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ORIGINAL RESEARCH

Clinical predictors of central sleep apnea evoked by positive airway pressure titration

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Purpose: Treatment-emergent central sleep apnea (TECSA), also called complex apnea, occurs in 5%–15% of sleep apnea patients during positive airway pressure (PAP) therapy, but the clinical predictors are not well understood. The goal of this study was to explore possible predictors in a clinical sleep laboratory cohort, which may highlight those at risk during clinical management.

Methods: We retrospectively analyzed 728 patients who underwent PAP titration (n=422 split-night; n=306 two-night). Demographics and self-reported medical comorbidities, medications, and behaviors as well as standard physiological parameters from the polysomnography (PSG) data were analyzed. We used regression analysis to assess predictors of binary presence or absence of central apnea index (CAI) ≥5 during split-night PSG (SN-PSG) versus full-night PSG (FN-PSG) titrations.

Results: CAI ≥5 was present in 24.2% of SN-PSG and 11.4% of FN-PSG patients during titration. Male sex, maximum continuous positive airway pressure, and use of bilevel positive airway pressure were predictors of TECSA, and rapid eye movement dominance was a negative predictor, for both SN-PSG and FN-PSG patients. Self-reported narcotics were a positive predictor of TECSA, and the time spent in stage N2 sleep was a negative predictor only for SN-PSG patients. Self-reported history of stroke and the CAI during the diagnostic recording predicted TECSA only for FN-PSG patients.

Conclusion: Clinical predictors of treatment-evoked central apnea spanned demographic, medical history, sleep physiology, and titration factors. Improved predictive models may be increasingly important as diagnostic and therapeutic modalities move away from the laboratory setting, even as PSG remains the gold standard for characterizing primary central apnea and TECSA.

Keywords: risk, prediction, central apnea, complex apnea, emergent, titration

Introduction

Treatment-emergent central sleep apnea (TECSA), also known as complex apnea or "CompSA", is a recognized cause of therapeutic failure occurring in a subset of patients with obstructive sleep apnea (OSA). The prevalence of TECSA has been reported in the range of 1.6%–20% in continuous positive airway pressure (CPAP)-treated OSA patients.[1] The natural history of TECSA remains uncertain, although a recent randomized trial of CPAP versus adaptive servoventilation suggested that it may resolve spontaneously in about half the PAP-treated patients,[2] consistent with prior retrospective and prospective studies.[2–5] In addition to mechanistic questions

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as to the basis of TECSA, the utility of clinical predictors may influence utilization decisions regarding diagnostic and therapeutic strategies in certain patients. TECSA is important to recognize, because if it persists in standard PAP therapy, then alternative treatments should be sought.[6] Before therapy is initiated, risk factors predicting TECSA could be used to stratify those who warrant closer evaluation or in-lab assessments, such as demographic or clinical information. Some clues may surface after the start of PAP therapy, such as elevated apnea–hypopnea index (AHI) detected by the PAP machine, or symptoms of air hunger or inadvertent mask removal,[7] although overall adherence may be similar in people with versus those without TECSA.[4] Several potential mechanisms may underlie central apnea pathophysiology, such as relative hypocarbia compared to the apnea threshold and relatively high loop gain,[8] with a potential impact on clinical history, medications, and titration.[1,9,10] During titration, rapid or excessively high titration, excessive mask leak, and use of bilevel positive airway pressure (BiPAP) may be contributors. These titration factors may result in reduced carbon dioxide and thus trigger central events. Male sex,[7,11–13] older age,[14] narcotic use,[3] severity of OSA,[3,11,12] non-rapid eye movement (NREM) dominance,[11,15] central apnea pre-PAP,[3,7,12,14,15] use of BiPAP,[16] increased nasal resistance,[17] cardiac history (especially atrial fibrillation heart failure),[12,18] and stroke[19] have been linked to central sleep apnea and/or TECSA, but the literature has not been consistent in that different studies do not always identify the same risk factors, and many studies excluded groups with potentially important risk factors (eg, heart failure and opiates). Other work suggests that untreated OSA alters chemosensitivity[20] and that sensitivity is restored by PAP therapy,[21] which in susceptible individuals might lead to transient vulnerability to central apnea.

Identifying TECSA typically requires laboratory polysomnography (PSG), as home sleep testing kits are not validated for detection of central apnea during diagnostic testing.[22] With increasing pressure toward home testing and auto-PAP approaches, it is possible that clinical clues could help risk-stratify patients for the potential for TECSA. To this end, we analyzed a large retrospective cohort of two-night PSG and split-night PSG (SN-PSG) to explore predictors of central apnea index (CAI) ≥5 based on three categories of clinical information: demographics and clinical information available before PSG; baseline sleep physiology that is observed during diagnostic PSG recordings; and factors associated with the PAP titration portion of PSG recordings. This approach adds to existing retrospective literature on risk factors, benefiting from diverse clinical populations and allowing large cohorts to be analyzed with fewer resources compared to prospective endeavors. Moreover, for any risk factor prediction assessment, it is important to recognize the limitations where, for example, the factors explain only a subset of the risk. This is important in light of increasing pressure to defer testing and treatment to the home, where no gold standard TECSA determination exists.

Methods

We performed a retrospective analysis on a cohort of patients who underwent SN-PSG (n=422) or full-night PSG (FN-PSG; n=306) testing in our clinical sleep laboratory. TECSA was defined as a CAI ≥5 during PAP titration ("Rx-CAI"). The International Classification of Sleep Disorders-Third edition uses the term treatment-emergent central apnea and defines it as CAI >5 and also lists central events comprising >50% of events;[23] we did not impose the latter criteria in our definition here. FN-PSG patients had their diagnostic PSG on one night and PAP titration on a different night (<1 year apart, median of 3 months). PSGs were conducted and scored according to the American Academy of Sleep Medicine criteria for diagnostic and titration protocols;[24] reasons to switch to BiPAP include patient comfort, high CPAP (usually 15 or more), or persistent hypoxemia despite the control of sleep-disordered breathing. We used the 4% rule for hypopneas; however, central hypopneas were not scored. Split-night protocol in our laboratory generally utilizes thresholds of 20 or 40 events per hour to trigger PAP trial, and thus, the SN-PSG data generally involved more moderate or severe OSA cases. We included both diagnostic PSG cases who returned for a second night (titration) as well as split-night studies, so as not to enrich the dataset for any particular severity (split nights tend to be more severe). The Partners Healthcare Institutional Review Board approved retrospective analysis of this database without requiring consent.

We divided the available information into three categories depending on when the information was available. Information available prior to the PSG night included demographics, self-reported medications, and comorbidities; we call this "pre-info". Self-reporting included free text for medications, and check boxes for common comorbidities as well as free text option, which was manually assessed. Information obtained during the diagnostic PSG recording ("Dx-info") included standard scoring of sleep stages, movements, and respiratory parameters. Finally, information obtained during the titration ("Rx-info") included whether a benzodiazepine was taken on the night of PSG, mask type (full-face mask or nasal mask) used, maximal CPAP observed, whether BiPAP was used. The

treatment CAI was taken as the outcome measure (dichotomized using a threshold of ≥5 as positive).

The PSG database is stored internally via the acquisition system (Grass Technologies, Knocksquire, Co. Carlow, Ireland), which is distinct from the hospital electronic medical record system. The presleep surveys are Word documents, the fields of which are batch-extracted by custom internal software. We used Statistica for all analyses, and significance was taken as a *P*-value of <0.05. Spearman correlations were performed because of the predominantly nonnormal distribution characteristics. Chi-square test was used for categorical variable comparisons. Logistic regression analyses using backward elimination steps, beginning with correlated factors identified in the initial correlation analysis, were implemented to identify significant clinical predictors for TECSA at each stage of information. Significant predictors were shown if 95% confidence intervals of their respective odds ratios did not include 1.0.

Results

We present our analysis of potential predictors of TECSA (titration CAI ≥5) according to three categories that represent when the predictors would be knowable: demographic and clinical information available before the titration (Pre-info; Table 1), diagnostic PSG physiology that would be available only after PSG is undertaken (Dx-info; Table 2), and titration PSG factors that become available in real-time during therapy (Rx-info; Table 3).

The occurrence of CAI ≥5 during PAP titration was higher in SN-PSG patients than in FN-PSG patients (24.4% versus 11.4%; *P*<0.05). The SN-PSG group had higher body mass index and higher frequency of hypertension than the FN-PSG group (Table 1). The SN-PSG group had lower total sleep time and higher AHI, as expected due to the nature of

Table 1 Demographics and clinical history

Characteristic	SN-PSG (N=422)	FN-PSG (N=306)	*P*-value
Sex (% male)	69.4	56.9	0.00[a]
Age	55.0 (13.6)	55.3 (13.1)	0.76
BMI	35.7 (7.8)	32.2 (7.1)	0.00[a]
Epworth sleepiness scale	9.5 (5.2)	8.0 (4.8)	0.00[a]
Heart failure	4.5	3.6	0.79
Stroke	3.5	4.6	0.49
Pacer	3.5	1.3	0.04[a]
Coronary disease	5.8	4.6	0.62
Hypertension	48.6	39.9	0.02[a]
Diabetes	20.5	18.3	0.47
Smoker	10.6	8.2	0.37
Atrial fibrillation	5.3	5.2	0.98
Narcotic use	5.9	8.2	0.24
Antidepressant	23.7	25.5	0.64

Notes: Data are either mean (SD), or percentage for clinical binary categories. Smoker refers to self-reported current smoking. [a]Significantly different between groups (*P*<0.05).

Abbreviations: SN-PSG, split-night polysomnography; FN-PSG, full-night polysomnography; BMI, body mass index; SD, standard deviation.

Table 2 Diagnostic PSG metrics

Variables	SN-PSG (N=422)	FN-PSG (N=306)	*P*-value
	Mean (SD)	Mean (SD)	
TST (min)	147.1 (36.5)	374.5 (57.7)	
N1 (min)	40.5 (31.0)	67.5 (40.9)	
N1 (%)	29.2 (22.7)	18.8 (12.9)	
N2 (min)	81.0(35.5)	206.4 (56.3)[a]	
N2 (%)	54.7 (20.0)	54.7 (11.4)	
N3 (min)	17.0(22.2)	47.5(37.1)	
N3 (%)	10.7 (12.9)	12.6 (9.8)	
REM (min)	8.7 (11.1)	53.1 (30.9)	
REM (%)	5.4 (6.7)	13.8 (7.3)	
Efficiency (%)	81.6 (13.0)	84.5 (11.7)	
REM AHI (/hr)	56.1 (28.5)	31.7 (22.3)	<0.00[b]
NREM AHI (/hr)	51.4 (27.8)	15.6 (12.9)	<0.00[b]
Supine sleep (min)	100.3 (51.8)	230.1 (104.0)	<0.00[b]
Supine sleep (% of TST)	68.2 (31.6)	60.6 (26)	<0.00[b]
Supine AHI	54.3 (29.6	25.4 (18.0)	<0.00[b]
Nonsupine AHI	36.9 (34.3)	8.9 (10.8)	<0.00[b]
CAI (/hr)	4.9 (10.6)	2.0 (4.4)	<0.00[b]
AHI (/hr)	52.1 (27.0)	17.9 (12.1)	<0.00[b]
Minutes of REM <88% O_2 REM	2.1 (4.4)	82.9 (7.4)	<0.00[b]
Minutes of NREM <88% O_2	17.4 (2.44)	83.7 (6.4)	<0.00[b]
Supine dominant AHI (ratio)	7.1 (13.5)	7.8 (9.7)	<0.00[b]
REM dominant AHI (ratio)	1.8 (2.1)	4.3 (9.4)	<0.00[b]

Notes: [a]Normal distributed (Shapiro–Wilk *P*<0.05). [b]Significantly different (*P*<0.01); tests not performed on stage information expected to differ in split- versus full-night PSG.

Abbreviations: PSG, polysomnography; SN-PSG, split-night polysomnography; FN-PSG, full-night polysomnography; SD, standard deviation; TST, total sleep time; REM, rapid eye movement; NREM, non-rapid eye movement; CAI, central apnea index; AHI, apnea–hypopnea index.

Table 3 Titration metrics

Variables	SN-PSG (N=422)	FN-PSG (N=306)	*P*-value
Benzo taken on PSG night (% of cohort)	6.4	8.5	0.35
Full-face mask (% of cohort)	31.7	12.1	<0.00[a]
Maximum CPAP	10.1 (2.9)	8.9 (2.6)	<0.00[a]
BiPAP (% of cohort)	18.7	5.6	<0.00[a]
Maximum IPAP	15.4 (3.2)[b]	11.5 (3.1)[b]	<0.00[a]
Maximum EPAP	11.8 (3.2)[b]	7.6 (3.3)	<0.00[a]
CAI (/hr) during titration	4.6 (9.0)	1.9 (3.5)	<0.00[a]

Notes: Data are either mean (SD), or percentage for benzo use on PSG night, full-face mask, and BiPAP (binary variables). [a]Significantly different (*P*<0.01). [b]Normally distributed (Shapiro–Wilk *P*<0.05).

Abbreviations: PSG, polysomnography; SN-PSG, split-night polysomnography; FN-PSG, full-night polysomnography; Benzo, benzodiazepines taken in lab; CPAP, continuous positive airway pressure; IPAP, inspiratory PAP; EPAP, expiratory PAP; BiPAP, bilevel positive airway pressure; CAI, central apnea index; SD, standard deviation.

Table 4 Logistic regression models and odds ratios

Variables	SN-PSG (N=422)				FN-PSG (N=306)			
	Log Reg estimates	OR	95% CI lower	95% CI upper	Log Reg estimates	OR	95% CI lower	95% CI upper
Clinical predictors for RxCAI ≥5								
Intercept	–0.81	–	–	–	–1.52	–	–	–
Male sex	0.45	1.56	1.20	2.05	0.43	1.54	1.02	2.32
Narcotic	0.63	1.89	1.22	2.89	–	–	–	–
Stroke	–	–	–	–	0.78	2.18	1.21	3.93
Diagnostic sleep physiology predictors for RxCAI ≥5								
Intercept	0.96	–	–	–	–1.80	–	–	–
N2 (hr)	–1.03	0.36	0.17	0.73	–	–	–	–
CAI (/hr)	–	–	–	–	0.10	1.10	1.02	1.19
REM dominance	–0.37	0.63	0.51	0.95	–0.20	0.82	0.67	0.99
Titration predictors for RxCAI ≥5								
Intercept	–2.37	–	–	–	–3.18	–	–	–
Max CPAP	0.15	1.16	1.05	1.28	0.24	1.27	1.11	1.46
BiPAP use	1.28	2.27	1.69	3.05	1.42	4.14	2.32	7.32

Notes: Sex, narcotic, self-reported stroke, and BiPAP are binary variables. REM dominance: ratio of REM AHI to NREM AHI; max CPAP is the maximum pressure reached during titration. All estimates are significant (*P*-value <0.05). Endash (–) represents not applicable.

Abbreviations: SN-PSG, split-night polysomnography; FN-PSG, full-night polysomnography; Log Reg, logistic regression; OR, odds ratio; CI, confidence interval; CAI, central apnea index; NREM, non-rapid eye movement; REM, rapid eye movement; CPAP, continuous positive airway pressure; BiPAP, bilevel positive airway pressure; AHI, apnea–hypopnea index.

SN-PSG protocols (Table 2). During the titrations, the SN-PSG group had a higher frequency of full-face mask, higher maximum CPAP, and more likely BiPAP use, than FN-PSG group (Table 3).

We used logistic regression to determine significant predictors of categorical CAI ≥5 (Table 4). From the demographic and clinical information category, male sex was a significant predictor for both groups. Self-reported narcotic use was a significant predictor for the SN-PSG group only, while self-reported stroke history was a significant predictor for the FN-PSG group only.

From the diagnostic PSG metrics, we observed that rapid eye movement (REM) dominance of OSA was a significant negative predictor of RxCAI ≥5 for both groups in the regression models (Table 4). Time spent in N2 sleep was also a significant negative predictor for SN-PSG only. The presence of baseline central apnea during the diagnostic recordings was a significant predictor for the FN-PSG group only. From the titration, PSG metrics, the maximum CPAP, and the categorical use of BiPAP were significant predictors of CAI ≥5 in the models. Individual correlations are given in Table S1.

Discussion

This retrospective study revealed that a substantial subset of patients undergoing PAP titration demonstrated TECSA defined by CAI ≥5 during full-night and split-night treatment pathways. Several predictors and contributors were identified, which are discernible at three different stages of patient flow through clinical care: clinical and demographic information that is available prior to PSG; sleep physiology that is observable during diagnostic recordings; and factors occurring during titration of PAP. The results suggest that multiple factors contribute to TECSA, each contributing a subset of the risk, the timing of which suggests different stages of prediction, recognition, and reaction to TECSA.

As discussed later, if at-home diagnostic and auto-PAP treatment pathways are solely utilized, then only the clinical and demographic factors (among those we identified herein) be available to the clinician. The literature, however, has not been consistent in regard to clinical predictors (Table 5). Different studies identified factors such as older age, male sex, or cardiac disease, while other studies did not find these factors predictive. For example, Dernaika et al[25] also failed to identify demographic or diagnostic physiology predictors of central sleep apnea, although in this study, patients were excluded if they had congestive heart failure, major comorbidities, or had central apnea observed during diagnostic testing. Among prospective studies of TECSA resolution, a recent randomized trial failed to identify clinical predictors of incomplete response to CPAP, with the exception of higher oxygen saturation during diagnostic testing.[2] Whether this observation was a surrogate for NREM dominance, for example, if REM-dominant phenotype generally results in more prominent hypoxia, remains uncertain. In our cohort, a REM-dominant phenotype during the diagnostic phase was negatively related to TECSA. There may be several reasons for this, including elevated carbon dioxide (CO_2)

Table 5 Risk factor studies of central apnea and TECSA

Reference	N	Comments
Morgenthaler et al[11]	243	Male sex was risk factor; no difference in clinical history otherwise to predict treatment-evoked centrals NREM dominance was more common during diagnostic PSG in complex apnea
Pusalavidyasagar et al[7]	167	20% with TECSA; male sex, lower BMI, and centrals at baseline, but no other clinical or demographic variables or PAP or medications, were linked to TECSA
Dernaika et al[25]	21	No demographic or baseline PSG differences. Titration PSG had higher CPAP, more fragmentation, 12 of 14 who had repeat PSG showed resolution of CSA Exclusion: CHF, COPD, narcotic use, patients with centrals during diagnostic PSG
Lehman et al[12]	99	Baseline central apnea, higher severity, male sex, and cardiac disease predicted treatment-evoked centrals
Endo et al[13]	1,312	6% with central or TECSA; male sex and higher AHI were predictors of TECSA, but no other clinical or demographic factors were identified
Kuzniar et al[4]	200	6.5% had TECSA; NREM dominance and higher ESS scores at baseline, but not age or sex or CPAP, were associated with TECSA
Javaheri et al[3]	1,286	6.5% of cohort had CAI >5. 42 of 84 returned for second PSG: n=9 with persistent CSA had more severe apnea, or were on opiates, or had centrals at baseline No difference in medical history of 84 CSA and 84 non-CSA matched for age, sex, and BMI
Yaegashi et al[15]	297	5.7% had TECSA; centrals at baseline and NREM dominance were predictors No clinical or comorbidity differences between groups
Bitter et al[8]	192	N=34 with complex apnea, no demographic or clinical predictors. Hypercapnic ventilator response was elevated (and small differences in diuretic use, CHF severity, and PCO_2).
Cassel et al[14]	675	Older age (but no other clinical factors) and centrals at baseline predicted TECSA. Some patients initially without TECSA developed it on subsequent retitration
Westhoff et al[28]	1,776	No difference in demographics or PSG features during diagnostic testing Exclusion: elevated BNP, central apnea with opiates
Montesi et al[26]	310	CAI >5 in n=30; no difference in demographics, but did show higher leak values than non-CSA group Exclusion: CHF, atrial fibrillation

Abbreviations: TECSA, Treatment-emergent central sleep apnea; CSA, central sleep apnea; NREM, non-rapid eye movement; PSG, polysomnography; BMI, body mass index; PAP, positive airway pressure; CPAP, continuous positive airway pressure; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CAI, central apnea index; AHI, apnea–hypopnea index; PCO_2, partial pressure of carbon dioxide; BNP, brain natriuretic peptide; ESS, Epworth Sleepiness Scale.

and decreased chemosensitivity during REM.[9] The observation that time spent in stage N2 was a negative predictor of TECSA warrants further investigation. For example, additional subclassification of NREM sleep by cyclic alternating pattern or cardiopulmonary coupling may prove informative.[26] To the extent that CO_2 dynamics contribute to TECSA, it was not unexpected that high CPAP or the use of BiPAP was predictive of elevated CAI, although this is not systematically seen in prior work (Table 5). High pressures may also cause arousals, or be associated with increased leak,[27] which might also contribute to TECSA. Of note, we did not find a significant relation with the type of mask (nasal or full-face).

We found a link between male sex and TECSA, but did not identify correlations with self-reported cardiac disease (coronary artery disease, congestive heart failure, or atrial fibrillation) and TECSA. Lehman et al[12] reported that TECSA was associated with male sex and cardiac history, as well as severity of OSA based on AHI (which itself is a marker of NREM dominance[28]). The link between central sleep apnea and atrial fibrillation has been reported elsewhere as well.[18] Other literature has focused on central apnea in cardiac patients, including the natural history and relation to cardiac function.[8,29,30] The potential reasons for the difference between our work and prior work regarding cardiac history and stroke include that comorbidity was identified by self-report and that variation in disease severity was not captured.

Beyond the (likely bidirectional) association of sleep apnea and stroke, several reports suggest that central apnea and/or TECSA is more likely poststroke.[19,31] Studies in this area have not consistently linked sleep apnea to stroke location, and teasing apart relationships with stroke itself, versus with clinical factors that may present risk for both stroke and apnea (and TECSA in particular), make mechanistic associations challenging. Our finding of relationship with self-reported stroke supports this prior work, although details such as location, severity, recovery, and proximity to PSG may each contribute to variance in this association.

Narcotic use has been linked to both obstructive and central apnea,[32] and clinical trials of adaptive PAP therapy have targeted this population.[33,34] The mechanism behind this may be due to respiratory depression or due to altered chemosensitivity of ventilator drive.[9] In our cohort, self-reported narcotic use was a predictor of TECSA. It is likely that further subclassification of use (dosing regimen and chronicity), as well as the extent to which pain itself leads to arousals that

alter nocturnal respiratory stability, could further clarify the role of this important predictor.

Practice implications

Recognizing TECSA is important for the subset in which it persists, as alternative treatments should be pursued in such patients. With increasing pressure to perform home testing to diagnose sleep apnea, and home autotitration for therapy, only pre-PSG factors (ie, demographics and clinical history) are available before testing/therapy begins. Current home diagnostic kits are not validated for central apnea, which might predict TECSA in some cases (Table 5); in fact, most limited channel devices were validated in populations that specifically excluded central apnea.[22] When therapy is initiated with auto-PAP machines, the capacity to distinguish central from obstructive events remains uncertain (though most machines purport to have this capacity), and recent work raises concerns about event detection itself by machine algorithms when compared to human scoring of raw flow data.[35] For this reason, central apnea is considered an exclusion to auto-PAP,[36] although its detection by home diagnostic kits is not validated, and thus, the practitioner is left to use other clues to identify the subset that may have persistent TECSA. After therapy starts, symptom reporting may provide such clues, including air hunger and inadvertent mask removal.[7] It is possible that improvements in the technology used for home diagnostics and home titrations will increase the recognition of central apnea and TECSA. Having a predictive model to risk-stratify patients for TECSA may help with diagnostic and titration decision making, with the caveat that prospective validation of such models is lacking and it is likely that only a portion of the variance in TECSA will be explained. Our study identified more factors than the prior literature, likely because of the much larger sample size. The differences between factors identified for full-night versus split-night titrations may relate either to titration dynamics (such as rate of increase pressure) or to underlying physiology (more severe cases in split-night group). Combining clinical clues, including machine data downloads, with some adjunctive monitoring methods may prove useful in those treated with PAP who have not undergone laboratory titration. For example, single-lead electrocardiogram analysis during sleep has been shown to distinguish central from obstructive events.[26]

Limitations

Several limitations warrant further investigation, some of which relate to the nature of a retrospective strategy. The clinical history was self-report, rather than sleep physician-obtained, and thus, do not capture variation in compliance with medications or severity of comorbidities. We did not subclassify hypopneas into central versus obstructive, which is now permitted by updated American Academy of Sleep Medicine guidelines, which may further inform the clinical significance and predictors of TECSA. We also do not have CO_2 measurements in our laboratory, which might account for some of the variance in TECSA occurrence. Finally, the retrospective design does not inform the long-term consequences or resolution of the TECSA observed in single-night PAP exposure via the laboratory, such as might be obtained with repeated titration studies.

Authors' contribution

M Moro and MTB performed the study design and analysis. M Moro, KG, KL, M Merlino, and MTB were responsible for data collection. M Moro, JM, and MTB were involved in the interpretation. All authors contributed toward data analysis, drafting, and critically revising the paper and agree to be accountable for all aspects of the work. All the authors have given their final approval of the manuscript.

Disclosure

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Supplementary material

Table S1 Correlated factors with RxCAI ≥5

Variables	SN-PSG (N=422)	FN-PSG (N=306)
	R-value	*R*-value
Clinical factors		
Male sex	0.15**	0.13*
Narcotic	0.14**	–
Stroke	–	0.17**
Diagnostic PSG factors		
TST (min)	–0.14**	–
N2 (min)	–0.14**	–
NREM AHI	0.16*	0.17**
Supine time (min)	–0.14**	–
Supine AHI (/hr)	0.15**	–
Nonsupine AHI (/hr)	0.17**	–
CAI (/hr)	0.37**	0.28**
AHI (/hr)	0.15**	0.13*
REM dominance	–0.18*	–0.19**
Titration PSG factors		
Maximum CPAP	0.30**	0.19**
Full-face mask use	0.25**	–
BiPAP use	0.41**	0.36**

Notes: Endash (–) represents data not correlated. **P*-value <0.05. ***P*-value <0.01.
Abbreviation: PSG, polysomnography; R, Spearman correlation coefficient; CAI, central apnea index; SN-PSG, split-night polysomnography; FN-PSG, full-night polysomnography; TST, total sleep time; NREM, non-rapid eye movement; AHI, apnea–hypopnea index; CPAP, continuous positive airway pressure; BiPAP, bilevel positive airway pressure.