Effect of Obstructive Sleep Apnea in Acute Coronary Syndrome

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The effect of obstructive sleep apnea (OSA) on clinical outcomes after acute coronary syndrome (ACS) is incompletely defined. We sought to determine the prevalence of OSA in patients with ACS and evaluate prognostic impact of OSA and continuous positive airway pressure (CPAP) therapy in these patients. This was a prospective longitudinal cohort study of 73 patients admitted on cardiac intensive care unit for ACS. Cardiorespiratory sleep study and/or polysomnography were performed in all patients. CPAP was recommended if Apnea−Hypopnea Index ≥5. The main study outcome was a composite of death for any cause, myocardial infarction, and myocardial revascularization. OSA was diagnosed in 46 patients (63%). Age and cardiovascular risk factors were not significantly different between groups. OSA was classified as mild (m-OSA) in 14 patients (30%) and as moderate-to-severe (s-OSA) in 32 patients (70%). After a median follow-up of 75 months (interquartile range 71 to 79), patients with s-OSA had lower event-free survival rate. After adjustment for gender, patients with s-OSA showed a significantly higher incidence of the composite end point (hazard ratio 3.58, 95% CI 1.09 to 17.73, p = 0.035). Adherence to CPAP occurred in 19 patients (41%), but compliance to CPAP therapy did not reduce the risk of composite end point (hazard ratio 0.87, 95% CI 0.31 to 2.46, p = 0.798). In conclusion, OSA is an underdiagnosed disease with high prevalence in patients with ACS. It is urgent to establish screening protocols because those have high diagnostic yield and allow identifying a group of patients with manifestly unfavorable prognosis. **(Am J Cardiol 2016;117:1084−1087)**

The association between obstructive sleep apnea (OSA) and cardiovascular disease has been previously described. A higher prevalence of OSA was found in those with hypertension and other cardiovascular disorders, including coronary artery disease, stroke, and atrial fibrillation.[1] A prevalence of OSA up to 66% has been reported in the early phase of acute coronary syndrome (ACS).[2] However, the role of OSA as an adverse prognostic marker after ACS, although plausible, remains to be proved. Findings from published reports on the effect of OSA on clinical outcomes after ACS are conflicting and existing reports were limited by short follow-up duration.[3−5] In this study, we sought to determine the prevalence of OSA in patients with ACS. We intend to evaluate the long-term prognostic impact of OSA in patients with ACS and the effect of continuous positive airway pressure (CPAP) therapy.

Methods

This was a prospective longitudinal cohort study of a sample of 73 patients admitted on cardiac intensive care unit for ACS. First patient admitted for ACS on a previously defined day of the week was selected to be included. Patients with known OSA diagnosis were excluded. After agreeing to participate, all patients underwent a cardiorespiratory sleep study after clinical stabilization.

Cardiorespiratory sleep studies were performed using a portable diagnostic device (Stardust II, Respironics, Murrysville, PA). The parameters measured included nasal airflow (nasal cannula), thoracoabdominal movements (inductive respiratory bands), arterial oxygen saturation (pulse oximetry), snoring episodes (derived from the integrated pressure transducer), and body position. An Apnea−Hypopnea Index (AHI) ≥30 was considered positive of OSA and treated. Patients with AHI <30 or suggestion of Cheyne-Stokes ventilation underwent polysomnography (PSG) to confirm diagnosis and quantify the breathing disorder, after discharge from index admission.

PSG was performed with the oversight of a sleep technologist using an Alice 4 device. The parameters measured were nasal airflow (nasal cannula thermistor), thoracoabdominal movements (inductive respiratory bands), arterial oxygen saturation (pulse oximetry), electroencephalography, electrooculogram, chin and tibial electromyograms, electrocardiogram, snoring episodes (derived from the integrated pressure transducer), and body position.

One reviewing physician interpreted polysomnographic recordings. The definitions of apneas and hypopneas were based on the American Academy of Sleep Medicine criteria that were valid at the time of the screening (2007/2008)[6]:

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apnea requires a decrease in peak thermal sensor excursion by >90% of baseline for >10 seconds; hypopnea requires a ≥30% decrease in the nasal pressure transducer signal for >10 seconds and a desaturation ≥4% compared with the previous event baseline.

OSA was defined as mild for AHI ≥5 and <15, moderate for AHI ≥15 and <30, and severe for AHI ≥30.

Patients with diagnosis of OSA were referred to CPAP therapy.

Clinical outcomes were collected through patient visit, telephone calls, and/or reviews of medical records. Clinical outcome measurements included death for any cause, myocardial infarction, and myocardial revascularization.

Continuous variables are described as mean and SD or median and interquartile range (IQR) as adequate, whereas categorical variables are described as numbers and percentages. Differences in clinical and procedural characteristics between patient groups were analyzed by the unpaired Student *t* tests or Mann−Whitney tests (continuous data) and chi-square tests or Fisher's exact tests (categorical data) as adequate. The time to event was calculated from the date of index admission to the date when the first adverse event occurred. Patients in whom there has been no evidence of an adverse event were censored at the date of last follow-up. Event-free survival curves were constructed using the Kaplan−Meier methods and compared using the log-rank test. Cox proportional hazards regression analysis was also performed. All statistical analyses were carried out using SPSS software version 20. A p value <0.05 was considered significant.

Results

Seventy-three patients presenting with ACS underwent a simplified sleep study after clinical stabilization. Simplified sleep study was positive (AHI >5) in 54 patients (74%). A complete sleep study was performed 55 days (IQR 31 to 77) after ACS admission and confirmed the diagnosis in 46 patients, representing a prevalence of 63%. In patients in whom OSA diagnosis was confirmed, the severity of disease was classified in the same way by both methods. Patient demographic and clinical characteristics are presented in Table 1. Most of the study patients (75%) were men, and the average age was 62.4 ± 11.3 years. No significant differences were observed between the 2 groups in terms of gender, cardiovascular risk factors (hypertension, diabetes mellitus, body mass index, dyslipidemia, and smoking), clinical presentation, or Killip's class during hospitalization. The vast majority of patients were in Killip I. Left ventricle ejection fraction assessed by echocardiography and infarct size estimated by troponin I levels were also comparable between the groups. The mean length of stay was 6.78 ± 0.44 days. Aspirin was prescribed for 89% of the patients, clopidogrel for 81%, β blockers for 73%, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers for 89%, and statins for 90% on discharge. There were no significant differences in the medications prescribed between groups.

Sleep related data are reported in Table 2. The average AHI and Epworth Sleepiness Scale score were higher in patients with OSA. OSA was classified as mild in 14 patients (30%), moderate in 11 patients (24%), and severe in 21 patients (46%).

The median follow-up time was 75 months (IQR 71 to 79). During the study period, 4 patients of non-OSA group had at least one event—3 deaths, 1 myocardial infarction, and 1 revascularization. Two patients of mild-OSA (m-OSA) group had events—1 death, 2 myocardial infarctions, and 1 revascularization. Thirteen patients of

Table 1
General characteristics of the study groups

Variable	Overall (n=73)	Obstructive Sleep Apnea		p value
		Yes (n=46)	No (n=27)	
Men	55 (75%)	38 (83%)	17 (63%)	0.060
Age (years), mean ± SD	62.4 ± 11.3	63.5 ± 10.3	60.6 ± 12.7	0.304
BMI (Kg/m^2), mean ± SD	27.6 ± 3.7	27.8 ± 3.8	27.2 ± 3.4	0.561
Hypertension	54 (74%)	36 (78%)	18 (67%)	0.276
Diabetes Mellitus	24 (33%)	16 (35%)	8 (30%)	0.651
Dyslipidemia	55 (75%)	37 (80%)	18 (67%)	0.188
Smoking	13 (18%)	8 (17%)	5 (18%)	0.768
COPD	15 (20%)	8 (17%)	7 (26%)	0.384
Clinical Presentation				
Unstable Angina Pectoris	12 (16%)	6 (22%)	6 (13%)	
NSTEMI	32 (44%)	20 (44%)	12 (44%)	0.518
STEMI	29 (40%)	20 (44%)	9 (33%)	
Killip class				
I	64 (88%)	40 (87%)	24 (89%)	
II	3 (4%)	2 (4%)	1 (4%)	0.889
III	1 (1%)	1 (2%)	0 (0%)	
IV	5 (7%)	3 (6%)	2 (7%)	
Lenght of stay (days), median (IQR)	6.0 (4.0-8.8)	7.0 (5.0-9.0)	5.5 (3.8-7.5)	0.292
Ejection Fraction (%), mean ± SD	50.1 ± 9.0	49.4 ± 9.2	51.2 ± 8.7	0.462
Peak Troponin I (ng/mL), mean ± SD	27.8 ± 35.5	27.7 ± 36.3	28.0 ± 34.8	0.974

BMI = body mass index; COPD = chronic obstructive pulmonary disease; IQR = interquartile range; NSTEMI = non−ST-elevation myocardial infarction; SD = standard deviation; STEMI = ST-elevation myocardial infarction.

Table 2
Sleep study characteristics

Variable	Overall	Obstructive Sleep Apnea		p value
		Yes (n=46)	No (n=27)	
No. of days from ACS to sleep study, median (IQR)	55 (31-77)	45 (23-77)	62 (50-77)	0.117
AHI (events/hour), mean ± SD	20.0 ± 22.8	30.6 ± 23.0	2.3 ± 3.2	<0.001
Epworth Sleepiness Scale, mean ± SD	7.3 ± 5.1	8.8 ± 5.5	5.1 ± 3.5	0.006

ACS = acute coronary syndrome; AHI = Apnea−Hypopnea Index; IQR = interquartile range; SD= standard deviation.