

# Predictors of long-term adherence to continuous positive airway pressure in patients with obstructive sleep apnoea and acute coronary syndrome

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**Background:** Continuous positive airway pressure (CPAP) is an effective treatment for obstructive sleep apnoea (OSA), but an evaluation of CPAP adherence is rarely carried out among patients with acute coronary syndrome (ACS). The goals of the study are to analyse long-term adherence and identify the predictors of non-compliance with CPAP treatment for patients with non-sleepy OSA and ACS.

**Methods:** This is an ancillary study of the ISAACC study, which is a multicentre, prospective, open-label, parallel, randomized, and controlled trial (NCT01335087) in patients with hospital admission for ACS. For the purpose of this study, only non-sleepy patients with moderate or severe OSA and randomized to receive CPAP treatment were analysed (n=357). Non-compliance was defined as CPAP dropout or average cumulative CPAP use of <4 hours/night. Multivariable logistic regression analysis was performed to identify predictors of CPAP adherence.

**Results:** Adherence to treatment was 35.3% at 12 months. According to the unadjusted analysis, higher apnoea-hypopnea index (AHI) ( $P<0.001$ ) and oxygen desaturation index (ODI) ( $P=0.001$ ) were associated with a lower risk of non-compliance. Multivariable logistic regression analysis showed that high AHI ( $P=0.0051$ ), high amounts of smoking pack-year ( $P=0.0170$ ), and long intensive care unit (ICU) stays ( $P=0.0263$ ) were associated with lower odds of non-compliance. It also showed a significant interaction between ACS history and age ( $P=0.0131$ ), such that young patients with their first ACS showed significantly lower odds of CPAP non-compliance than patients with recurrent ACS and significantly lower odds of CPAP non-compliance were associated with ageing only in patients with recurrent ACS.

**Conclusions:** Protective factors against non-compliance with CPAP treatment in non-sleepy patients with ACS were illness severity (high values of AHI or ICU stay length) or smoking amount. Patients with no previous history of ACS showed lower odds of CPAP non-compliance than patients with a recurrent ACS with younger age.

**Keywords:** Obstructive sleep apnoea (OSA); acute coronary syndrome (ACS); continuous positive airway pressure adherence (CPAP adherence); continuous positive airway pressure compliance (CPAP compliance)

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## Introduction

Obstructive sleep apnoea (OSA) is a highly prevalent respiratory disorder that affects 6–13% of the general population or more, depending on gender and age group (1,2). OSA is characterized by recurrent episodes of upper airway collapse that result in sleep fragmentation, intermittent hypoxia and the disruption of sleep architecture. OSA is associated with daytime symptoms, a decrease in the quality of life and an increase in morbidity and mortality from metabolic, neural and cardiovascular alterations (3-5).

Continuous positive airway pressure (CPAP) is an effective treatment for OSA and is recommended for symptomatic patients with an apnoea-hypopnea index (AHI)  $\geq 5$  and for patients with an AHI  $\geq 15$  regardless of symptoms (6). The effectiveness of CPAP therapy in improving clinical symptoms, quality of life and potential consequences associated with OSA is strongly related to compliance (7-10); nevertheless, the predictors of adherence to this therapy are still not well known.

The most typical symptom of OSA is excessive daytime sleepiness. Most of the studies assessing compliance have been conducted on patients with hypersomnia, where excessive daytime sleepiness has been suggested as one of the most important determinants of adherence to CPAP. Although several studies have reported that excessive daytime sleepiness is absent in approximately 50% of all OSA patients (11), very few studies have focused on non-sleepy patients. The results of these studies are contradictory (10,12-14), with some authors reporting similar CPAP adherence regardless of daytime sleepiness and others finding differences.

It is estimated that in patients with acute coronary syndrome (ACS) the prevalence of sleep apnea hypopnea syndrome (SAHS) is higher than in the general population (15). Nevertheless, the evaluation of respiratory disorders during sleep is not routinely considered in guidelines for diagnosis and evaluation of patients with ACS (16). In addition, CPAP adherence has been rarely carried out among patients with ACS and it may be different from that of other OSA patients.

In this context, we designed this study to analyse long-term adherence and identify the predictors of non-compliance with CPAP treatment for patients with non-sleepy OSA who have suffered an ACS.

## Methods

### Patients

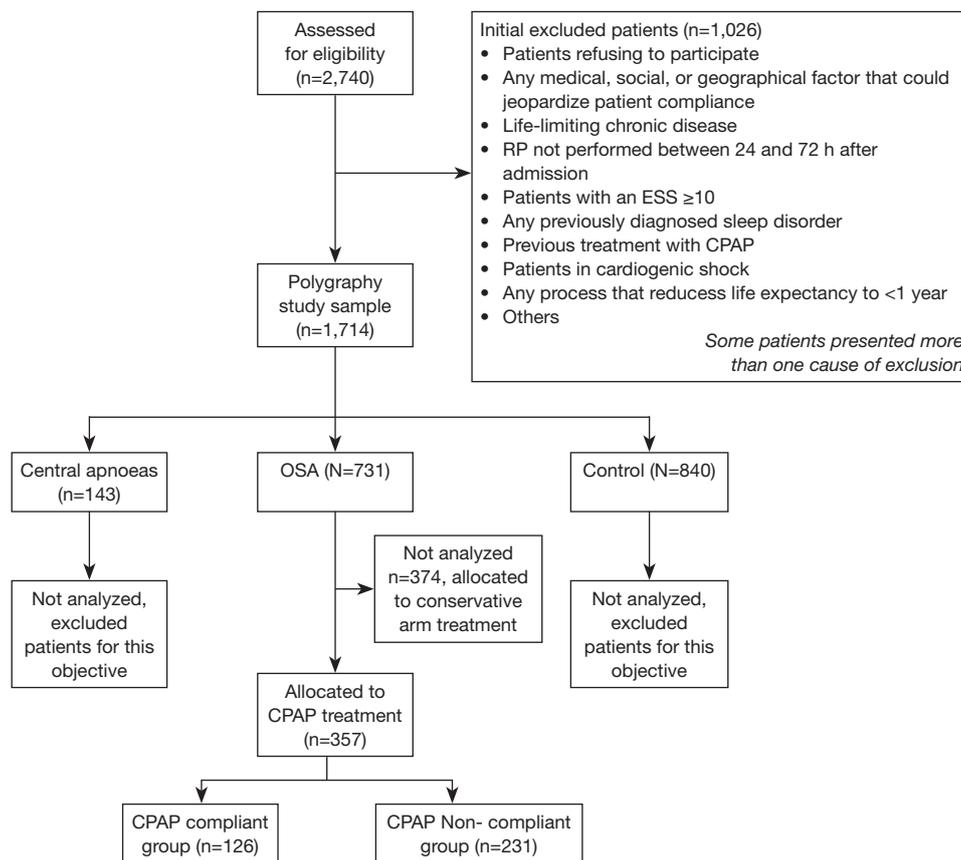
This is an ancillary study of the ISAACC study, which is a multicentre, prospective, open-label, parallel, randomized, controlled trial (NCT01335087) to evaluate the effect of CPAP treatment on the recurrence of cardiovascular events in non-sleepy patients with ACS and co-occurring OSA (17). Briefly, the study started in June 2011, and patients consecutively admitted for ACS to coronary care units or cardiology hospitalization rooms at 15 teaching hospitals in Spain were evaluated in regard to the inclusion and exclusion criteria. The ethics committee of each participating centre approved the study (CEIC-852).

ACS was defined as the acute presentation of coronary disease with or without ST-elevation infarction, unstable angina or type 1 myocardial infarction (18). The inclusion criteria were patients aged greater than 18 years, admitted to the hospital for ACS with or without ST-segment elevation, without excessive daytime sleepiness [Epworth Sleepiness Scale (ESS) score  $\leq 10$ ], and having signed informed consent.

The exclusion criteria included previous treatment with CPAP, psychophysical inability to complete questionnaires, having 50% central apnoea or Cheyne-Stokes respiration, having a previously diagnosed sleep disorder or chronic disease (neoplasm, renal failure, severe chronic obstructive pulmonary, chronic depression, or other limiting chronic diseases), having a medical history that could interfere with the study objectives, having a life expectancy lower than 1 year or being in cardiogenic shock.

All patients included underwent cardiorespiratory polygraphy during the first 24–72 hours after admission, and patients presenting an (AHI)  $\geq 15$  events/hour were randomized to receive conservative care or CPAP treatment.

Between June 2011 and June 2014, the ISAACC study included 731 patients aged more than 18 years old who were diagnosed with moderate or severe OSA (AHI  $\geq 15$ ) without excessive daytime sleepiness (ESS  $\leq 10$ ). For the purpose of this study, only patients who were randomized to receive CPAP treatment (n=357) were considered for analysis of adherence to CPAP treatment. A flowchart for study participation in the study period is provided in *Figure 1*.



**Figure 1** Study flowchart showing recruitment in the study. CSA, central sleep apnoea; RP, cardiorespiratory polygraphy; ESS, Epworth Sleepiness Scale; CPAP, continuous positive airway pressure.

### Procedures

All participants underwent overnight cardiorespiratory polygraphy with the same model of device (Embletta; ResMed, Australia). Nasal flow, thoracoabdominal effort and oximetry were recorded. All sleep studies were manually scored by trained personnel at each participating centre according to standard criteria (19). Apnoea was defined as an absence of airflow lasting  $\geq 10$  seconds. Hypopnea was defined as a reduction in airflow lasting  $\geq 10$  seconds associated with a decrease in arterial oxygen saturation ( $\text{SaO}_2$ )  $\geq 4\%$ . The AHI was defined as the number of episodes of apnoea and hypopnea per hour of recording.

Baseline variables were systematically recorded using a standardized protocol. These variables included clinical and anthropometric data, subjective sleepiness/drowsiness based on the Spanish version of the ESS (20), quality of life (EuroQol test), smoking habit, and alcohol intake, and cardiovascular health was assessed through by collecting

information regarding a history of diabetes, hypertension, dyslipidaemia, first episode of ACS, cardiomyopathy, stroke, neuropathy and neurological disease.

CPAP titration was performed by automatic CPAP following a validated protocol (21) on a second night. After titration, the patients were treated with fixed CPAP. The optimal pressure was determined visually on the raw data of the automatic CPAP device by analyzing the pressure that included 90% of the periods with a leak lower than 0.4 L/second (percentile 90). All these patients also received advice on conservative treatment based on dietary-hygienic measures.

### Follow-up and endpoints

The follow-up period was extended until June 2015. Thus, CPAP treatment continued on an updated basis for at least 1 year for all the participants. Patients who interrupted

CPAP treatment continued with their scheduled clinical visits. Patients were followed up and were evaluated at baseline, 1, 3, 6 and 12 months.

The goal of the visits at baseline and 1 month was to facilitate adaptation and adherence to CPAP treatment and to insist on dietary-hygienic advice. At each visit, CPAP use was reinforced and side effects or concerns related to treatment were addressed. All collaborating centres have extensive experience in the management of CPAP treatment. All the patients had a phone number that allowed them to contact the research team at any time. If any problems related to the adaptation to CPAP occurred, additional visits were scheduled in order to immediately resolve them. CPAP devices were provided free of charge. Compliance with CPAP treatment was objectively assessed by reading the internal counter of the device at each follow-up visit.

The endpoints of this study were CPAP treatment compliance and variables associated with adherence to treatment. For this purpose, lack of adherence was defined as mean CPAP use less than 4 hours per day at 12 months of CPAP treatment. Those patients with early known withdrawals from the trial or CPAP treatment were classified in the lack of adherence group. Patients who dropped out before completing 12 months of follow-up (and therefore who had missing compliance, including patients who were completely or partially lost to follow-up) were also classified in the lack of adherence group.

### Data analysis

Non-normally distributed quantitative variables were summarized by their median (and interquartile intervals via the 25<sup>th</sup> and 75<sup>th</sup> percentiles). Qualitative variables were summarized by absolute and relative frequencies.

The association between CPAP lack of adherence at 12 months of follow-up and patient characteristics of clinical interest at baseline was tested using a Mann-Whitney U-test for continuous variables and/or a *t*-test for continuous non-normally or normally distributed variables. A Chi-square test was used to test qualitative variables.

Independent predictors of CPAP adherence were identified by performing multivariable logistic regression analysis starting with a model of all variables with a *P* value lower than 0.20 associated with their coefficients in the unadjusted analysis. The selection of variables included in the final model was based on the statistical significance of their coefficients. The final model was

adjusted by hospital. Model calibration and discrimination were assessed, and the Hosmer-Lemeshow test and area under the curve (AUC) were estimated. Additionally, a mixed-effect logistic regression model was adjusted to test the random effects of the hospitals. A significance level of 0.05 was applied. R statistical software was used for data processing and analysis (22).

### Results

The first 357 ACS patients who were diagnosed with OSA and randomized to CPAP treatment were analysed.

The patients' baseline characteristics are described in *Table 1*. Briefly, 82.5% were men, the median age was 59 years (IQR, 52–67), and the median body mass index (BMI) was 29 kg/m<sup>2</sup> (IQR, 26.3–32.4). For most patients, it was their first episode of ACS (82%). Concerning the respiratory variables, the patients had severe OSA (median AHI of 34 events/hour; IQR, 24.4–51.3), with a median time with SaO<sub>2</sub> below 90% (TC90) of 4.7% (IQR, 1–19.9) and a median ESS score of 6 (IQR, 4–8).

After 12 months, 4 patients had died and 88 were lost to follow-up (last bar in *Figure 2*). At the end of the study, 126 patients (35.3%) completed the 12-month follow-up period and reported good compliance, 54 (15.1%) reported good compliance after 1, 3 or 6 months but discontinued CPAP treatment before the last 12-month visit, and 177 (49.6%) showed non-compliance.

According to the unadjusted analysis (*Table 2*), higher AHI and oxygen desaturation index (ODI), both of which are indicators of OSA severity, were associated with a lower risk of becoming a non-complier of CPAP treatment after 12 months. No statistically significant differences were identified between the groups in their sociodemographic characteristics, medical history or ACS variables, such as ACS type, Killip class, left ventricle ejection fraction or number vessels affected.

The results of multivariable analysis to identify the characteristics of patients associated with an increased risk of non-adherence to CPAP in a 12-month treatment period are shown in *Table 3*. The identified patient characteristics significantly associated with a lower risk of long-term non-compliance with CPAP treatment were high AHI values, high amounts of smoking pack years, and longer intensive care unit (ICU) stays. The same adjusted regression model identified a significant interaction between age and ACS personal history with a lower risk of non-compliance with CPAP treatment among patients without a personal history

**Table 1** Baseline characteristics of the patients included in this study

Characteristics	Data
Male	295 (82.5%)
Age (years)	59 [52; 67]
Alcohol (gr)	13 [1.50; 21]
Smoking	
Never	88 (25.1%)
Current	167 (47.6%)
Former	96 (27.4%)
Smoking (pack-year)	30 [16.8; 42]
First episode of ACS	279 (82%)
Type of ACS	
Unstable angina	32 (11.3%)
ACS without ST-elevation	149 (52.5%)
ACS with ST-elevation	103 (36.3%)
Killip class	
1	293 (90.2%)
2	30 (9.23%)
3	2 (0.62%)
Left ventricular ejection fraction (%)	55 [49.0; 60.0]
Number of vessels affected	1 [1; 2]
Hospitalization stay (days)	5 [4; 7]
ICU stay (days)	2 [1; 3]
BMI (kg/m <sup>2</sup> )	29 [26.3; 32.4]
ESS score	6 [4; 8]
AHI (events/hour)	34 [24.4; 51.3]
ODI >4%	27.5 [18.2; 43.7]
TC90 (%)	4.7 [1.0; 19.9]
Mean oxygen saturation (%)	92.6 [91; 94]
Hypertension	191 (54.3%)
Diabetes Mellitus	84 (23.9%)
Dyslipidaemia	192 (54.4%)
Previous heart disease	77 (21.9%)
Stroke	10 (2.87%)
Lung disease	18 (5.14%)

The data are summarized as the median [25<sup>th</sup> percentile; 75<sup>th</sup> percentile] or n (%) for non-normally distributed quantitative or qualitative variables, respectively. ACS, acute coronary syndrome; BMI, body mass index; ESS, Epworth Sleepiness Scale; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; SaO<sub>2</sub>, arterial oxygen saturation; TC90, time with an arterial oxygen saturation below 90%.

of ACS (for younger patient age) in comparison to patients with recurrent ACS. In addition, patients with recurrent ACS showed lower odds of CPAP non-compliance associated with ageing. The calibration and discrimination capability of this multivariable model to predict long-term non-compliance is shown in *Figure 3*, which indicates no significant lack of calibration (Hosmer-Lemeshow test, P=0.44) and an AUC of 0.736.

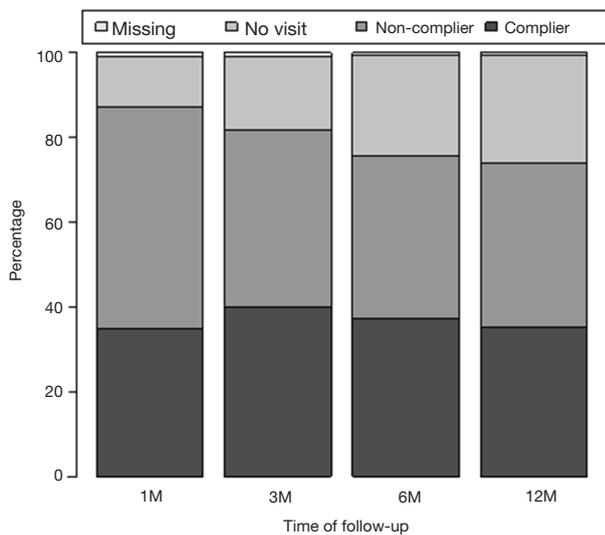
## Discussion

This study shows that patients hospitalized due to an ACS who were newly diagnosed with OSA without sleepiness and who started CPAP treatment had low adherence to treatment, which was approximately 35.3% at 12 months. Predictors of compliance with CPAP treatment at 12 months were OSA severity, smoking pack years, ICU stay length, age and a personal history of ACS. High values of AHI, smoking pack years or ICU stay length were associated with a lower risk of non-compliance with CPAP treatment. The adjusted analysis also showed a significant interaction between age and a previous ACS personal history associated with CPAP compliance. Thus, younger patients showed the highest non-compliance rates when having a recurrent ACS compared to patients without any previous history of ACS.

A better understanding of the predictors of CPAP compliance is interesting because adherence to CPAP treatment is essential to achieving the beneficial effects of CPAP (23,24). Therefore, knowing the predictors of non-compliance may help in the development of clinical practice strategies directed towards improving adherence to treatment in groups with a high risk of poor compliance.

In most studies assessing this topic, sleepiness is suggested as the most relevant predictor of CPAP compliance. Nevertheless, approximately 40–50% of patients suffering from OSA do not report sleepiness (11,25,26); thus, it is also important to determine which variables can predict compliance in these patients. However, few studies have focused on non-sleepy patients, and the results of those studies have been conflicting.

In our study, only 35.3% of patients reported good compliance with CPAP treatment after 12 months. Although CPAP compliance is usually higher in patients with sleepiness than in non-sleepy ones (27,28), our results differ from adherences reported in other studies performed in non-sleepy patients. This fact could be related to the place where patients were recruited or the symptoms that they presented at baseline. Campos-Rodriguez *et al.* (12)



**Figure 2** Detailed information on compliance throughout the study period (12 months). M, month.

and Gagnadoux *et al.* (13) reported adherences to CPAP treatment of approximately 64% and 67%, respectively, in non-sleepy patients. The difference between our results and these studies might be explained by the fact that both of the previous studies included patients who were recruited in sleep clinics. Thus, despite not having sleepiness, the patients probably exhibited other symptoms, such as snoring or witnessed apnoea, because they were suspicious of having OSA, and these other symptoms may motivate compliance. In contrast, our non-sleepy patients were evaluated during an ACS but were not being evaluated for suspected OSA. Nevertheless, there are also studies describing poor compliance in clinical trials performed in non-sleepy patients recruited in sleep units (10). The adherence shown in our study is similar to the values reported by Chai-Coetzer *et al.* (14) in the SAVE trial in which patients did not present to a sleep clinic and were mainly recruited in neurology or cardiology clinics, as in our study. The values

**Table 2** Compliance versus non-compliance in univariate analysis

Parameter	Compliance (n=126)	Non-compliance (n=231)	OR	P. ratio	P. overall
Sex					0.444
Male	101 (34.2%)	194 (65.8%)			
Female	25 (40.3%)	37 (59.7%)	0.77 [0.44, 1.36]	0.366	
Age (years)	60 [54; 67]	59 [52; 67]	1 [0.98; 1.02]	0.784	0.706
Smoking					0.548
Never	28 (31.8%)	60 (68.2%)	Ref.	Ref.	
Former	38 (39.6%)	58 (60.4%)	0.71 [0.39; 1.31]	0.278	
Current	60 (35.9%)	107 (64.1%)	0.83 [0.48; 1.44]	0.517	
Smoking pack years	28.0 [0.00; 40.0]	18 [0; 37.5]	0.99 [0.98; 1.00]	0.025	0.055
Hypertension					1.000
No	58 (36.0%)	103 (64.0%)	Ref.	Ref.	
Yes	68 (35.6%)	123 (64.4%)	1.02 [0.66; 1.58]	0.934	
Diabetes					0.683
No	98 (36.6%)	170 (63.4%)	Ref.	Ref.	
Yes	28 (33.3%)	56 (66.7%)	1.15 [0.69; 1.95]	0.596	
Dyslipidaemia					0.650
No	60 (37.3%)	101 (62.7%)	Ref.	Ref.	
Yes	66 (34.4%)	126 (65.6%)	1.13 [0.73; 1.76]	0.574	
BMI (kg/m <sup>2</sup> )	28.8 [26.1; 32.3]	29.1 [26.4; 32.5]	1.01 [0.97; 1.05]	0.682	0.865

**Table 2** (continued)

Table 2 (continued)

Parameter	Compliance (n=126)	Non-compliance (n=231)	OR	P. ratio	P. overall
ESS score	6.00 [4.00; 8.00]	6.00 [4.00; 7.00]	0.96 [0.97; 1.05]	0.388	0.466
AHI (events/hour)	41.8 [30.0; 53.8]	31.0 [22.1; 48.6]	0.98 [0.97; 0.99]	0.003	<0.001
ODI >4%/h	30.3 [21.2; 50.5]	25.5 [15.4; 41.5]	0.98 [0.97; 0.99]	0.001	0.001
Mean SaO <sub>2</sub> (%)	95.2 [90.8; 93.4]	92.8 [91.3; 94.0]	1.00 [0.98; 1.02]	0.848	0.142
Minimum SaO <sub>2</sub> (%)	82.0 [77.0; 86.0]	83.0 [78.0; 86.0]	1.01 [0.99; 1.04]	0.335	0.320
TC90 (%)	6.70 [1.20; 26.9]	3.70 [0.90; 18.4]	0.99 [0.98; 1.00]	0.138	0.054
CPAP pressure	8.00 [7.00; 9.00]	8.00 [7.00; 9.00]	0.97 [0.84; 1.13]	0.721	0.939
ACS category					0.884
Non-STEMI	51 (34.2%)	98 (65.8%)	Ref.	Ref.	
Unstable angina	10 (31.2%)	22 (68.8%)	1.14 [0.51; 2.70]	0.761	
STEMI	37 (35.9%)	66 (64.1)	0.93 [0.55; 1.58]	0.782	
KILLIP class					0.516
Killip 1	106 (36.2%)	187 (63.8%)	Ref.	Ref.	
Killip 2 or 3	14 (43.8%)	18 (56.2%)	0.73 [0.35; 1.56]	0.406	
Ejection fraction	55.0 [49.0; 60.0]	55.0 [50.0; 62.0]	1.01 [0.99; 1.04]	0.250	0.201
First ACS					0.786
Yes	101(36.2%)	178 (63.8%)	Ref.	Ref.	
No	20 (33.3%)	40 (66.7%)	1.13 [0.63; 2.08]	0.683	
Days in hospital	5.00 [4.00; 7.00]	5.00 [4.00; 7.00]	0.97 [0.91; 1.03]	0.257	0.465
Days in ICU	2.00 [1.25; 3.00]	2.00 [1.00; 3.00]	0.91 [0.80; 1.03]	0.144	0.226

The data are summarized as the median [25<sup>th</sup> percentile; 75<sup>th</sup> percentile] or n (%) for non-normally distributed quantitative or qualitative variables, respectively. BMI, body mass index; ESS, Epworth Sleepiness Scale; AHI, apnea-hypopnea index; ODI, oxygen desaturation index; SaO<sub>2</sub>, arterial oxygen saturation; TC90, time with SaO<sub>2</sub> below 90% (%); STEMI, ST-elevation myocardial infarction; CPAP, continuous positive airway pressure; ACS, acute coronary syndrome; ICU, intensive care unit.

of CPAP use and adherence reported in the SAVE trial did not significantly differ from those reported in our study (CPAP mean use: 3.3±2.4 hours per night and adherence of approximately 39%). Therefore, in line with the existing literature, our findings suggest that adherence to CPAP therapy is more difficult in non-sleepy patients than in more symptomatic ones, especially when treatment is initiated outside of a sleep unit and during hospitalization.

This study also shows that compliance rate remains fairly similar between the first follow-up visit at 1 month and at the end of the study at 12 months. These data are concordant with studies reporting that use obtained within the first months is an important determinant of long-term compliance (28,29). This fact suggests that patient's early

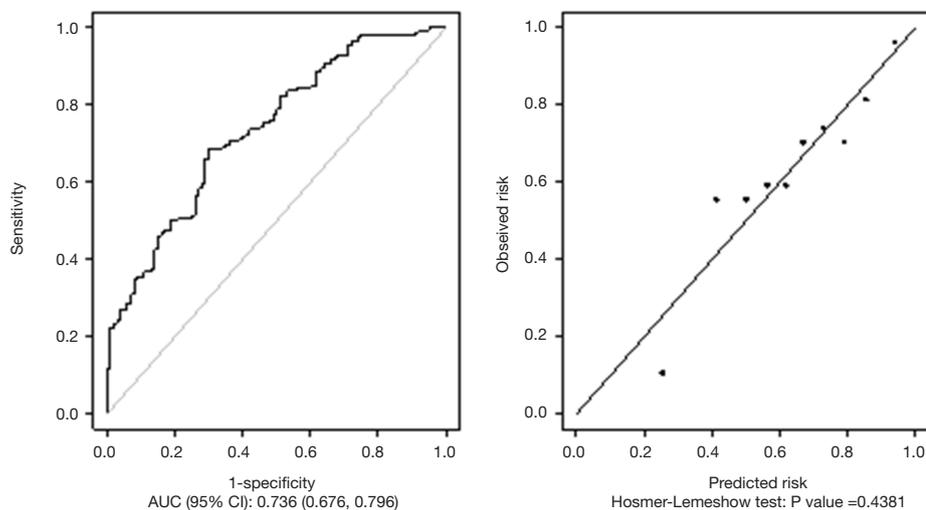
experience and initial comfort with CPAP, even during the titration night, may impact future compliance (30). Moreover, it suggests that there is probably a window of opportunity shortly after starting CPAP treatment to influence future compliance. Early identification of these patients could be useful to increase patient education and motivation (when possible) and improve compliance (31) or to allocate resources and propose alternative treatments in the other cases.

Moreover, our data also depict that after CPAP titration, there is a non-negligible percentage of patients with poor compliance or those who do not continue with follow-up visits. On one hand, these data could be related to the hospital admission for an ACS and not for suspected OSA.

**Table 3** Regression logistic analysis adjusted by centre for non-compliant CPAP patients

Parameter	Adjusted by centre as fixed effect			Adjusted by centre as random effect		
	OR	95% CI	P value	OR	95% CI	P value
AHI	0.976	0.961–0.991	0.0025	0.980	0.966–0.994	0.0051
Smoking pack years	0.985	0.973–0.997	0.0194	0.986	0.975–0.997	0.0170
Days in ICU	0.795	0.635–0.959	0.0318	0.821	0.691–0.977	0.0263
1 <sup>st</sup> ACS, depending on age						
If median age	0.312	0.088–0.891	0.0457	0.396	0.138–1.136	0.0849
If younger (1 <sup>st</sup> quartile)	0.133	0.022–0.570	0.0140	0.190	0.043–0.832	0.0275
If older (3 <sup>rd</sup> quartile)	0.826	0.324–2.005	0.6788	0.917	0.395–2.131	0.8411
Age, depending on 1 <sup>st</sup> ACS						
If 1 <sup>st</sup> ACS	0.997	0.968–1.028	0.8572	0.998	0.971–1.027	0.9162
If not 1 <sup>st</sup> ACS	0.883	0.803–0.955	0.0045	0.899	0.831–0.973	0.0080

CPAP, continuous positive airway pressure; AHI, according to the unadjusted analysis, higher apnoea-hypopnea index; ICU, intensive care unit; ACS, acute coronary syndrome.



**Figure 3** Discrimination and calibration analysis and plots. The model adjusted by the fixed effect of centre does not show any significant lack of fit with an AUC of 0.736 (0.676, 0.796). AUC, area under the curve.

Thus, these patients probably have low awareness of the importance of OSA diagnosis and treatment. On the other hand, the patients included in our study are minimally symptomatic and probably could not perceive clear benefits from the treatment, which has been reported in previous studies as the main cause for discontinuing CPAP treatment (28).

The study also shows that high values of AHI, smoking pack years or ICU stay length were associated with a

lower risk of non-compliance. Our results agree with previous studies reporting that the severity of OSA was a determinant of long-term adherence in non-sleepy (12,13) and sleepy patients (27). These results could be explained by more symptomatic diseases (aside from sleepiness) in patients with higher AHI. Moreover, smokers and patients with longer ICU stays could have greater comorbidities and worse overall health status, which may increase their awareness of the disease and motivate CPAP compliance.

The adjusted regression model also identified a significant interaction between age and ACS personal history, with a lower risk of non-compliance with CPAP treatment among patients without a personal history of ACS (in younger patients) in comparison to patients with recurrent ACS. These findings could be related to the impact of a new diagnosis of cardiovascular disease, and therefore, adherence to CPAP may have been encouraged by the patients' recent awareness of increased cardiovascular risk. Furthermore, patients with recurrent ACS showed lower odds of CPAP non-compliance associated with ageing. These patients with recurrent ACS and advanced age may be the ones who have a good complier profile and they could also show better adherence to cardiovascular medications apart from CPAP.

In contrast to the results of Campos-Rodriguez *et al.* (12), we did not find that hypertension predicted compliance in our sample. This result could be related to the fact that all included patients have suffered an ACS and therefore were aware of their cardiovascular health status regardless of hypertension. In our study, instead of hypertension, ACS could be the main factor in increasing awareness of the importance of treatment.

### Strengths and limitations

The main strength of this study is that it provides information on predictors of CPAP compliance in a group of patients in which poor adherence was recently described in the context of important clinical trials. Therefore, identifying predictors of compliance in patients with cardiovascular diseases could be useful in clinical practice and may also be helpful in additional research trials.

Another strength of our study is its multicentre design with a large number of patients. All participating centres performed the same methodology, and the sleep study was performed with the same model of polygraph; furthermore, the study includes the measurement of a broad range of sociodemographic, anthropometric, clinical, pharmacological and cardiovascular variables.

The following limitations should be acknowledged. First, the study was not originally designed to analyse compliance; therefore, some interesting variables, such as side effects, type of interface, humidification, medications and personal or social factors that could influence compliance were not considered. Second, sleepiness was evaluated in our study with ESS, a subjective scale. This scale could have limitations compared to objective methods and has not been validated in women or elders; however, we chose to use

ESS because it is a widely used tool to evaluate sleepiness in clinical practice. Third, other OSA-related complaints and symptoms (snoring, fatigue, breathing pauses and choking) were not considered. Fourth, this study was conducted in a health system where CPAP treatment has no cost to the patient; thus, we cannot exclude that cost could be a determinant of compliance in systems where treatment is not free, even though the available data argue against a significant effect of cost on continued use (32).

### Conclusions

In non-sleepy patients with ACS and OSA, the main predictors of low risk of non-CPAP compliance were high values of AHI, smoking pack years, and ICU stay length. A previous personal history of ACS was also associated with CPAP non-compliance, although it was dependent on patient age, such that younger patients with recurrent ACS displayed the worst CPAP compliance. This study sheds light on clinical profiles that could benefit from closer follow-up or more personalized visits in order to encourage and increase adherence to CPAP treatment.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The ethics committee of each participating centre approved the study (CEIC-852). Written informed consent was obtained from the patient for publication of

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