Title: Complex sleep apnea at auto-titrating CPAP initiation: prevalence, significance and predictive factors.

Running head: Prevalence and predictive factors of complex apnea

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Abstract

**Introduction:** Obstructive sleep apnea (OSA) patients may develop central respiratory events under continuous positive airway pressure (CPAP), referred to as complex sleep apnea (CompSA).

**Objective:** We aimed to assess prevalence and predictive factors of complex apnea and to evaluate treatment response to CPAP.

**Methods:** Within a retrospective cohort study, we assessed clinical data of OSA patients, attending the sleep lab during a 15-months period. Included participants underwent two consecutive polysomnographies; baseline diagnosis and treatment trial. Complex apnea patients, defined by a central apnea index $\geq 5$ per hour during pressure auto-titration, were compared to remainders.

**Results:** Among 263 included patients, the prevalence of complex apnea was 9.1%. The mean apnea hypopnea index only dropped from 52.7 to 39.9 per hour in CompSA patients, while it improved from 40.9 to 7.3 in patients without CompSA. Although a decreased sleep-fragmentation under CPAP was observable in both groups, the enhancement of Non-REM sleep was superior in patients without CompSA. The CompSA patients showed higher median apnea-hypopnea, mixed apnea and central apnea indices at baseline and displayed higher rates of co-morbid heart failure and obstructive pulmonary disease, but no higher severity of associated daytime fatigue and sleepiness symptoms.

**Conclusion:** Despite evidenced partial improvement of obstructive events, nocturnal hypoxemia and sleep fragmentation, the occurrence of complex apnea presented here as a clear therapeutic failure of auto-titrating CPAP and was associated with heart failure, COPD and higher central and mixed apnea indices at baseline.
Keywords: sleep apnea, complex apnea, central apnea, CPAP, sleep quality, polysomnography

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Introduction

According to the International Classification of Sleep Disorders (ICSD-3), central apneas (CA) during sleep are defined as recurrent apneic events in the absence of upper airway collapse or obstruction episodes (1). CA are presumably attributed to dysfunctions of the central nervous system (CNS) and related ventilatory control mechanisms (2,3). CA are either referred to as being idiopathic, related to periodic breathing (Cheyne-Stokes) or occurring as high altitude related apneas (2-4). Despite the fact that CA may represent about only 5 percent of encountered disorders in sleep labs, increased incidences are observable in co-morbid conditions like heart failure or renal insufficiency and certain CNS related disorders (3).

CA might also occur in obstructive sleep apnea (OSA) patients at the initiation of a continuous positive airway pressure (CPAP) treatment (2,5-7). The latter are generally referred to as complex sleep apnea (CompSA) (2,8,9). Previously mentioned hypotheses about CompSA mainly concerned the sudden CPAP-induced decline of upper airway resistance, associated with a decrease of PaCO$_2$. Arterial CO$_2$ is thereupon potentially lowered for any given set of ventilatory condition (10). If PaCO$_2$ values drop below the so-called CO$_2$ apnea threshold, then central apnea can be expected. Indeed, high upper airway resistance can modify ventilatory control mechanisms and therewith reduce CO$_2$ excretion efficacy (10,11). Whether predictive parameters for the occurrence of CompSA can be defined after diagnosis of OSA or whether certain pre-existing or co-morbid conditions might be more systematically related to CompSA remains however uncertain. Hence, the main purpose of the present study was: (a) to assess the prevalence of CompSA during CPAP pressure titration in a population sample of OSA patients and (b) aimed at the identification of potential predictive factors for CompSA. In addition, it remains also unclear if whether CompSA patients present systematically with more severe sleep impairment or higher intensities of associated daytime symptoms. Therewith, we also compared sleep variables between nights and clinical complaints (i.e. fatigue, sleepiness,
affective symptoms and perceived sleep quality) in CompSA patients versus patients without CompSA.

Methods

Patients

Medical files from all patients which underwent diagnostic polysomnography recording and subsequent CPAP pressure titration in the sleep laboratory of a general University Hospital during a 15 months period (between January 2012 and March 2013) were considered for eligibility. During the study period, patients with an apnea-hypopnea index (AHI, see below) > 20 per hour and an arousal index (ArI) (see below) > 30 per hour during the first diagnostic PSG were invited to benefit from a CPAP treatment trial, with pressure titration, in accordance with the convention requirements for supported care from the Belgian health insurance system.

Patients who underwent CPAP during a second night were then considered for inclusion, and electronic data of interest for clinical and PSG variables were extracted. Upper pressure limit, during automated titration was calculated by adding 4 cm H$_2$O to the estimated optimal pressure according to the prediction equation: pressure = [(0.16 × BMI) + (0.13 × neck circumference) + (0.04 × AHI) − 5.12] (12). Lower pressure bound was set at 4 cm H$_2$O for all patients.

Patients with a CA index (CAI) ≥ 5 per hour during the CPAP pressure titration were considered as presenting with CompSA (13). Patients with incomplete medical files (i.e. lacking clinical data, incomplete psychometric scales, electronic storage problems…) or incomplete CPAP pressure titration were excluded from further analysis. According to inclusion and exclusion criteria and for the purpose of comparisons, subjects were therewith divided in two groups: CompSA patients and the remainders further referred here to as patients without CompSA.
Demographical data including age, gender, body mass index (BMI in kg/m²) and neck circumference (in cm) were assessed for each subject. Co-morbid clinically significant medical conditions (stroke, heart failure, chronic renal failure, hypertension, chronic obstructive pulmonary disease (COPD), gastro-esophageal reflux, diabetes mellitus), and ongoing current or recent (past month) and potentially sleep-interfering neuropharmacological treatments (benzodiazepines (BZD); antidepressants (AD), opioids) were also recorded for all patients. However, intake of BZD during PSG recording was not allowed and no opioid drugs were administered during hospitalization. All participants admitted to the sleep unit were prepared for PSG recording between 9 pm and 11 pm and allowed to retire when they wished. Morning arousal was spontaneous in most cases.

Material

The recordings included three or more electroencephalograms recorded at least from Fp2-A1, C4-A1, O2-A1, sites, two electrooculograms, submental and bilateral anterior tibial electromyograms. Oral and nasal airflow were recorded by an oro-nasal cannula (Pro-Flow Plus™ Pro-Tech® Mukilteo, WA, USA), respiratory effort was measured by thoracic and abdominal belts (Pro-Tech® CT2™, Mukilteo, WA, USA). Capillary oxygen saturation was monitored by photosensitive finger-oxymetry (Nonin® Flexi-Form® II 7000A Nonin Medical Inc, Minneapolis, MN USA and LINOP® Adt Masimo corp. Irvine, CA, USA). All PSG recordings were analyzed on 21” screens displaying 30 second polysomnograph epochs (Philips Respironics Inc™ Alice5®, Philips Healthcare™, Eindhoven, The Netherlands, European Union) by trained technicians unaware of the aims of the study. Auto-adjusting pressure titration, was performed by means of REMstar® (Philips Respironics Inc™) CPAP devices in all patients.
Polysomnography

Sleep onset latency was defined as the time from lights-off to the first 30 seconds epoch of sleep. Sleep period time (SPT) is the time interval from sleep onset to final awakening. Total sleep time (TST) is defined as SPT minus the total duration of cumulated intra-sleep awakenings (wake time after sleep onset, WASO). The internal sleep efficiency index (SEI), expressed in percent, is defined here as the ratio between TST and SPT (SEI = (TST/SPT)*100). NREM (Non Rapid Eye Movement) sleep included sleep stages N1, N2 and N3 (or slow wave sleep, SWS). Light sleep (LS) was defined as the sum of N1 and N2 (14). REM (Rapid Eye Movement) sleep latency (REMLAT) was defined as the time between sleep onset and the first epoch of REM sleep. An episode of sleep apnea was defined as a more than an 80% reduction in airflow for at least 10 seconds during sleep. A sleep hypopnea was defined as a ≥ 30% reduction of airflow amplitude accompanied by either a 3% or greater reduction in oxygen saturation or an arousal. Oxygen desaturation index (ODI) was defined here as the number of 3% or greater reductions in oxygen saturation per hour. Arousals were defined according to AASM criteria (1) and the arousal index (ArI) represented the number of arousals divided by TST.

Clinical assessment

During the study period, all patients in our lab completed questionnaires about life style, drinking habits and sleep. Patients with reported daily smoking habits were considered as smokers (irrespective of the number of cigarettes or other) and patients with a consumption of more than two units of alcohol per day were encoded as alcohol consumers (see also result section and table 1). Patients reporting sleep initiation, maintenance difficulties or early arousals (> 3 times per week during the past month) were considered here as presenting co-morbid insomnia complaints.
Self-reporting psychometric scales with classical semantic instructions for fatigue and sleepiness were given to all participants on the first day of their stay in our unit at the same daytime (between 5 p.m. and 7 p.m.) before their first night of polysomnographic recording during the study period.

The **Fatigue Severity Scale** (FSS) is a self-reporting tool used to assess symptomatic intensity levels of fatigue and its effect on daily functioning (15). The FSS is a 9 item 7-point Likert-type scale. Scores are usually reported as ‘mean scores’ (ranging from 1 to 7) obtained by dividing the total score (ranging from 7 to 63) by 9. For clinically significant pathological daytime fatigue, a cut-off >5 on mean scores is often proposed (16).

The **Epworth Sleepiness Scale** (ESS) is the most widely used scale of subjective sleepiness and daytime sleep propensity. The ESS consists of 8 items (described situations) arranged on a 4-point Likert scale ranging from 0 (“never doze”) to 3 (“high chance of dozing” during daytime). The summed scores range from 0 to 24 and scores above 10 are commonly interpreted as clinically relevant increased daytime sleepiness (17).

The **Pittsburgh Sleep Quality Index** (PSQI) assesses subjective sleep quality. The 19 items are grouped into seven component scores, each weighted equally on a scale from 0-3. These components are subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication and daytime dysfunction. The component scores are then summed to yield the global PSQI score. In validation studies, a global PSQI score > 5 indicates that a subject is having severe difficulties in at least two areas, or moderate difficulty in more than three areas (18).

**Affective symptoms:** the Hospital Anxiety and Depression rating scale (HADRS) is a self-report rating scale of 14 items on a 4-point Likert scale (with a range from 0–3). It is the most commonly used psychometric tool in general internal medicine designed to measure the
intensity of anxiety and depression symptoms (7 items for each subscale, HAD-A and HAD-D with respective scores ranging from 0–21). The reliability and validity of the HADRS have been tested in a vast number of studies. Scores ≥ 11 on each subscale have previously been considered as clinically significant (19).

**Statistics**

Group differences for nominal variables were computed using Fisher’s exact tests. Violations of normality were assessed by means of one-sample Kolmogorov-Smirnov tests. Between-group comparisons of demographic and psychometric variables were either computed using univariate analysis of variance (ANOVA) or using non-parametric Mann-Whitney U tests. Non-normally distributed PSG variables were further rank-transformed. Two-way mixed analyses of variance (Mixed ANOVA) were then used to test effects within groups, between nights and their interactions. Multivariate logistic regression was carried out for predictive outcome value of nominal variables. Hypothesis tests were performed two-sided at the 5% significance level. Trends were reported at the 10% level of significance. Statistical analyses were computed using IBM SPSS 22® (Industrial Business Machines, SPSS™ Inc., Chicago, IL).

The study was approved by the local ethical committee and conducted in accordance with the rules and regulations for the conduct of clinical trials stated by the World Medical Assembly in Helsinki.

**Results**

During the study period, 1560 PSGs had been performed. 936 patients presented with other sleep disorders or primary diagnoses than OSA or with mild OSA not fulfilling the inclusion
criteria. Among 312 patients which had initially included after baseline polysomnography and referred for CPAP titration, 49 patients were excluded for incomplete data or lacking information within the medical files. Finally, 263 patients were definitely included for further analysis (see figure1).

**Prevalence of complex apnea**

Among the 263 included subjects, 24 patients presented with CompSA at CPAP trial, depicting a prevalence of 9.1% (5.6-12.6, 95%CI).

**Baseline characteristics of the study sample**

Table 1 summarizes the study sample’s demographical data, clinical findings, co-morbid conditions and psychometrics. Age, gender and BMI distributions showed respectively 184 male (70.0%) and 79 female (30.0%) patients, mean age of 54.8(13.3) years and a mean BMI of 31.9(6.6) kg/m\(^2\) for the total sample. Gender distribution was similar between CompSA and the remainders (table 1). BMI, age and neck circumference were also similar between groups (table 1). In CompSA patients, heart failure and COPD showed significantly higher prevalence, while a medical history of stroke showed a trend for higher prevalence. In addition, a trend for more smokers in the CompSA group was also found. All other co-morbid conditions including reported insomnia complaints showed similar frequencies between groups (table 1).

**Risk factors associated with CompSA**

According to multivariate logistic regression, independent predictive factors for CompSA were higher CAI and MAI at baseline, prior to CPAP, with respective odds ratios (95% CI) of 1.10(1.02-1.19) for an increase of 1 in CAI and 1.09(1.01-1.18) for an increase of 1 in MAI.
**Polysomnography**

For descriptive purposes, table 2 summarizes mean or median values from all PSG derived variables of both groups for both nights (baseline diagnosis and CPAP pressure titration). All comparison outcomes between groups and conditions (baseline night and CPAP trial) are given here below by means of mixed ANOVAs.

**Within group and between nights comparisons (Factorial plots, Figure 2 a and b)**

*Respiratory variables (Figure 2a)*

Statistically significantly higher AHI (F(1,260)= 36.911, p< .001), MAI (F(1,209)= 52.262, p< .001), CAI (F(1,208)= 65.741, p< .001) and ODI (F(1,254)= 21.334, p< .001) were found in the in the CompSA group. Except for a worsening of CAI during CPAP trial (CAI: F(1,208)= 6.136, p= .014) and a trend for a decrease of the percent of TST spent snoring (F(1,247)= 3.160, p= .077), all other respiratory indices showed a statistically significant improvement during CPAP pressure titration (AHI: F(1,260)= 15.445, p< .001; OAI: F(1,209)= 6.326, p= .013; MAI: F(1,209)= 7.900, p= .005; HI: F(1,210)= 17.863, p< .001; ODI: F(1,254)= 11.482, p< .001). As evidenced by interaction effects, a statistically significantly larger improvement was found in the group without CompSA for AHI (F(1,260)= 22.710, p< .001), OAI (F(1,209)= 7.011, p= .032), HI (F(1,210)= 24.676, p< .001), MAI (F(1,209)= 10.426, p= .001), ODI (F(1,254)= 16.486, p< .001) and the percentage of TST spent snoring (F(1,247)= 4.597, p= .033). CAI increased significantly higher in the CompSA group during the CPAP trial (F(1,208)= 7.815, p= .006).

*Sleep variables (Figure 2b)*

Sleep fragmentation was significantly higher in the CompSA group (F(1,256)= 10.410, p= .001). Albeit the latter improved significantly in both groups during the CPAP trial (F(1,256)= 4.074, p= .045), the improvement was significantly higher in the group without CompSA (F(1,256)= 7.087,
p = .008). SWS proportions of TST increased significantly during CPAP titration (F(1,237) = 3.801, p = .05). REM sleep proportions increased mostly in the group without CompSA, as evidenced by an interaction effect significant at the trend level (F(1,255) = 3.489, p = .063). LS proportions of TST decreased significantly during the CPAP night (F(1,226) = 9.252, p = .003) with a significant interaction effect between groups and conditions (F(1,226) = 6.053, p = .015). All other tested comparisons returned non-significant.

**Discussion**

CompSA is not a rare condition. In our study sample of 263 patients, the overall prevalence of CompSA was 9.1%. Previous findings reported slightly divergent prevalence rates for CompSA. These ranged, in larger retrospective studies, from 5% in 1312 patients (5) to 6.5% (with monthly varying incidences between 3% and 10% over a 1-year period) in 1286 patients (20), and went up to 12.2% at CPAP initiation in a prospective study (21) and 13.1% in another smaller retrospective study of 99 consecutive OSA patients (2). Hence, the presently found prevalence is agreeably within the boundaries of these former reports. Discrepancies between studies may in fact essentially be attributable to study designs; manual (vs. automated) pressure titration procedures (5,20) with different lower pressure bounds (i.e. starting at 5 cm H\textsubscript{2}O) (20), inclusion criteria (i.e. AHI thresholds or partially allowing split-nights) (2) or the type of positive airway pressure device (Bi-level vs. CPAP).

The main finding of the present study is the lack of adequate treatment response to CPAP in patients with CompSA. Indeed, in these patients, the mean AHI of 52.7 events per hour only dropped to 39.9 events per hour of sleep under CPAP. The latter was not only a clinically irrelevant reduction, but was even not statistically significant. In contrast, the mean AHI, of patients without complex apnea, improved from 40.9 to 7.3 during pressure titration. Albeit that, respiratory indices decreased to small extents, CompSA patients also showed a further significant worsening of CAI under CPAP. Moreover, with respect to the pressure titration night,
AHI, MAI, OAI, HI and ODI were all still significantly increased in the CompSA group. Therewith, the improvement of sleep related respiratory events was expectedly significantly larger for all variables in patients without CompSA. Despite the fact, that CO$_2$ apnea-thresholds can evolve and that CPAP treatment-emerging CA might resolve over a given time course (days or mostly weeks) in some cases (10,21); the occurrence of CompSA under CPAP was associated in our study with a clear therapeutic failure at the point of pressure titration. Similar observations were made for sleep fragmentation, showing clinically significant improvement of arousals solely in patients without CompSA. While, from a statistical point of view, sleep fragmentation decreased undeniably in both groups during CPAP, the latter also showed a much larger effect in the group without CompSA. The mean ArI under CPAP remained above 30 per hour of sleep in CompSA patients, which is not satisfactory at all from a clinical point of view. Likewise in previous study reports (9,20), measured sleep efficiency was also similar between groups here. Regarding the impact on sleep structure, an increase of LS at the expense of SWS is a commonly observable physiopathological phenomenon in primary sleep disorders like OSA (14). Although SWS proportions increased here in both groups during CPAP, the dynamic exchange in NREM sleep, between LS and SWS proportions solely showed a significant improvement in patients without CompSA (as evidenced by significant interactions and depicted by respective slopes of factorial plots). Meanwhile, despite evidenced partial improvements of obstructive events, nocturnal desaturation and sleep fragmentation, the incidence of complex apneas during pressure titration can, also with respect to the observed effect on sleep composition, mostly be considered as a treatment letdown of CPAP, at least at its initiation.

An important objective of our study was to identify potential predictive factors for CompSA. In accordance with previous reports (5,9,20), we did not find significant differences in demographics or BMI. Moreover, though being clinically significant, perceived sleep quality impairment was also equally altered in both groups here. Hence, CompSA patients did not
present with a higher impact on sleep quality than patients without CompSA. Patients from both groups showed comparable moderate fatigue severity levels and subjective sleepiness levels were, on average, similarly borderline with respect to clinical thresholds for excessive daytime sleepiness. Furthermore, affective symptom intensities (anxiety and depression scores) showed no differences between groups and remained below clinical significance. Even though most previous studies did not systematically report measurements of clinical symptoms other than subjective sleepiness, our results are at least in accordance with those reporting no significant difference in Epworth scores between patients with vs without CompSA (9,20,21). On the other hand, we found that heart failure and COPD are more prevalent in CompSA patients. This may come to no surprise; heart failure in particular has consistently been associated to higher risks of developing CompSA (22). Given that heart failure implies potential circulatory instability and delay, the latter can lead to a number of changes in ventilatory control including enhanced chemoreceptor sensitivity and delayed ventilatory responsiveness (22). The higher prevalence of COPD is less straightforward here. Although OSA may exist as an overlap with COPD, a specifically increased risk for central events in COPD without cor pulmonale or congestive heart failure remains undetermined. An increased nocturnal hypoventilation, associated to hypercapnia in some COPD patients could however in the long term also lead to changes in chemoreceptor sensitivity (23). Our findings also showed, in line with previous reports (2,5,20,21), significantly higher severity of sleep related respiratory disturbance (AHl, MAI, CAI and ODI) at baseline. However, these findings make part of the ongoing debate about CompSA being solely treatment-emergent or transient CA, which could in many cases resolve spontaneously over time (10,21). In a very recent prospective randomized trial (CPAP versus adaptive servo-ventilation device (ASV)), Morgenthaler and colleagues (24) showed in an intention-to-treat analysis that, after 90 days of therapy, significantly more CompSA patients improved under ASV (89.7%) than under CPAP (64.5%). Whether pre-existing supposed chemo-reflex dysfunction can positively evolve in any patient is therefore questionable. For
patients with co-morbid cardio-vascular or respiratory conditions, this may even be unlikely and part of these patients may need adequate care with non-invasive positive pressure ventilation, either using bilevel positive airway pressure with a back-up ventilatory rate, or using ASV (7,24,25).

At last, auto-titrating procedures may be more prone to induce CompSA in certain patients. The fact that we did not perform control PSG with manual titration or fixed CPAP pressure could on one hand be considered as a limitation here. On the other hand these considerations do not interfere with the significance of our findings. With respect to predictive values of respiratory events (types and indices) and clinical status at baseline, the outcomes of PSG-derived parameters at CPAP initiation were indeed obtained under the same conditions and by means of identical procedures in all patients of our sample.

In summary, almost 1 in every 10 patients presented here with CompSA during CPAP pressure auto-titration. The occurrence of CompSA was clearly associated with some degree of therapeutic failure. CompSA patients showed increased co-morbid heart failure and COPD, but no higher severity of associated daytime symptoms. Significant associated risk factors for the occurrence of CompSA were the presence of central or mixed apneas prior to CPAP treatment.

Alternative pressure titration pathways, in patients displaying such respiratory events at diagnosis, may help to reduce CompSA in some patients, in order to permit adaptation of dysfunctional chemo-reflexes (10), but more sophisticated non-invasive ventilation may be needed for others (7,24,25). Additional large prospective and/or long-term follow-up studies of patients with CompSA at CPAP initiation, might still be mandatory for documenting long-term evolution of central apneas in these patients and in order to establish clear algorithmic treatment guidelines for CompSA.
References


### Table 1: Demographics, co-morbid conditions and psychometrics

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<th>CompSA (n=24)</th>
<th>without CompSA (n=239)</th>
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<td>Age (years)</td>
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<td>Opioids</td>
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**Legend (Table 1):**

- Body mass index (BMI); Chronic obstructive pulmonary disease (COPD); mean scores of the Fatigue severity scale (FSS); Epworth sleepiness scale (ESS); Depression (HAD-D) and Anxiety (HAD-A) scores; Pittsburgh sleep quality index (PSQI); Benzodiazepines (BZD); Antidepressants (AD). Values are expressed as means +/- (standard deviation) or median (interquartile range) for non-normally distributed variables. For nominal variables, respective percent values are given between brackets. P values express significance of group comparisons performed by parametric tests for continuous and normally distributed variables and non-parametric tests for non-normal distributions or nominal variables (see also methods and results sections). Trends are given between brackets. Non-significant outcomes are given in light-grey.
Table 2: Polysomnography

<table>
<thead>
<tr>
<th>PSG variables</th>
<th>Night 1 (Baseline)</th>
<th>Night 2 (CPAP trial)</th>
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<tbody>
<tr>
<td></td>
<td>CompSA (n=24)</td>
<td>without CompSA (n=239)</td>
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<tr>
<td>TST (min)</td>
<td>395 (307.5-476.2)</td>
<td>398.7 (344.5-448.5)</td>
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<tr>
<td>WASO (min)</td>
<td>72.5 (50.0-111.2)</td>
<td>69.7 (39.5-116.5)</td>
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<td>REMLAT (min)</td>
<td>138.0 (77.5-245.0)</td>
<td>117.0 (74.0-219.6)</td>
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<td>SEI (%)</td>
<td>83.5 (72.0-90.0)</td>
<td>85.1 (77.3-91.4)</td>
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<td>REM (%)‡</td>
<td>7.8 (5.3-16.0)</td>
<td>10.0 (4.5-14.0)</td>
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<tr>
<td>N1 (%)</td>
<td>9.3 (6.5-19.6)</td>
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<tr>
<td>N2 (%)</td>
<td>57.9 (16.4)</td>
<td>59.5 (13.9)</td>
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<tr>
<td>LS (%)§‡</td>
<td>74.4 (16.8)</td>
<td>74.3 (13.7)</td>
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<tr>
<td>SWS (%)§‡</td>
<td>9.5 (4.9-23.7)</td>
<td>14.6 (7.4-21.4)</td>
</tr>
<tr>
<td>CAI (/h)§‡‡</td>
<td>3.7 (1.3-7.5)</td>
<td>0.2 (0-1.2)</td>
</tr>
<tr>
<td>OAI (/h)§‡‡</td>
<td>6.4 (1.3-15.2)</td>
<td>7.1 (2.3-17.9)</td>
</tr>
<tr>
<td>MAI (/h)§‡‡</td>
<td>2.3 (0.3-8.3)</td>
<td>0.3 (0-1.2)</td>
</tr>
<tr>
<td>HI (/h)§‡‡</td>
<td>16.8 (10.5-26.3)</td>
<td>20.5 (16.6-27.5)</td>
</tr>
<tr>
<td>AH (/h)§‡‡</td>
<td>49.6 (24.9-79.5)</td>
<td>30.5 (23.2-51.2)</td>
</tr>
<tr>
<td>ARI (/h)§‡‡</td>
<td>44.0 (35.6-73.8)</td>
<td>43.0 (36.3-56.0)</td>
</tr>
<tr>
<td>ODI (/h)§‡‡</td>
<td>42.1 (25.8-69.6)</td>
<td>29.2 (17.9-52.2)</td>
</tr>
<tr>
<td>Snoring (%)‡</td>
<td>11.9 (4.1-26.3)</td>
<td>26.8 (9.6-43.2)</td>
</tr>
</tbody>
</table>

Legend (Table 2):

Polysomnography (PSG). Total sleep time (TST), wake after sleep onset (WASO) and REM latency (REMLAT) in minutes (min). NREM sleep stages 1 & 2 (N1 & N2), slow wave sleep (SWS/N3), Light sleep (LS, sum of N1 and N2) and Rapid Eye Movement (REM) sleep in percent (%). Sleep efficiency index (SEI=(TST/SPT)*100) in percent (%); Complex Sleep Apnea (CompSA), apnea-hypopnea index (AHI), oxygen desaturation index (ODI) and arousal index (ArI) are ratios per hour of sleep without units. Snoring expresses sleep time spent snoring in percent (%). Values are expressed as means +/- (standard deviation) or median (interquartile range). Statistically significant effects (at least at the p<.05 level) are depicted by the following symbols: # (group), § (condition) and ‡ (interactions). Detailed statistical outcomes of comparisons are reported in the results section.
Figure 1: Flow-chart of inclusion procedure

Legend (Figure 1):

During the study period, 1560 polysomnographies (PSGs) had been performed. 936 patients presented with other primary disorders, not corresponding to initial inclusion criteria. 312 patients had initially been referred to CPAP pressure titration and underwent 2 consecutive nights of PSG. 49 out of these 312 patients were further excluded for incomplete data or lacking information within the medical files. 263 patients were definitely included for further analysis.
Figure 2: Factorial plots displaying differences between groups and nights

2a: Respiratory variables

Legend (Figure 2a and b):
Figures depict values of obstructive apnea index (OAI), hypopnea index (HI), apnea-hypopnea index (AHI), central apnea index (CAI), mixed apnea index (MAI), oxygen desaturation index (ODI) snoring (percentage of TST spent snoring), Total sleep time (TST), wake after sleep onset (WASO), arousal index (ArI), Rapid Eye Movement sleep (REM), slow wave sleep (SWS), Light sleep (LS, sum of NREM N1 and NREM N2) and Sleep efficiency index (SEI = (TST/SPT)*100). Dark grey lines depict CompSA and light grey lines, patients without (w/o) CompSA. Error bars represent +/- 1 standard deviation. Statistical outcomes are reported in the results section.