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TIME COURSE OF CARDIAC TROPONIN IN PATIENTS WITH ACUTE CORONARY SYNDROME AND SLEEP APNOEA: A PILOT STUDY

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ABSTRACT

We compared the time course of cardiac troponin-I (cTn-I) in patients admitted for acute coronary syndrome (ACS) with and without obstructive sleep apnoea (OSA).

Blood samples were collected every 6 hours from the time of admission until 2 consecutive assays showed a downward trend for the cTn-I assay.

We included 89 OSA and 38 non-OSA patients with an apnoea-hypopnoea index (AHI) (median [interquartile ranges (IQR)] of 32 [20.8, 46.6] h⁻¹ and 4.8 [1.6, 9.6] h⁻¹, respectively. The daytime peak cTn-I levels were significantly higher in the non-OSA than in the OSA patients (p=0.04). In the non-OSA patients, a variation in the peak daytime cTn-I levels was observed compared with those at night: median [IQR] 54.9 [7.6,81.2] vs. 7.9 [1.2,23.1] ng·ml⁻¹; p=0.03, respectively. In the OSA group, no significant cTn-I diurnal variation was observed. However, when the OSA patients were stratified according to the median AHI, a significant diurnal variation in the peak cTn-I levels was evident in the mild-to-moderate OSA patients (AHI <32h⁻¹) that was not observed in the severe OSA patients.

This study suggests that OSA and its severity are associated with a different cTn-I time course, a finding that might indicate possible myocardial protection from severe OSA.

INTRODUCTION

Acute coronary syndrome (ACS) affects 1% of the adult world population and is a leading cause of death worldwide, wherein one-third of all deaths are due to cardiovascular disease (CVD) [1]. Obstructive sleep apnoea (OSA) is a highly prevalent breathing disorder that affects at least 10% of middle-aged men and 3% of middle-aged women [2, 3]. The risk of developing OSA increases with age [4]; moreover, OSA has been associated with major cardiovascular morbidity and mortality and is likely to be an independent risk factor for CVD [5, 6].

OSA is characterized by recurrent episodes of partial or total upper airway obstruction during sleep, which leads to intermittent hypoxia, brain arousal and intrathoracic pressure changes. These events activate underlying intermediate mechanisms that predispose OSA patients to the initiation and aggravation of CVD [6].

Because of their potential negative effects when coexistent, the relationship between OSA and CVD has received increasing attention among scientists. In fact, patients with ACS are at an increased risk for fatal and non-fatal cardiac events, and the prevalence of OSA has been reported to be as high as 65.7% in patients admitted for ACS [7]. However, the interaction and impact of OSA on ACS severity and prognosis is mostly unknown. Moreover, despite the existence of closely interrelated and detrimental mechanisms that link OSA and CVD, epidemiological studies suggest that a protective mechanism may exist in patients with OSA [8]; although such a mechanism may have a pertinent clinical impact, its presence remains under debate. While several studies described superior post-operative survival in patients with OSA compared to that of patients without OSA [9] along with studies that showed increased survival of elderly patients with mild OSA [10], other authors described worse post-operative outcomes after an episode of ACS, such as myocardial infarction in patients with sleep disordered-breathing (SDB), compared with patients without SDB [11-13].

OSA may confer a degree of myocardial protection by activating ischaemic preconditioning mechanisms primarily through intermittent hypoxia. This sequence appears particularly evident in patients with acute myocardial injury and mild-to-moderate OSA [8] due to adaptive mechanisms associated with cardioprotection. Moreover, in animal models, exposure to mild or moderate intermittent hypoxia is compatible with the activation of cardio- and neuro-protection pathways. In these models, a reduction of tissue damage (infarct size) was observed in relation to the

time and degree of intermittent hypoxia (IH) exposure[14]. In contrast, other groups of investigators found deleterious effects of IH in animal models and recently described IH exposure as having potentially detrimental effects causing vascular remodelling in a mice model [15].

Cardiac troponin (cTn) is a sensitive marker of cardiac injury and is the preferred clinical biomarker for the diagnosis or exclusion of acute myocardial infarction in the acute care setting; thus, cTn has become the biomarker of choice in the assessment and evaluation of myocardial injury [16]. The magnitude of cTn elevation correlates with the extent of myocardial necrosis and is related to the subsequent risk of adverse outcomes, thereby predicting poor prognosis [17]. cTn levels are more sensitive for the diagnosis of myocardial infarction than to other clinically available biomarkers, such as myoglobin, the MB fraction of creatine kinase (CK-MB), myeloperoxidase, and heart fatty acid-binding protein [18]. Recently, more sensitive cTn assays (high-sensitivity cTn) have been developed. Interestingly, studies suggest that high-sensitivity cTn-T is elevated in patients with OSA [19, 20] . A recent study found that based on cTn-T levels, patients with OSA had less severe cardiac injury during an acute non-fatal myocardial infarction than patients without OSA [21].

Previous studies have suggested that OSA is associated with CVD. Paradoxically, as some studies have suggested, the presence of OSA might activate mechanisms with cardioprotective effects that might be reflected by a change in the expression of cardiac damage markers. The study of the time course of cardiac injury markers in patients with OSA who sustain an episode of ACS may contribute to a better understanding of the interactions and potentially the impact of OSA among ACS subjects. We sought to investigate the impact of OSA on the time course of markers of severity in ACS patients. We hypothesized that the presence of chronic intermittent hypoxia episodes during sleep in OSA patients affects cTn expression in patients who sustain an episode of ACS.

METHODS

Study Design and Subjects

This observational, prospective study of 127 patients admitted to the University Hospital Arnau de Vilanova (Lleida, Spain) (Fig. 1) is an ancillary study of the ISAACC

cohort (a randomized trial of NCT01335087 (Continuous Positive Airway Pressure (CPAP) in Patients with Acute Coronary Syndrome and Obstructive Sleep Apnoea (ISAACC)). The aim of that multicentre, open-label, parallel, prospective, randomized controlled trial [22], was to evaluate the effect of CPAP treatment on the incidence of new cardiovascular events in patients with an episode of ACS and OSA. The ISAACC study includes non-sleepy patients due to the ethical issues involved in withholding treatment for OSA patients with excessive daytime sleepiness. In this study, we evaluated patients consecutively admitted to the coronary care unit or hospital cardiology room with a diagnosis of ACS. The criteria for inclusion were the detection of a rise and/or fall of cardiac biomarker values [preferably cTn] with at least one value above the 99th percentile upper reference limit (URL). Additionally, patients were required to have at least one of the following: symptoms of ischaemia; new or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBBB); development of pathological Q waves in the ECG; and imaging evidence of new loss of viable myocardium or new regional wall motion abnormality [23].

After patients agreed to participate and the consent form was signed, all patients underwent respiratory polygraphy in the first 24-72 hours after admission to assess the presence of OSA. Those patients with an apnoea-hypopnea index (AHI) of ≥ 15 events \cdot h⁻¹ were considered to have OSA and were randomized to conservative or CPAP treatment. Those with an AHI of < 15 events \cdot h⁻¹ were included in the non-OSA group. Considering the higher number of patients with an AHI of < 15 events \cdot h⁻¹ than those with an AHI of ≥ 15 events \cdot h⁻¹ and that the rate of inclusion into the reference group (non-OSA patients) needed to match that of the randomized patients, a probabilistic mechanism integrated into the web-based program randomly selected patients once the sleep test results were known. This probabilistic mechanism follows a random selection that includes one of each three patients with an AHI < 15 events \cdot h⁻¹. The randomization is generated by the computer automatically through an internal function of the computer mathematical processor, as performed by statistical packages. No external factor can affect the results of the manoeuvre. This method guarantees that the group of patients with an AHI < 15 events \cdot h⁻¹ includes a similar and proportional number of patients with an AHI ≥ 15 events \cdot h⁻¹, the latter constituting the group of patients randomized to conservative or CPAP treatment in the ISAACC study. For the present study, we included all patients with an AHI ≥ 15

events·h⁻¹ and the randomly selected patients with an AHI <15 events·h⁻¹

Only patients selected by the website were included in the study. Additionally, during the hospital stay, we analysed the time course of cTn-I expression in all the included patients. In the current study, we compared the time course of cTn-I expression in patients with ACS included in the OSA group versus the non-OSA group.

The ethics committee approved the study (approval number: 2010-852) and informed consent was obtained from all subjects.

Procedures

Clinical Examinations and Questionnaires

Demographic and anthropometric characteristics, a medical history and a detailed medication history were obtained, and questionnaires were administered the day before the sleep study. Cardiovascular health was assessed through the collection of information regarding a history of diabetes, hypertension, dyslipidaemia, first episode of ACS, cardiomyopathy, stroke, neuropathy and neurological disease.

Sleep Study

The diagnosis of OSA was made according to the guidelines of the national consensus on the apnoea-hypopnea syndrome [24]. All participants underwent overnight cardio-respiratory polygraphy with the same model of device (Embletta; ResMed, Bella Vista, Australia). The variables measured included oronasal flow, thoracoabdominal movements, ECG, and pulse oximetry. An obstructive apnoea episode was scored when a complete cessation of airflow lasted for ≥10 seconds. An episode of hypopnea was defined as a reduction in airflow for ≥10 seconds associated with a >4% decrease in arterial oxygen saturation. Cardio-respiratory polygraphy studies were performed without supplemental oxygen.

Cardiac Biomarkers

We assessed the expression of cTn-I as a marker of myocardial injury. Routine biochemical analyses in patients admitted for ACS were performed during the hospital stay. To evaluate the time course of cTn-I, blood samples were drawn at six-hour intervals from the time of admission until decrements in two consecutive cTn-I measurements ensued. The peak cTn-I value provides a relative estimate of infarct size [25]. The quantitative determination of cTn-I levels was performed via

chemiluminescence immunoassay (AccuTnI+3 Beckman-Coulter. Unicel Dxl 600 Beckman-Coulter autoanalyser).

Statistical Analysis

Continuous variables were summarized as the means (standard deviations) or medians [interquartile ranges] when distributions were skewed. Participant characteristics were compared using Student's test, analysis of variance (ANOVA), or non-parametric Mann-Whitney and Kruskal-Wallis tests for skewed data.

We determined at which time of day the peak cTn-I level was reached for each patient. Then, we compared the diurnal variation in peak cTn-I for the groups analysed.

The diurnal variation in cTn-I expression was assessed using non-parametric smoothing splines to represent the observed nonlinearity of the cTn-I peak. The time course of peak cTn expression was compared between patients with and without OSA. Stratified comparisons of the peak cTn-I time course for OSA patients by AHI levels (15-32 events·h⁻¹ vs. >32 events·h⁻¹) and by oxygen desaturation index (ODI) levels (<20.2 h⁻¹ vs. >20.2 h⁻¹) were performed.

Additionally, this study used cluster analysis to prove whether distinct patient subgroups would emerge based on the time course of cTn-I expression. Cluster analysis is a mathematical approach to identify the existence of subgroups of individuals who cluster closer together in key measures but are dissimilar to individuals in other clusters.

All tests were two-tailed, and p-values of <0.05 were considered statistically significant. The R statistical software, version 3.3.1, was used for all the analyses.

RESULTS

Among the 127 patients enrolled, 89 were found to have OSA (AHI ≥15 events·h⁻¹). The clinical characteristics and demographic variables of the patients are shown in Table 1. No significant differences were observed between the OSA and non-OSA patients in terms of gender age and prevalence of cardiovascular risk factors (hypertension, diabetes mellitus, body mass index, dyslipidaemia and smoking). Compared with the non-OSA patients, the OSA patients had a higher number of stents placed during percutaneous coronary intervention (PCI) (p=0.007). The peak cTn was not associated with the number of stents (Spearman's rho correlation

coefficient=0.13, $p=0.16$). We also found that a higher percentage of OSA patients than non-OSA patients were treated with a calcium-channel antagonist ($p=0.032$), likely due to the known association between OSA and hypertension [26]. Regarding the timing of the PCI (before or after the peak cTn-I), no difference was observed between the non-OSA and OSA patients ($p=0.85$).

No significant differences were observed between the OSA and non-OSA patients regarding, respectively, the mean values (SD) for the time of admission (7:17 am (8 h and 41 min) and 8:39 am (8 h and 26 min); $p=0.58$), time of the onset of symptoms (10:45 am (6 h and 24 min) and 11:35 am (6 h and 13 min); $p=0.55$) or time to peak cTn-I levels (after 9 h and 23 min (8 h and 14 min) and after 9 h and 19 min (7h and 35 min); $p=0.97$).

Three clusters of patients were identified based on the cTn-I curves obtained during the hospital stay after admission for ACS. We found a tendency towards a higher percentage of OSA patients in the cluster with lower cTn-I levels ($p=0.05$) (Fig. S1 and Table S1 in the online supplemental material).

The number of cTn-I levels measurements between the non-OSA and OSA groups did not differ significantly during the hospital stay (median [IQR] 2.00 [2.00, 3.00] and 2.00 [2.00, 3.00] for the OSA and non-OSA groups respectively; $p=0.65$).

For the non-OSA patients, a diurnal variation in peak cTn-I was observed, with significantly higher peak cTn-I levels during the daytime (10 am to 8 pm) than during the night-time (8 pm to 10 am) (median [IQR] 54.9 [7.6, 81.2] vs. 7.9 [1.2, 23.1] ng·ml⁻¹ for daytime and nighttime, respectively; $p=0.03$). In the OSA group, no significant diurnal variation was observed (median [IQR] 4.2 [0.3, 26.5] vs. 3.8 [0.6, 13.8] ng·ml⁻¹, for daytime and nighttime, respectively) (Figs. 2-3 and Table 2). Additionally, we found that the diurnal variations in the peak cTn-I levels were significantly higher in non-OSA patients than in OSA patients ($p=0.04$).

To further investigate the strength of the impact of OSA severity-related variables on the time course of cTn-I expression, we classified the OSA patients into two groups according to the observed AHI median value (median AHI for OSA patients =32 events·h⁻¹). We differentiated between OSA patients with mild-to-moderate OSA (AHI

15-32 events·h⁻¹) and OSA patients with high-severity OSA (AHI >32 events·h⁻¹). The characteristics and demographic variables of the patients groups are shown in Table S2 in the online supplemental material. We found that in patients with high OSA severity, no diurnal variation was observed in the peak cTn-I levels (median [IQR] 2.2 [0.1, 5.0] vs. 4.5 [0.7, 35.6] ng·ml⁻¹, for daytime and nighttime, respectively; p=0.22). However, in patients with mild-to-moderate OSA, a diurnal variation in peak cTn-I expression existed with significantly higher peak levels during the daytime than during the night-time (median [IQR] 24.4 [1.8, 66.7] vs. 3.5 [0.5, 8.9] ng·ml⁻¹ for daytime and nighttime, respectively; p=0.01) (Figs. 4-5 and Table 3). These results confirm that patients with mild-to-moderate OSA were similar to non-OSA patients in that the peak cTn-I levels showed significant diurnal variations that were not observed in those patients with high OSA severity. Moreover, the patients with severe OSA exhibited a significantly lower median peak cTn-I levels during the daytime than those without OSA (p=0.004). To confirm the relationship between OSA severity and diurnal variation in peak cTn-I, we also classified the patients according to the severity of OSA based on an ODI of >4% h⁻¹. We classified the OSA patients into two groups based on the observed median ODI value (20.2 h⁻¹). Similar to our observations when patients were stratified by AHI severity, we observed a diurnal variation in peak cTn-I expression with significantly higher levels during the daytime than the nighttime in non-OSA subjects and patients with mild-to-moderate OSA (ODI ≤20.2 h⁻¹) (p=0.03 and p=0.008, respectively). Moreover, this diurnal variation was not found in patients with a more severe OSA (ODI >20.2 h⁻¹) (p=0.48) (Fig. S2 and Table S3 in the online supplemental material).

DISCUSSION

The results of this observational study suggest that the presence of OSA has an effect on the time course of peak cTn-I in patients with ACS. We found that patients without OSA exhibited a diurnal variation in peak cTn-I levels with significantly higher peak levels during the day than at night. In contrast, patients with OSA did not show such a diurnal variation. Among the OSA patients, we found that the diurnal variation in peak cTn-I was observed only in patients with mild-to-moderate OSA (AHI =15-32 events·h⁻¹) but not in those with high OSA severity (AHI >32 events·h⁻¹). These results indicate that patients with mild-to-moderate OSA behave similarly to non-OSA patients. Additionally, these results suggest that patients with higher AHI are

significantly more likely to have low cTn-I levels than patients without evidence of OSA, which could imply that patients with elevated AHI, particularly those with severe OSA, may experience less severe myocardial injury.

In the present study, we have explored the extent of myocardial injury as assessed by the peak cTn-I levels. Cardiac troponins, which are structural proteins unique to the heart, are sensitive and specific biochemical markers of myocardial damage. cTn levels are superior to all other clinically available biomarkers, including myoglobin, CK-MB, myeloperoxidase, and heart fatty acid-binding protein, for the diagnosis of acute myocardial infarction [18]. The magnitude of cTn elevation correlates with the extent of myocardial necrosis and is related to subsequent risk of adverse outcomes indicating a worse prognosis [17].

The consequences of OSA have been well established to involve the activation of several intermediate mechanisms that associate OSA with cardiovascular disease [6]. The repetitive cycle of an apnoeic event during sleep leads to brain arousal, changes in intrathoracic pressure, and intermittent episodes of hypoxia and reoxygenation. These events induce the activation of intermediate mechanisms linking OSA with CVD [6]. Moreover, previous studies have postulated that OSA consequences might also promote ischaemic preconditioning [21]. Previous animal model-based studies have hypothesized the promotion of protective mechanisms related to IH exposure. A study in a rat model of hind limb ischaemia suggested that hypoxic/normoxic treatment significantly increased endothelial progenitor cell (EPC) proliferation and function and augmented the efficacy of these cells for therapeutic neovascularization [27]. Furthermore, exposing rats to brief episodes of hypoxia has been shown to protect the heart against ischaemia/reperfusion injury by enhancing the mobilization of CD34+ progenitor cells from the bone marrow via an ischaemic preconditioning effect. Thus, although the IH model does not mimic sleep-disordered breathing, it might be considered an ischaemic preconditioning model [27, 28]. In animal models, exposure to mild or moderate intermittent hypoxia is compatible with the activation of cardio- and neuro-protection pathways. In these animal models, the reduction of infarct size was dependent on the depth and duration of exposure to intermittent hypoxia [14].

Berger et al. [8] demonstrated that recurrent episodes of hypoxia/reoxygenation in

patients with acute myocardial injury with mild-to-moderate SDB activated adaptive mechanisms that improved endothelial function, providing cardioprotection in the context of acute myocardial injury. These authors also showed that the proliferative and angiogenic properties of EPC from healthy individuals were increased after exposure to IH *in vitro*, implicating the IH associated with SDB in the alterations of EPC numbers and functions.

Despite the existence of closely interrelated and detrimental mechanisms that link OSA and CVD, epidemiological studies suggest that a protective mechanisms may be activated in patients with OSA [8]. This possibility is germane from a clinical perspective and remains under debate. Whereas several studies described better post-operative survival in patients with OSA than in patients without OSA [9] along with studies that showed the increased survival of elderly patients with mild OSA [10], others studies described less optimal post-operative recovery after myocardial infarction in SDB patients compared with that of patients without SDB [11-13].

In contrast to our results that suggest that OSA may correlate with a reduction in infarct size, Belaidi et al. [29] showed that chronic IH in OSA patients resulted in the development of enhanced hypertension and an increase in infarct size. Conversely and in accordance with our results, a previous study suggested that patients with OSA have less severe cardiac injury during an acute non-fatal MI than patients without OSA. The authors postulate a cardioprotective role of sleep apnoea during acute MI via ischaemic preconditioning in patients with severe OSA [21].

In addition to the relationship between OSA and myocardial damage, the relationship between OSA and vascular damage has also been explored. Two animal-based studies concluded that IH exposure might have deleterious effects causing vascular remodelling [15, 30]. Moreover, previous clinical studies have indicated that OSA might be associated with increased vascular damage. Nakashima et al. [12] showed that in patients with OSA, an increased risk of ACS exists along with a higher incidence of PCI for progressive lesions. These authors suggested that increased plaque vulnerability might be related to these clinical manifestations. In our study, we observed that the number of stents implanted was significantly higher in the OSA group than in the non-OSA group. Nevertheless, the relationship between the number of stents and the cTn-I level was not statistically significant. We hypothesize that OSA patients, despite having a higher degree of coronary artery disease, have smaller

infarct sizes, as determined by the peak cTn level, which may be due to ischaemic preconditioning.

Moreover, in our study, the observed relationship between ODI and cTn-I levels, as well as AHI and cTn-I levels, suggests that ODI provides a similar representative index of chronic intermittent hypoxic stress as AHI, representing specific hypoxia-related airway obstruction. We have shown previously that OSA influences the severity of ACS [31]. In that previous study, we observed that OSA was related to a significant increase in peak cTn-I levels after adjusting for confounding variables ($p=0.03$). This observation contrast with the current reported findings, which show that the peak cTn-I levels were significantly higher in the non-OSA group than in the OSA group ($p=0.04$). A potential explanation is that although both patient populations are from the parent ISAACC study, the current study was performed in a single-centre in a subpopulation of individuals with different clinical and anthropometrical baseline variables compared to the parent published data. Our cohort was composed of older subjects with a significantly higher prevalence of hypertension and/or diabetes.

The current study has several strengths, including the analysis of cTn-I that are superior to all other clinically available biomarkers for the diagnosis of acute myocardial infarction [18]. Additionally, the novelty of the setting, the assessment of non-sleepy patients with an episode of ACS, and the measurement of a broad range of sociodemographic, anthropometric, clinical, pharmacological and cardiovascular variables, while using respiratory polygraphy to determine OSA status, are advantages of this study. Nevertheless, several limitations of this analysis should be noted. First, we excluded patients with more severe ACS, as these patients represented a low proportion of the patient population (3.6% of patients assessed). Second, this study excluded sleepy subjects (Epworth Sleepiness Scale (ESS) >10), which could have included the patients who exhibited the most severe OSA. However, the number of patients excluded for these causes was relatively low (6.9% of patients assessed).

CONCLUSIONS

Patients with ACS and OSA were found to have overall lower cTn-I levels than non-OSA patients. OSA patients did not show the time effect on peak cTn-I levels that was observed in the non-OSA group. Moreover, patients with low OSA severity showed a

diurnal variation of peak cTn-I similar to non-OSA patients. Therefore, it is plausible that the existence of ischaemic preconditioning mechanisms may confer a degree of cardioprotection and potentially reduce the severity of acute ischaemic events in patients with severe OSA. However, this hypothesis should be investigated in future studies that specifically evaluate the role of OSA as a preconditioning factor in ischemic damage.

Spanish Sleep Network

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Author Contributions: Study design: AST, XS, FB, AM and MST; data acquisition: AST, FB, MF, AA, FW, CT, EG, JB and MST; data analysis and interpretation: AST, XS, FB, AM, MR, SB, AA, FW, JV, CHL, JB and MST; drafting of the manuscript: AST, XS, FB, AM and MST; revision of the manuscript for intellectual content and approval of the final version: AST, XS, FB, MF, AM, AM, MR, SB, AA, FW, JV, CHL, CT, EG, JB and MST; guarantor of the study: MST.

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Conflict of Interest Statement

FB received research grants from ResMed Inc., Australia, a company that develops products related to sleep apnoea; the Health Research Fund, Spanish Ministry of Health; the Spanish Respiratory Society (SEPAR); the Catalan Cardiology Society;

Esteve-Teijin (Spain); Oxigen Salud (Spain); and ALLER to develop the ISAACC clinical trial (NCT01335087). All other authors declare that they have no conflicts of interest.

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Table 1. Anthropometric, clinical, and treatment characteristics in the non-obstructive sleep apnoea and obstructive sleep apnoea groups.

| | <i>Group</i> | | |
|--|---|---------------------------------------|----------------|
| | <i>non-OSA (AHI<15) (n=38)</i> | <i>OSA (AHI>15) (n=89)</i> | <i>p-value</i> |
| Age, years, mean (SD) | 64.4 (13.1) | 63.6 (11.5) | 0.739 |
| Gender, n (%) | | | 0.966 |
| Male | 32 (84.2%) | 73 (82.0%) | |
| Female | 6 (15.8%) | 16 (18.0%) | |
| Apnoea-hypopnoea index events·h ⁻¹ , median [IQR] | 4.8 [1.6, 9.6] | 32.0 [20.8, 46.6] | <0.001 |
| Oxygen desaturation index >4% h ⁻¹ , median [IQR] | 4.7 [3.5, 10.1] | 20.2 [6.6, 38.1] | <0.001 |
| Minimum SaO ₂ , %, median [IQR] | 87.0 [84.0, 89.0] | 83.0 [78.0, 87.0] | 0.002 |
| Mean SaO ₂ , %, median [IQR] | 93.3 [92.1, 94.1] | 93.0 [91.7, 94.2] | 0.614 |
| Time with SaO ₂ <90%, %, median [IQR] | 1.6 [0.2, 10.0] | 4.20 [0.9, 15.6] | 0.130 |
| Epworth Sleepiness Scale, median [IQR] | 3.0 [3.0, 4.3] | 5.0 [3.0, 6.0] | 0.021 |
| Hypertensive patients, n (%) | 24 (63.2%) | 61 (68.5%) | 0.701 |
| Body mass index, kg·m ⁻² , median [IQR] | 26.4 [24.6, 30.0] | 27.7 [25.0, 30.1] | 0.402 |
| Neck circumference, cm, n (%) | 42.0 [39.5, 43.5] | 41.0 [39.5, 42.0] | 0.247 |
| Diabetes mellitus, n (%) | 10 (26.3%) | 33 (37.5%) | 0.312 |
| Dyslipidaemia, n (%) | 18 (47.4%) | 53 (59.6%) | 0.284 |
| First episode of ACS, n (%) | 28 (73.7%) | 70 (78.7%) | 0.704 |
| Cardiomyopathy, n (%) | 11 (28.9%) | 28 (31.8%) | 0.912 |
| Stroke, n (%) | 1 (2.7%) | 3 (3.5%) | 1 |
| Killip class, median [IQR] | 1.0 [1.0, 1.0] | 1.0 [1.0, 1.0] | 0.98 |
| Number of affected vessels, median [IQR] | 1.0 [1.0, 2.0] | 1.5 [1.0, 3.0] | 0.622 |
| Number of stents, median [IQR] | 1.0 [0.0, 1.0] | 1.0 [1.0, 2.0] | 0.007 |
| Smoker, n (%) | | | 0.883 |
| Former smoker | 11 (28.9%) | 24 (27.0%) | |
| No | 13 (34.2%) | 28 (31.5%) | |
| Yes | 14 (36.8%) | 37 (41.6%) | |
| Total tobacco exposure, pack-years, median [IQR] | 20.0 [15.0, 30.0] | 28.2 [17.0, 43.8] | 0.354 |
| Alcohol use, n (%) | | | 0.333 |
| Former alcoholism | 2 (6.5%) | 1 (1.56%) | |
| No | 24 (77.4%) | 54 (84.4%) | |
| Yes | 5 (16.1%) | 9 (14.1%) | |
| Diuretics, n (%) | 17 (44.7%) | 26 (29.9%) | 0.161 |
| Anticoagulants, n (%) | 6 (15.8%) | 16 (18.6%) | 0.902 |
| Antacids, n (%) | 11 (28.9%) | 35 (40.7%) | 0.295 |
| Hypolipidaemics, n (%) | 12 (31.6%) | 36 (41.4%) | 0.403 |
| β-blockers, n (%) | 17 (44.7%) | 33 (37.9%) | 0.606 |
| Antiplatelet agents, n (%) | 6 (15.8%) | 15 (17.4%) | 1 |
| Bronchodilators, n (%) | 3 (7.9%) | 5 (5.9%) | 0.701 |
| Oral antidiabetic drugs, n (%) | 7 (18.4%) | 26 (29.9%) | 0.264 |
| Insulin, n (%) | 1 (2.6%) | 10 (11.8%) | 0.170 |
| Calcium antagonists, n (%) | 2 (5.3%) | 20 (23.0%) | 0.032 |

IQR, interquartile range; AHI, apnoea-hypopnoea index (number of events·h⁻¹).

Table 2. Peak troponin levels observed throughout the day in patients with and without obstructive sleep apnoea.

| | <i>Total</i> | <i>Nighttime (From 8 pm to 10 am)</i> | <i>Daytime (From 10 am to 8 pm)</i> | |
|-----------------------------|------------------|---|---|----------------|
| Total | n=127 | n=77 | n=50 | 0.17 |
| <i>Peak troponin-I</i> | 4.7 [0.8, 25.9] | 4.5 [0.9, 15.2] | 6.4 [0.7, 52.6] | |
| Non-OSA (AHI <15) | n=38 | n=26 | n=12 | 0.03 |
| <i>Peak troponin-I</i> | 10.7 [1.8, 40.1] | 7.9 [1.2, 23.1] | 54.9 [7.6, 81.2] | |
| OSA (AHI ≥15) | n=89 | n=51 | n=38 | 0.5 |
| <i>Peak troponin-I</i> | 3.8 [0.4, 24.3] | 3.8 [0.6, 13.8] | 4.2 [0.3, 26.5] | |
| | 0.04 | 0.3 | 0.04 | p-value |

Data are presented as the medians [IQR]. The peak troponin level is expressed in ng·ml⁻¹. AHI, apnoea-hypopnoea index (number of events·h⁻¹). P-value obtained by Mann-Whitney test.

Table 3. Peak troponin levels observed throughout the day in patients without obstructive sleep apnoea and in patients with mild-to-moderate and high severity obstructive sleep apnoea. The severity is based on the apnoea-hypopnea index.

| | <i>Total</i> | <i>Nighttime (From 8 pm to 10 am)</i> | <i>Daytime (From 10 am to 8 pm)</i> | |
|-----------------------------|------------------|---|---|----------------|
| Total | n=127 | n=77 | n=50 | 0.17 |
| <i>Peak troponin-I</i> | 4.7 [0.8, 25.9] | 4.5 [0.9, 15.2] | 6.4 [0.7, 52.6] | |
| Non-OSA (AHI <15) | n=38 | n=26 | n=12 | 0.03 |
| <i>Peak troponin-I</i> | 10.7 [1.8, 40.1] | 7.9 [1.2, 23.1] | 54.9 [7.6, 81.2] | |
| OSA (AHI =15-32) | n=45 | n=26 | n=19 | 0.01 |
| <i>Peak troponin-I</i> | 5.2 [0.9, 24.3] | 3.5 [0.5, 8.9] | 24.4 [1.8, 66.7] | |
| OSA (AHI >32) | n=44 | n=25 | n=19 | 0.22 |
| <i>Peak troponin-I</i> | 2.4 [0.2, 20.0] | 4.5 [0.7, 35.6] | 2.2 [0.1, 5.0] | |
| | 0.06 | 0.36 | 0.004 | p-value |

Data are presented as the medians [IQR]. The peak troponin level is expressed in ng·ml⁻¹. AHI, apnoea-hypopnoea index (number of events·h⁻¹). P-value obtained by Mann-Whitney test.

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