Continuous Positive Airway Pressure Treatment and Anxiety in Adults with Coronary Artery Disease and Nonsleepy Obstructive Sleep Apnea in the RICCADSA Trial

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ABSTRACT

Background: Anxiety and obstructive sleep apnea (OSA) coexist among adults with coronary artery disease (CAD) following revascularization. Continuous positive airway pressure (CPAP) is the first line treatment of OSA patients with daytime sleepiness. The current study evaluated the effect of CPAP on anxiety in CAD patients with nonsleepy OSA.

Methods: Two hundred forty-four revascularized CAD patients with nonsleepy OSA (apnea-hypopnea index ≥ 15 /h, Epworth Sleepiness Scale score < 10) were randomly assigned to CPAP or no-CPAP between 2005 and 2010. Zung Self-rating Anxiety Scale (SAS) was administered at baseline, and after 3 and 12 months with higher scores suggesting more anxiety.

Results: A total of 208 patients with complete SAS scores at baseline and 12-month follow-up were included (CPAP, $n=103$; no-CPAP, $n=105$). In the intention-to-treat analysis, CPAP had no significant effect on the SAS scores. On-treatment analysis revealed a significant increase in the median of delta SAS score (+3.75) after three months among the participants using the device 2.8 hours/day or more while there was a decline in the median of delta SAS score (-1.25) in the non-adherent or no-CPAP group ($p=0.031$). The increase in the SAS score (+1.25) in the adherent group, and the decline (-1.25 points) in the non-adherent/no-CPAP group remained significant after one year ($p=0.011$). Baseline SAS score predicted non-adherence (adjusted odds ratio 1.11; 95% confidence interval [CI] 1.04-1.18; $p=0.003$), and there was an association between the increase in the SAS scores and accumulated CPAP hours/day (standardized $\beta=0.144$ [95% CI 0.005-0.695], $p=0.047$).

Conclusion: Our results suggest that anxiety should be considered in the management of CAD patients with nonsleepy OSA following revascularization.

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INTRODUCTION

Coronary artery disease (CAD) is a common disorder leading to enhanced morbidity and mortality worldwide (1). Although traditionally recognized cardiovascular risk factors play an important role on the pathogenesis of CAD, there is also data indicating that psychological factors should also be considered in this context (2). As also emphasized in a recent review, cardiac patients are more likely to report impaired sleep with reduced sleep duration and quality, and also, sleep interruptions due to nocturnal dyspnea or arrhythmias (3).

Anxiety is one of the prominent psychological symptoms with an estimated prevalence rate ranging from 20 to 50% among adults with CAD (4, 5). Previous studies on anxiety have been generally performed among cardiac patients before and after mechanical revascularizations such as percutaneous coronary intervention (PCI) (6), and coronary artery bypass grafting (CABG) surgery (7-9). The results of these studies imply that preoperative anxiety aggravates complications experienced during early postoperative period including hemodynamic consequences, prolonged mechanical ventilation, higher postoperative pain, increased analgesic and anaesthetic requirements (10). Consequently, postoperative anxiety has also been related with a 4-year mortality among patients undergoing CABG and valve surgery (11).

Obstructive sleep apnea (OSA) is also a common disorder (12), and anxiety has been reported among 32% of OSA patients according to a recent systematic review and meta-analysis (13). On the other hand, there have also been reports suggesting no association between OSA and anxiety symptoms (14, 15). Continuous positive airway pressure (CPAP), which is the first line treatment of symptomatic OSA patients, has been shown to improve health related quality of life (16) and comorbid depression (17, 18) but not anxiety (19). In the secondary analysis of the Sleep Apnea Cardiovascular Endpoints (SAVE) trial, that involved 2410

patients with cardiovascular and/or cerebrovascular disease and co-existing OSA, there were no significant changes in anxiety symptoms following CPAP treatment (20). No reports regarding the association between OSA treatment and anxiety are yet available from other recently completed or ongoing RCTs evaluating the cardiovascular effects of the OSA treatment as primary outcomes (21-25).

The RICCADSA (Randomized Intervention with CPAP in CAD and OSA) trial primarily addressed the effects of CPAP on the composite of repeat revascularization, myocardial infarction, stroke, and cardiovascular mortality in revascularized patients with CAD and nonsleepy OSA (26). In the current work, we evaluated the impact of CPAP on anxiety in the same cohort as one of the secondary outcomes of the RICCADSA trial.

METHODS

Study Design and Participants

The study design has been reported in detail elsewhere (27). In brief, all consecutive CAD patients undergoing PCI or CABG in the Skaraborg County of West Götaland, Sweden between 2005 and 2010 (n=1,291) were invited to participate (Figure 1). The participants with nonsleepy OSA (apnea–hypopnea index [AHI] >15/h) based on home sleep apnea testing [HSAT], and Epworth Sleepiness Scale [ESS] scores less than 10 points), were included in the randomized controlled trial (RCT) arm for the main protocol. For the purpose of the current study, the patients who completed Zung Self-rating Anxiety Scale (SAS) at baseline and follow-ups were included. The main study was completed in May 2013. The study protocol was approved by the Ethics Committee of the Medical Faculty of the University of Gothenburg (approval no. 207-05; 09.13.2005; amendment T744-10; 11.26.2010; amendment T512-11; 06.16.2011), and written informed consent was provided by all patients. The trial was registered (FoU i Sverige—Research and Development in

Sweden; researchweb.org; VGSKAS-4731; 04.29.2005; and www. clinicaltrials.gov; NCT00519597).

Home Sleep Apnea Testing

As previously described in detail (27), the Embletta Portable Digital System device was used for the HSAT recordings. The system contains a detector for nasal pressure, a finger pulse oximeter to detect both oxyhemoglobin saturation and heart rate as well as two respiratory belts for body position and thoraco-abdominal movements. Since the study protocol was established in 2005, the Chicago criteria were applied for apnea and hypopnea definitions (28); *i.e.*, at least 90% cessation of airflow was recognised as an apnea, and at least 50% decrease in nasal pressure amplitude and/or thoracoabdominal movement for 10 seconds or longer, irrespective of an oxyhemoglobin desaturation was scored as a hypopnea. The total number of oxyhemoglobin desaturations of at least 4% from the immediately preceding baseline, was also measured, and oxygen desaturation index (ODI) was calculated.

Epworth Sleepiness Scale

ESS, a self-administered questionnaire with eight questions to address the possibility of dozing off while performing eight different activities in the past month, was used to determine excessive daytime sleepiness (29). The participants with an ESS score less than 10 points were categorized as the nonsleepy phenotype.

Zung Self-rated Anxiety Scale

Participants were requested to answer the Zung SAS at baseline and 3 and 12 months after randomization. The Zung SAS is a likert scale which comprises 20 items to measure physiological and psychological symptoms (30). Each item was rated on a 4-point scale

ranging from 1 (none, or a little of the time) to 4 (most, or all of the time), and the raw scores (range 20-80) were converted into index scores (range 25-100) by multiplying 1.25. The SAS items include both affective and somatic symptoms; 15 items defining a negative experience such as “I feel afraid for no reason at all”, and 5 items expressing a positive experience such as “I can breathe in and out easily”. The positive items were recoded reversely (30).

Individuals with a SAS score of at least 45 points were defined as having a clinically significant anxiety, and higher scores indicate more anxiety (31). The questionnaire is provided in the online supplement (eTable 1). As item 19 (“I fall asleep easily and get a good night’s rest”) as well as item 20 (“I have nightmares”) may overlap symptoms related to OSA, a separate analysis was performed by excluding these questions from the total scores. All responses were recorded in the local database by a research nurse blinded to the group allocation and clinical data.

Comorbidities

Information regarding anthropometrics, smoking habits, comorbidities and use of medications were obtained at baseline. Obesity was defined as a body mass index (BMI) of 30 kg/m² or greater (32).

Group Assignment, Randomization, Interventions, and Follow-Up

As illustrated in Figure 1, the group assignment of the RCT arm was based on the HSAT results and the ESS scores. Nonsleepy OSA patients, who were randomly allocated to CPAP were provided with an automatic (self-titrating) CPAP device (S8 or S9; ResMed) with a nasal or full-face mask and humidifier. As previously described elsewhere (27), the CPAP group were contacted by telephone after 1 week, and both groups were followed after 1 month, 3 months, 6 months, 1 year, and then yearly until the end of the main study.

Adherence to CPAP

Participants allocated to CPAP brought the machines to the clinic at each follow-up, and CPAP use (hours/night) were downloaded from the device and entered into the database. Technical adjustments were done according to the clinical routines by the sleep medicine unit staff. Participants who stopped using their devices were followed as part of the ITT population (27). Accumulated CPAP usage (CPAP hours per day adjusted for percentage of CPAP days per 3 months and 12 months, respectively) was documented for each participant allocated to CPAP. Adherence was defined as CPAP usage at least 4 hours/day and 70% CPAP days/period (33), corresponding 2.8 hours/day/all days.

Outcomes and the sample size

The major outcome of the current study, which was one of the secondary endpoints of the RICCADSA trial, was absolute change from baseline in the SAS scores at 3 and 12 months, respectively. The sample size estimation for the RICCADSA trial was based on the calculations for the primary composite endpoints (*i.e.*, long-term cardiovascular adverse events) (26).

Statistical analysis

For descriptive statistics, the data are presented as medians and boundaries of interquartile ranges (continuous variables), and as percentages (categorical variables). Mann-Whitney U test was used to compare the difference between two study groups for continuous variables. Chi-Square test (or, when appropriate, Fisher's exact test) was conducted to compare categorical variables. Primary analysis was conducted in intention-to-treat population. Additional analyses were conducted to compare the anxiety levels of participants allocated to no-CPAP and nonadherent OSA with participants who were adherent to CPAP. Pearson

correlation coefficient was calculated between delta SAS scores and accumulated CPAP hours/day at 12-month follow-up. To be in line with the recent guidelines(34), the covariates for multivariate analyses were selected carefully. Age, sex, type of revascularization, comorbidities, ESS scores, Zung Self-rating Depression Scale scores, and CPAP usage were entered into the model to address the correlates of delta SAS scores. Baseline SAS scores were not included into the model due to multicollinearity. The tests were performed as two-sided and p value less than 0.05 was considered as statistically significant. The data was analysed by using Statistical Package for Social Sciences, version 26.0 for Windows system (SPSS Inc.).

RESULTS

Clinical Characteristics of the Study Cohort

As shown in Figure 1, 244 revascularized CAD patients with nonsleepy OSA was included in the RCT arm of the main trial. After excluding 34 patients who did not respond to the Zung SAS at baseline and/or at 12 month follow-up, 208 (mean age 65.9 +8.1 years; 83.7% men) remained for the current study (103 allocated to CPAP, 105 to no-CPAP). As shown in Table 1, diabetes mellitus was more common among patients allocated to CPAP whereas the distribution of the SAS scores and other baseline characteristics were similar. In all, 37 patients (17.8%) presented SAS scores ≥ 45 with a slightly higher occurrence in the no-CPAP group (Table 1). None of the patients was on hypnotics or anxiolytic drugs as continuous medication. As shown in online supplement eTable 2, baseline characteristics of participants with SAS scores ≥ 45 did not differ significantly between the CPAP vs no-CPAP groups except depressive mood which was more common among the participants allocated to the no-CPAP at baseline. Within the CPAP group with anxiety at baseline (n=14), seven returned the

device within one year, and four out of remaining seven were using the device less than 2.8 hours/day at the 12-month follow-up.

As illustrated in online supplement eFigure 1, 34.0% in the CPAP group, and 38.1% in the no-CPAP group had answered as “little of the time” or “some of the time” to the item 19 (I fall asleep easily and get a good night’s rest), and 3.9% in the CPAP group, and 4.8% in the no-CPAP group had answered as “most of the time” or “good part of the time” to the item 20 “I have nightmares”. Items 5 and 17 were the other questions that were rated more frequently in the entire population (39.0% and 41.3%, respectively) with no between-group differences.

CPAP Usage

In the CPAP group, 31 (30.1%) stopped using the device within 12 months. As shown in online supplement eTable 3, the patients who stopped using the device within one year had similar characteristics at baseline compared with the ones remaining on CPAP. The main reasons for returning the CPAP device were stated as “discomfort” (51.6%), “anxiety” (25.8%), insomnia (16.1%), and “others (the partner dislikes the device, etc.)” (6.5%). In the no-CPAP group (n=103), five patients had crossed-over to the CPAP arm within the follow-up period (Figure 1).

Outcomes

Intention-to-treat population

The distribution of the SAS scores were similar at baseline and at follow-ups (Table 2). As illustrated in Figure 2A, there was a non-significant decrease in change from baseline after 3 months in both groups, and this was more prominent after 12 months, especially in the no-CPAP group. Among patients with no anxiety at baseline (n=171), 11 in the CPAP group, and

7 in the no-CPAP group demonstrated SAS score ≥ 45 at 12 month-follow-up (n.s.). No changes were observed regarding prescription of anti-depressive medications during the follow-up period, and none of the patients were hospitalized due to psychiatric reasons.

As illustrated in Figure 3, there was a weak but significant association between accumulated CPAP hours/day and change from baseline on the SAS scores at 12-month follow-up ($r=0.14$, $p=0.042$). Among the patients randomized to CPAP, the baseline SAS scores predicted non-adherence (adjusted odds ratio 1.11; 95% confidence interval [CI] 1.04-1.18; $p=0.003$) (Table 3). In the entire study population, accumulated CPAP hours/day remained as the only significant variable associated with the delta SAS scores at 12-month follow-up in the multivariate analysis (Table 4).

On-treatment population

As shown in Table 2, the on-treatment analysis revealed that the median SAS score at baseline was significantly higher in the non-adherent/no-CPAP group compared to the participants who were using CPAP ≥ 2.8 hours/day/all days at the 12-month follow-up. As illustrated in Figure 2B, the patients in the non-adherent/no CPAP group rated lower anxiety scores at follow-ups compared to baseline while there was an increased anxiety in the adherent group, which was more prominent after 3 months. Analysis showed that the median delta score (+3.75) in the adherent group was significantly higher than the median delta score in the non-adherent/no-CPAP group (-1.25) after 3 months ($p=0.031$). The difference in the median SAS scores remained significant after 12 months follow-up (+1.25, and -1.25, $p=0.011$, respectively).

DISCUSSION

The present study showed no significant difference in anxiety levels among the CAD patients with nonsleepy OSA, who were randomized to CPAP or no-CPAP in intention-to-treat population. On-treatment analysis revealed a significant increase in the anxiety levels after three months among the individuals using the device at least 2.8 hours/day. The magnitude of the increase in the anxiety level reduced but remained significant at 12-month follow-up.

To the best of our knowledge, the present study is the first RCT evaluating the effect of CPAP treatment on anxiety in a CAD population with concomitant OSA. In the SAVE trial, that involved a larger number of participants with CAD and cerebrovascular disease, CPAP treatment had a neutral impact on anxiety scores based on the Hospital Anxiety and Depression Scale-Anxiety (HADS-A) (20). In the detailed analysis of these results, there was a significant decrease in anxiety symptoms after six months of CPAP treatment among the cases with high scores at baseline, but not at the subsequent assessments. It was argued in an editorial that the lack of improvement in the anxiety scores after CPAP treatment could be due to the low occurrence of anxiety cases at baseline (19). However, the magnitude of the reduction in the scores among the cases did not differ between the CPAP and usual care groups, indicating a poor efficacy of OSA treatment. Indeed, our results suggest that CPAP treatment is associated with an increase rather than a decrease of the anxiety symptoms in CAD patients who are nonsleepy. Given that a large number of the SAVE cases had mild sleepiness (ESS 10-15) at baseline, the improvement in the ESS following CPAP treatment may have contributed to the reduction observed in the anxiety scores at 6 months follow-up in that trial.

Anxiety is defined as a state of uncertainty about future threats, which is accompanied by concern, stress, negative emotions and sense of insecurity (35). It is associated with several cardiovascular pathophysiological processes such as cardiac arrhythmias and increased

autonomic nervous activity (11). Previous studies have demonstrated that the “heart-focused” anxiety symptoms including, fear, tension, high stress, headache, sweating, muscle spasms and palpitations are common in cardiac populations (36). Anxiety as a state can be a transient reaction directly associated to a specific health-related intervention (37). This transient anxiety may expand to a persistent state, namely, trait anxiety. This type of anxiety has been reported in CAD patients who were hospitalized for cardiovascular events during a four-year period after CABG (11). Hence, comorbid anxiety appears to be a risk factor for CAD, and may play crucial roles on the onset, development, management and response to treatment in these high-risk populations. Previous studies have been focused on the incidence and course of the anxiety among CAD cohorts before and after the revascularization procedures (38, 39). However, neither of them has considered OSA in the evaluation of anxiety in revascularized CAD patients. In the present study, not only the traditionally defined OSA in sleep clinic cohorts, but also the nonsleepy phenotype as well as response to CPAP treatment has been examined.

Other studies conducted in sleep clinic cohorts have mainly addressed the relationship between OSA severity and anxiety symptoms (14, 15, 40, 41), and a recent meta-analysis found no significant association (20). It is noteworthy that there was no association between type of questionnaire and the anxiety prevalence in the subgroup of studies included in that meta-analysis (20).

In the current study, approximately one fifth of the cohort was categorized as having anxiety based on the suggested SAS score threshold (≥ 45) with no significant difference between the CPAP and no-CPAP groups. Compared to the previous occurrence rates ranging from 20 to 50% among adults with CAD (4, 5), the prevalence of anxiety in our cohort was at the lower edge. One possible explanation could be the demographic, cultural and clinical differences

between the studied cohorts as well as the scales used in evaluating anxiety. Most of the studies had reported results based on the HADS-A (20); however, no significant difference has been found between HADS-A and SAS in classifying the severity of anxiety (42). In the SAVE trial, the prevalence rates were similar in both CPAP and usual care groups (%14.4 vs %17.0) at the end of the follow-up (20).

We observed no significant change in the SAS scores after 12 months in the entire nonsleepy OSA population. A possible argument for this finding could be the fact that the overall scores were below the threshold among 80% of the population, *i.e.*, the majority of the CAD patients had no or mild symptoms of anxiety at baseline. However, in the subgroup of participants with the SAS scores over the cut-off value, there was an improvement in the state anxiety among the participants allocated to no-CPAP whereas the severity of anxiety remained unchanged among the cases randomized to CPAP. Though the sample size of clinically anxious patients (SAS score ≥ 45) allocated to CPAP at baseline was small, the most of them had returned the device within one year. Moreover, there was a significant association between the baseline SAS scores and non-adherence among the CPAP group, which may imply that subclinical anxiety should be considered in the management of CPAP treatment of CAD patients with the nonsleepy OSA.

Remarkably, there was a significant increase in the delta SAS scores already after 3 months in the whole population among the patients using the device at least 2.8 hours/night, while there was a decline in the non-adherent/no-CPAP group. The significant association between increase in the anxiety scores and CPAP use in the multivariate analysis may suggest that CPAP treatment may worsen symptoms of anxiety among CAD patients with nonsleepy OSA following PCI or CABG. This increase might be temporary given that the magnitude of the

change was reduced at the 12-month follow-up. It is also probable that nonsleepy cardiac patients develop a higher degree of anxiety when they are asked to use CPAP in order to avoid adverse cardiovascular effects of OSA.

Of note, the results of the current study are not applicable to CAD patients with sleepy OSA phenotype. Given that sleepy patients are more prone to be adherent to CPAP therapy compared to the nonsleepy individuals (43), it may be argued that the reduction in excessive daytime sleepiness after CPAP treatment counteracts the anxiety symptoms in the sleepy OSA phenotype. Further analysis of the RICCADSA cohort comparing anxiety symptoms in sleepy vs nonsleepy OSA patients and adherence to CPAP treatment is in progress, and will be reported in future work.

Limitations

This study has a number of limitations that need to be acknowledged. First, the power estimate for the RCT population was done for the primary outcome (composite of repeat revascularization, myocardial infarction, stroke, and cardiovascular mortality), and not for the outcomes addressed in the current study. Second, there is yet no consensus regarding how much change in SAS scores should be considered as minimum clinically important difference (MCID) in CAD patients with concomitant OSA following CPAP treatment. Though 2 points of change in HADS-A scores was suggested as MCID (44), the studies summarized in the recent meta-analysis failed to show such a significant effect of CPAP treatment (20). In the current study, we found a 3.75 points of increase in the median of delta anxiety scores after 3 months among the nonsleepy OSA patients using the device at least 2.8 hours/night. Third, CPAP usage data were downloaded at each follow-up period for the main trial after 3 months, 6 months, 12 months, and yearly up to 6 years, so the downloaded CPAP usage data for the

month prior to completing the questionnaire were not recorded separately. Thus, the patient's CPAP use during the last month prior to the 12-month follow-up could possibly better reflect the association between CPAP usage and anxiety state. Fourth, results of the on-treatment analysis should be interpreted cautiously, because no randomization at baseline to "adherent" versus "nonadherent" is possible. Given that device usage and non-usage is patient-driven, a self-selection bias can therefore not be excluded. Finally, the age distribution of the study cohort is not typical for the OSA population, and our results are, therefore, not generalizable to younger sleep clinic cohorts with symptomatic OSA. Nevertheless, the secondary outcome analysis of the current study gives important insight into how anxiety level is affected by CPAP in revascularized patients with CAD and nonsleepy OSA.

CONCLUSIONS

CPAP prescription to nonsleepy CAD patients with OSA had neutral effect on anxiety levels in intention-to-treat population. However, on-treatment analysis revealed a significant increase in anxiety levels after three months among patients using the device at least 2.8 hours/day. The magnitude of the increase in the anxiety level reduced but remained significant as well at 12-month follow-up. Thus, it seems crucial to personalize the management of CAD patients to include early diagnosis and treatment of anxiety. This is particularly important among nonsleepy OSA phenotype in cardiac populations undergoing PCI or CABG, for whom CPAP treatment is considered in order to decrease the risk for adverse cardiovascular outcomes.

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Data sharing statement

Individual participant data that underlie the results reported in this article can be obtained by contacting the corresponding author, yuksel.peker@lungall.gu.se.

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Figure legends

Figure 1. Flow of patients through the study.

Definition of abbreviations: AHI = apnea-hypopnea index; CAD = coronary artery disease; CPAP = continuous positive airway pressure; CSA-CSR = central sleep apnea-Cheyne Stokes respiration; ESS = Epworth Sleepiness Scale; OSA = obstructive sleep apnea; RCT = Randomized Controlled Trial; RICCADSA = Randomized Intervention with CPAP in Coronary Artery Disease and Sleep Apnea.

Figure 2A. Distribution of delta scores on Zung Self-rated Anxiety Scale at 3- and 12-month follow-ups in intention-to-treat population.

Figure 2B. Distribution of delta scores on Zung Self-rated Anxiety Scale at 3- and 12-month follow-ups in on-treatment population.

Definition of abbreviations: CPAP = continuous positive airway pressure.

Figure 3. Correlation between accumulated CPAP hours/day and change on Zung Self-rated Anxiety Scale scores from baseline at 12-month follow-up in the entire study population.

Definition of abbreviations: CPAP = continuous positive airway pressure.

Table 1. Baseline characteristics of the entire study population with coronary artery disease and nonsleepy obstructive sleep apnea (n=208).

	CPAP (n=103)	No-CPAP (n=105)
<i>Demographic characteristics</i>		
Age, y	65.9 (60.5-70.8)	67.4 (61.0-73.1)
Age $\geq$ 65 y, %	53.4	55.2
BMI kg/m ²	27.8 (25.6-30.1)	28.7 (26.7-30.1)
Obesity, %	26.2	26.7
Male sex, %	83.5	83.8
<i>Home sleep apnea testing</i>		
AHI, events/h	23.9 (17.9-36.8)	24.8 (18.8-35.4)
<i>Comorbidities</i>		
Current smoking at baseline, %	15.5	13.3
CABG before inclusion,%	26.2	25.7
AMI at baseline,%	55.3	48.6
Former revascularization, %	19.4	17.1
Hypertension,%	68.9	60.0
Diabetes mellitus,%	28.2	16.2*
Stroke,%	7.8	6.7
Pulmonary disease, %	3.9	8.6
Anti-depressive medication, %	4.0	1.9
<i>Questionnaires</i>		
ESS score	6.0 (4.0-8.0)	5.0 (4.0-7.0)
Zung SDS score $\geq$ 50, %	29.0	26.0
Zung SAS score	37.5 (32.5-41.3)	37.5 (32.5-43.8)
Anxiety (Zung SAS score $\geq$ 45), %	13.6	21.9

Continuous variables are expressed as median and boundaries of interquartile ranges.

Definitions of abbreviations: AMI, acute myocardial infarction; AHI, apnea hypopnea index; BMI, body mass index; CABG, coronary artery bypass graft; CPAP, continuous positive airway pressure; ESS, epworth sleepiness scale; PCI, percutaneous coronary intervention; SAS, self-rating anxiety scale; SDS, self-rating depression Scale.

* $p < 0.05$

Table 2. Between-group comparisons of the absolute values of the Zung SAS scores in the entire study cohort at baseline and follow-ups.

		Baseline	After 3 Months	After 12 Months
	n	Median (25 th %- 75 th %)	Median (25 th %-75 th %)	Median (25 th %-75 th %)
Intention-to-treat population				
CPAP	103	37.5 (32.5-41.3)	36.9 (31.3-41.3)	36.3 (31.3-40.0)
No-CPAP	105	37.5 (32.5-43.8)	38.2 (32.5-42.5)	36.3 (31.3-42.5)
		<i>n.s.</i>	<i>n.s.</i>	<i>n.s.</i>
On-treatment population				
CPAP usage $\geq$ 2.8 hours/day	59	36.3 (31.3- 41.3)	37.5 (31.3- 41.3)	36.3 (30.0-42.5)
CPAP usage < 2.8 hours/day or no-CPAP	149	38.8 (33.8-43.8)	37.5 (32.5- 42.5)	36.3 (31.3-41.3)
		<i>p</i> = 0.009	<i>n.s.</i>	<i>n.s.</i>

Definitions of abbreviations: CPAP, continuous positive airway pressure; SAS, self-rated anxiety scale. P-values refer to between-group differences in absolute values of the SAS scores.

Table 3. Predictors of nonadherence among patients randomized to CPAP at baseline (n=103).

Multivariate	Odds Ratio	95% CI	<i>p</i>-values
Age	1.00	0.95, 1.05	0.912
Male sex	1.09	0.35, 3.46	0.879
CABG at baseline	0.83	0.32, 2.16	0.832
ESS score at baseline (0-9)	0.99	0.82, 1.19	0.933
Zung SAS score at baseline	1.11	1.04, 1.18	0.003

Definition of the abbreviations: CABG, coronary artery bypass grafting; CI, confidence interval; CPAP, continuous positive airway pressure; ESS, epworth sleepiness scale; SAS, self-rated anxiety scale.

Table 4. Predictors of change from baseline in SAS scores at 12- month-follow-up in the entire study population (n=208).

Multivariate	Standardized β	95% CI	<i>p</i>-values
Age	0.001	-0.108, 0.107	0.990
Male sex	-0.096	-3.893, 0.748	0.183
CABG at baseline	-0.077	-3.139, 0.984	0.304
AMI at baseline	-0.066	-2.602, 0.981	0.373
Pulmonary disease	0.023	-3.031, 4.168	0.756
Accumulated CPAP hours/day	0.144	0.005, 0.695	0.047

Definition of the abbreviations: AMI, acute myocardial infarction; CABG, coronary artery bypass grafting; CI, confidence interval; CPAP, continuous positive airway pressure; SAS, self-rated anxiety scale.