
- This association may have important clinical implications in ischemic stroke risk stratification.

Key Takeaways

- The high rates of OSA in patients with AF and the elevated risk of first-time stroke at AF patients with OSA, demonstrate the importance of screening in this patient population.
- Treatment of OSA with CPAP may result a lower rate of stroke at patients with AF. This emphasizes the importance of early detection and treatment of OSA in this group of patients.
- The presence of OSA is suggested to be considered in the cardioembolic risk assessment in AF patients, emphasizing even more the importance of OSA diagnosis.



Design of the study

Obstructive Sleep Apnea- Hypopnea and Incident Stroke

Redline, Yenokyan, Gottlieb, et al. AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 182 2010

Objective

- To quantify the incidence of ischemic stroke with sleep apnea in a community-based sample of men and women across a wide range of sleep apnea.
- The objective of this study was to investigate the impact of OSA on stroke rate in patients with AF.

Methods

- Baseline polysomnography was performed over participants between the years 1995-1998, in a longitudinal cohort study.
- The primary exposure was the obstructive apnea–hypopnea index (AHI) and outcome was incident ischemic stroke.
- Incident stroke was defined as the first occurrence of stroke between the date of the baseline polysomnogram and the end of follow-up.

Results

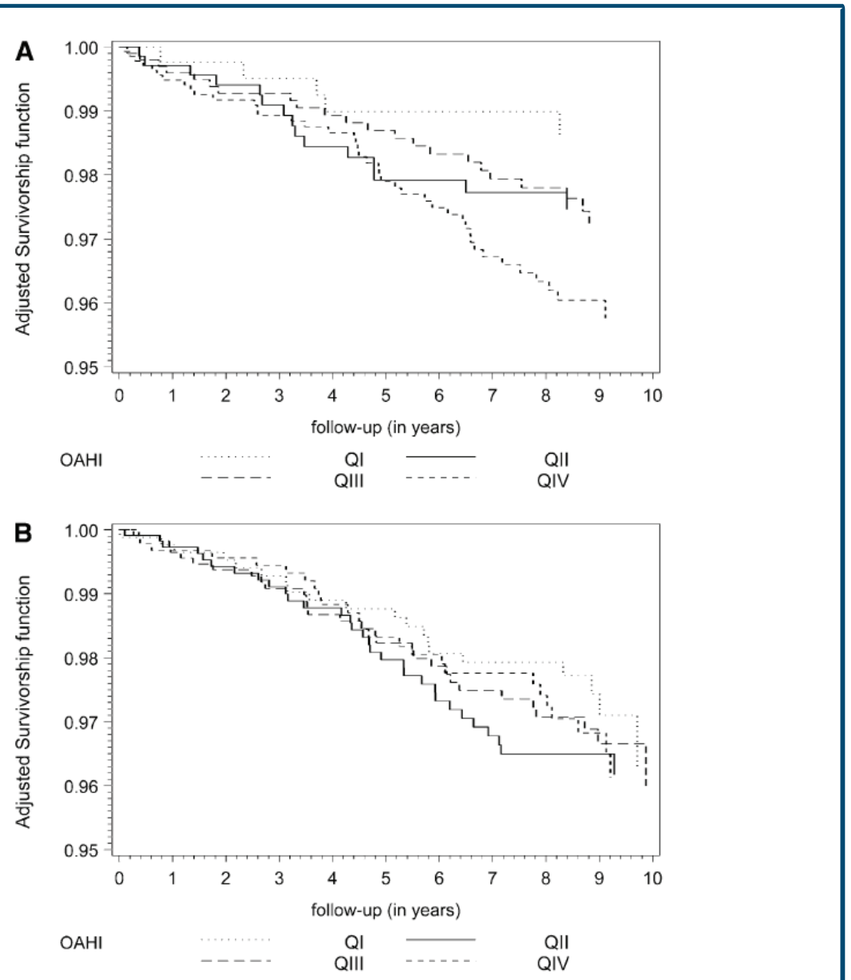
- A total of 5,422 participants, without a history of stroke at the baseline examination and untreated for sleep apnea, were followed for a median of 8.7 years. 193 ischemic strokes were observed.
- In covariate-adjusted Cox proportional hazard models, a significant positive association between ischemic stroke and AHI was observed in men (P value for linear trend: P = 0.016).
- Men in the highest AHI quartile (AHI>19) had an adjusted hazard ratio of 2.86 (95% confidence interval, 1.1–7.4).
- In the mild to moderate range (AHI = 5–25), each one-unit increase in AHI in men was estimated to increase stroke risk by 6% (95% confidence interval, 2–10%).
- In women, stroke was not significantly associated with AHI quartiles, but increased risk was observed at an AHI>25.

Conclusion

- Men with increasing AHI levels experience an increased risk of stroke.
- The effect size for stroke for OAHI levels in the upper quartile was comparable to that for a 10-year increase in age or atrial fibrillation.

Key Takeaways

- The strong adjusted association between ischemic stroke and AHI in community-dwelling men with mild to moderate sleep apnea suggests that this is an appropriate target for future stroke prevention trials.
- The evaluation of OSA in patients, as well as OSA treatment, might both have a key role in ischemic stroke risk reduction.



Adjusted Kaplan-Meier stroke-free survival estimates as a function of obstructive apnea–hypopnea index (AHI) quartile. Values are modeled in this graph for white current smoker (A) men and (B) women, with no use of antihypertensive medications, with mean values of other covariates.
The first (AHI, 4.5), second (4.05–9.5), third (9.5–19.1), and fourth quartiles (.19.1) of the AHI are shown by the various solid and dashed lines indicating the quartiles.

Sudden Cardiac Death

Day-Night Variation of Acute Myocardial Infraction in Obstructive Sleep Apnea

Sert Kuniyoshi et al JACC Vol. 52, No. 5, 2008 July 29, 2008:343–6

Objective

- To evaluate the day–night variation of acute myocardial infarction (MI) in patients with obstructive sleep apnea (OSA).
- The objective of this study was to investigate the impact of OSA on stroke rate in patients with AF.

Methods

- 92 patients were prospectively studied with MI for which the time of onset of chest pain was clearly identified.
- The presence of OSA was determined by overnight polysomnography.
- An apnea–hypopnea index (AHI) ≥5 established the diagnosis of OSA.

Results

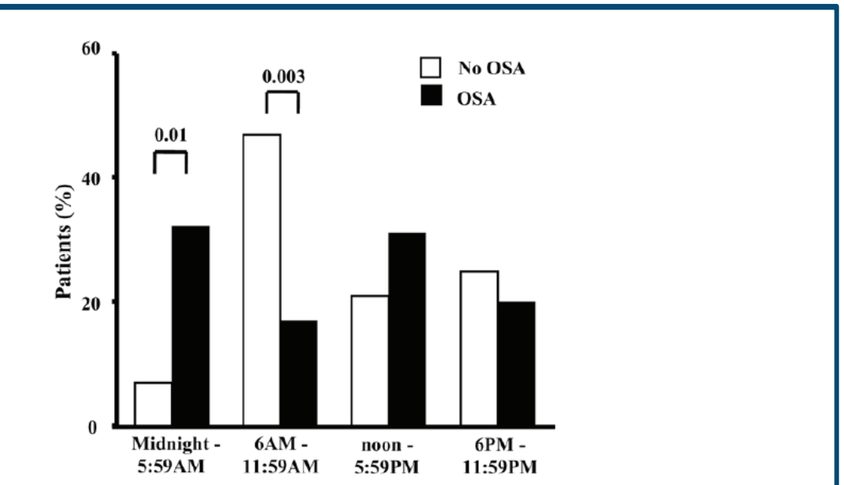
- For patients with and without OSA, the frequency of MI during different intervals of the day based on the onset time of chest pain was compared.
- The groups had similar prevalence of comorbidities.
- Myocardial infarction occurred between 12 AM and 6 AM in 32% of OSA patients and 7% of non-OSA patients (p = 0.01).
- The odds of having OSA in those patients whose MI occurred between 12 AM and 6 AM was 6-fold higher than in the remaining 18 h of the day (95% confidence interval: 1.3 to 27.3, p = 0.01).
- Of all patients having an MI between 12 AM and 6 AM, 91% had OSA.

Conclusion

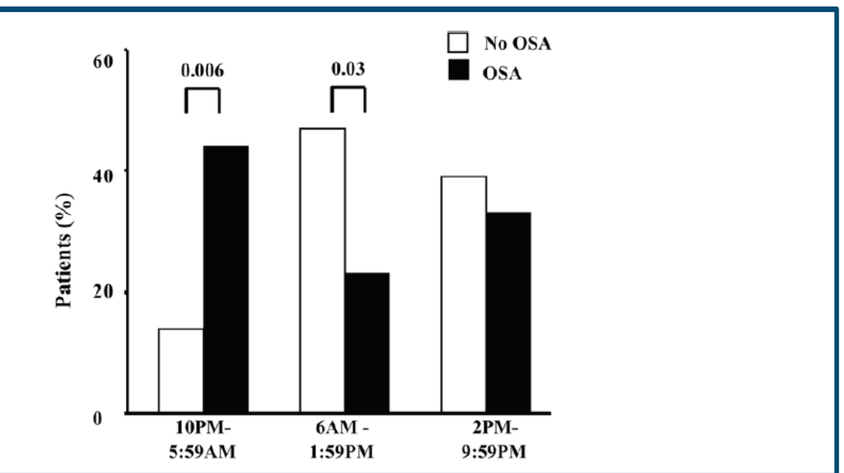
- OSA patients have an increased risk of MI between 12 AM and 6 AM, compared with non-OSA patients.
- The diurnal variation in the onset of MI in OSA patients is strikingly different from the diurnal variation in non-OSA patients.
- Patients with nocturnal onset of MI have a high likelihood of having OSA.

Key Takeaways

- TOSA might be a trigger for MI.
- Patients having nocturnal onset of MI should be evaluated for OSA.
- Treatment of OSA might have a great importance in future prevention of nocturnal cardiac events.



6-h Epochs of MI Occurrence: Day–night pattern of myocardial infarction based on four 6-h time intervals in OSA (n = 64) and non-OSA (n = 28) patients.



8-h Epochs of MI Occurrence: Day–night pattern of myocardial infarction based on three 8-h time intervals in OSA (n = 64) and non-OSA (n = 28) patients

Obstructive Sleep Apnea and the Risk of Sudden Cardiac Death: A Longitudinal Study of 10,701 Adults

Gami et al. J Am Coll Cardiol. 2013 August 13; 62(7)

Objective

- To identify the risk of sudden cardiac death (SCD) associated with obstructive sleep apnea (OSA).
- OSA is linked to cardiovascular disease and arrhythmias, and has been shown to increase the risk of nocturnal SCD.
- The objective of this study was to investigate the impact of OSA on stroke rate in patients with AF.

Methods

- 10,701 participants, consecutive adults undergoing their first diagnostic polysomnogram between the years 1987-2003, were included in the study.
- The indication for sleep studies in the vast majority of subjects was suspected sleep disordered breathing.
- During follow-up up to 15 years, incident resuscitated or fatal SCD have been assessed in relationship to the presence of OSA, physiological data including the apnea-hypopnea index (AHI) and nocturnal oxygen saturation (O2sat) parameters, and relevant comorbidities.

Results

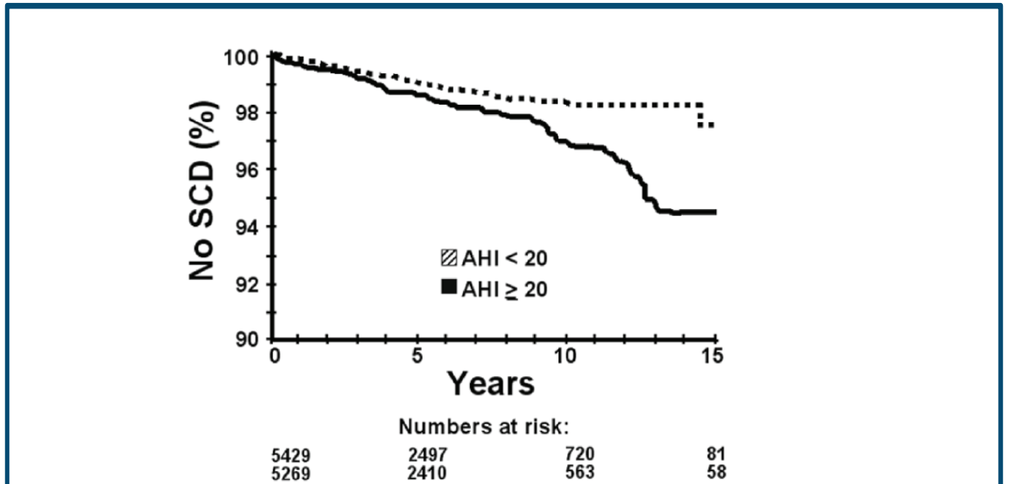
- During an average follow-up of 5.3 years, 142 patients had resuscitated or fatal SCD (annual rate 0.27%).
- In multivariate analysis, independent risk factors for SCD were age, hypertension, coronary artery disease, cardiomyopathy or heart failure, ventricular ectopy or non-sustained ventricular tachycardia, and lowest nocturnal O2sat (per -10%, HR 1.14, P=0.029).
- SCD was best predicted by age >60 years (HR 5.53), AHI >20 (HR 1.60), mean nocturnal O2sat <93% (HR 2.93), and lowest nocturnal O2sat <78% (HR 2.60, all P<0.0001).

Conclusion

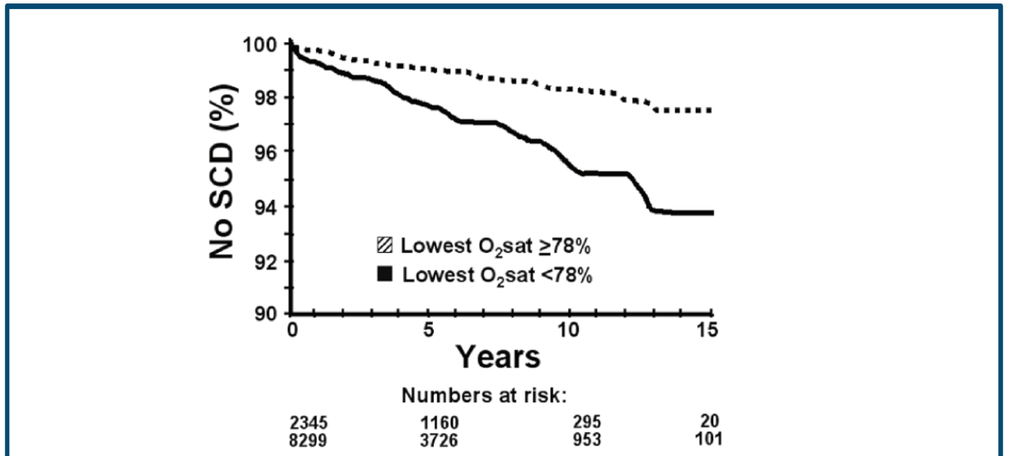
- In a population of 10,701 adults referred for polysomnography, OSA predicted incident SCD and the magnitude of risk was predicted by multiple parameters characterizing OSA severity.
- Nocturnal hypoxemia, an important pathophysiological feature of OSA, strongly predicted SCD independently of well-established risk factors.

Key Takeaways

- OSA, a prevalent condition, is implicated as a novel risk factor for SCD.
- Early diagnosis of OSA, as well as treatment, might be highly important for patients in select populations at risk for SCD.



Survival based on apnea hypopnea index:
Survival free of fatal or resuscitated sudden cardiac death (SCD) in the total study population, based on the apnea hypopnea index (AHI) threshold determined by classification and regression tree analysis (AHI < 20 vs. AHI ≥ 20).



Survival based on oxygen saturation:
Survival free of fatal or resuscitated sudden cardiac death (SCD) in the total study population, based on the lowest nocturnal oxygen saturation (O2sat) threshold determined by classification and regression tree analysis.

WatchPAT™

Sleep Apnea in Cardiac Diseases

Cardiology Clinical Compendium

REF MM219871.2 Edition 1

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