Auto-Titrating Continuous Positive Airway Pressure for Patients With Acute Transient Ischemic Attack

A Randomized Feasibility Trial

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Background and Purpose—Transient ischemic attack (TIA) patients are at risk of recurrent vascular events. The primary objectives were to evaluate among TIA patients the prevalence of sleep apnea and among patients with sleep apnea auto-titrating continuous positive airway pressure (auto-CPAP) adherence. The secondary objective was to describe among TIA patients with sleep apnea the recurrent vascular event rate by auto-CPAP use category.

Methods—All intervention patients received auto-CPAP for 2 nights, but only intervention patients with evidence of sleep apnea received auto-CPAP for the remainder of the 90-day period. Intervention patients received polysomnography at 90 days after TIA. Control patients received polysomnography at baseline and at 90 days. Acceptable auto-CPAP adherence was defined as ≥4 hours per night for ≥75% of nights. Vascular events included recurrent TIA, stroke, hospitalization for congestive heart failure, myocardial infarction, or death.

Results—We enrolled 70 acute TIA patients: 45 intervention and 25 control. The majority of patients had sleep apnea: 57% at baseline and 59% at 90 days. Among the 30 intervention patients with airflow obstruction, 12 (40%) had acceptable auto-CPAP adherence, 18 (60%) had some use, and none had no use. Three intervention patients (12%) had recurrent events compared with 1 (2%; $P=0.13$) control patient. The vascular event rate was highest among sleep apnea patients with no CPAP use: none, 16%; some, 5%; acceptable adherence 0% ($P=0.08$).

Conclusions—Sleep apnea is common among acute TIA patients. It appears feasible to provide auto-CPAP in the acute TIA period. Larger studies should evaluate whether a strategy of diagnosing and treating sleep apnea can reduce recurrent vascular events after TIA. **(*Stroke*. 2010;41:1464-1470.)**

Key Words: sleep disorders ■ TIA ■ treatment

An estimated 300 000 transient ischemic attacks (TIAs) occur annually in the United States.[1] TIA patients are at increased risk of recurrent vascular events; 25% of TIA patients will have a cerebrovascular or cardiovascular event or death in the 90 days after TIA, and over the long term, 11% per year will have a stroke, myocardial infarction, or vascular death.[2–4] Half of the recurrent events occur in the first 2 days after TIA.[3] Given that the recurrent event rate is highest early after TIA, new interventions are needed that can be applied in the acute TIA period.

The treatment of sleep apnea may provide a novel therapeutic target to improve outcomes for patients with TIA. Sleep apnea occurs in one in 5 adults in the general population[5] and in at least 60% of patients with stroke or TIA.[6,7] Auto-titrating continuous positive airway pressure (auto-CPAP) safely and effectively treats sleep apnea.[8]

The primary objective of this feasibility study was to evaluate the prevalence of sleep apnea among TIA patients and the adherence to auto-CPAP among TIA patients with sleep apnea. The secondary objectives were to compare the

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recurrent vascular event rate among TIA patients according to an intention-to-treat analysis and among patients with sleep apnea by auto-CPAP use category. This feasibility trial was designed as a randomized study of patients with acute TIA, comparing an intervention group who received a strategy of diagnosing and treating sleep apnea and a control group who received diagnostic testing but who did not receive sleep apnea treatment.

Methods

Sample

TIA patients cared for at 3 hospitals in Connecticut (December 2004 to February 2008) were included if they had a TIA and were ≥45 years of age. Patients were excluded for a known diagnosis of sleep apnea, respiratory distress requiring mechanical ventilation, oxygen-dependent chronic obstructive pulmonary disease, pregnancy, time from symptom onset to emergency department arrival >72 hours, life expectancy <6 months, non–English- speaking status, or residence outside of Connecticut.

Randomization

Patients were randomly assigned to the intervention or control group in a 1 (control):1.75 (intervention) ratio to ensure a sufficient number of patients in the intervention group given that a primary outcome was CPAP adherence. A randomization scheme was developed before the start of the study. Because patients were often recruited and randomized in the evening hours, our randomization system could not involve a call to the coordinating center (which operated only during regular daytime office hours). For this reason, the randomization system was converted into a package of sealed envelopes that the field staff opened in consecutive order. Randomization was not stratified by any baseline patient characteristic.

Baseline Measurements

A baseline assessment included a medical record review, an interview of patients or proxies, and physical measurements. The following data were collected at baseline: demographics, comorbidities, medications, blood pressure, heart rate, neck circumference, height, and weight. The ABCD^2 score, a system used to predict short-term recurrent event rates among patients with TIA, was calculated from: age (≥60 years, 1 point); blood pressure (systolic ≥140 mm Hg or diastolic ≥90 mm Hg, 1 point); symptom type (unilateral weakness with or without speech impairment, 2 points; speech impairment without weakness, 1 point); symptom duration (≥60 minutes, 2 points, 10 to 59 minutes, 1 point), and a history of diabetes (1 point).[3] The care the patients received to evaluate the etiology of the TIA and to prevent recurrent vascular events was measured and included the following: brain imaging, evaluation of the carotid arteries, echocardiography use, smoking cessation counseling, antithrombotic medication use, statin medication use, and angiotensin converting enzyme inhibitor or angiotensin receptor blocker medication use. Excessive daytime sleepiness was defined as a score of ≥10 on the Epworth Sleepiness Scale.[9]

Control Group Protocol

Control patients received portable unattended polysomnography at baseline and at 90 days after TIA (Figure 1). The primary care providers of the control patients were notified of the polysomnography results, but control patients were not given CPAP as part of the study. Although it was theoretically possible for control patients with sleep apnea to receive CPAP, none of them actually received CPAP during the 3-month study period.

Polysomnography was performed by a trained staff member at the patient's bedside. The patients were not moved off their unit if they were admitted to the hospital. The polysomnography included electroencephalogram, respiratory inductive plethysmography, body position, ECG, blood pressure, and oxygen saturation.[10] We used portable unattended polysomonography (LifeShirt; Vivometrics) because it has been validated against the gold standard of polysomnography in a sleep laboratory, has been successfully used in clinical trials of sleep apnea, and can be used throughout the hospital or at a patient's residence.[11]

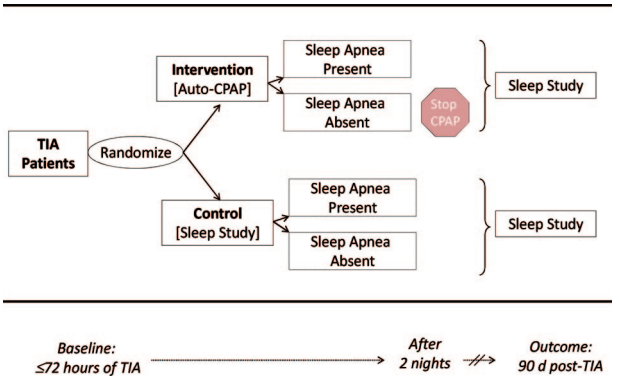

Figure 1. Research design.

Diagnosis of Sleep Apnea

Apnea was defined as an airflow cessation of ≥10 seconds, and hypopnea was defined as a reduction in airflow of ≥10 seconds or a decrease in amplitude of breathing by ≥30%, followed by an oxygen desaturation of ≥4%.[12–14] The apnea–hypopnea index (AHI) was calculated from the sum of the number of apneas and hypopneas per hour of sleep. Sleep apnea was diagnosed when the AHI was ≥5.[13]

Intervention Group Protocol

All intervention patients received auto-CPAP. The traditional approach to the treatment of sleep apnea is to use fixed-pressure CPAP. This approach requires a 2-step process. First, a sleep study is performed to diagnose sleep apnea. Then, CPAP titration is performed by a sleep therapist who increases the fixed-pressure CPAP until the apneas and hypopneas are eliminated. This approach is usually conducted on 2 nights. In cases in which patients have many apneas and hypopneas, a split-night study can be conducted in which both the diagnostic component and the CPAP titration can be performed on the same evening. Whether or not a split-night study is performed, the use of fixed-pressure CPAP requires that the patient have a sleep study in the presence of a sleep technician. Auto-CPAP machines eliminate respiratory disturbances by varying the pressure delivered depending on the patients' respiratory efforts. Auto-CPAP compared with fixed-pressure CPAP is equally efficacious but has improved patient adherence and comfort.[15,16] We used auto-CPAP because it is equally as effective as fixed-pressure CPAP and because it does not require the presence of a sleep therapist for titration.

The auto-CPAP machine (AutoSet Spirit; ResMed) measured and stored information about respiratory events (apneas and hypopneas), patient use (minutes used and nights used), mask leak, and pressure delivered. Auto-CPAP adherence was categorized as no use, any use (more than no use but <4 hours per night for <75% of nights), or acceptable adherence (≥4 hours per night for ≥75% of nights).[8,17]

The machine was interrogated after 2 nights. If there was no evidence of airflow limitation (AHI <5 or median pressure <6 cm H_2O), then the auto-CPAP was discontinued. If there was evidence of airflow limitation, then the auto-CPAP was continued for the remainder of the 90-day period (Figure 1). Intervention patients received information about sleep apnea, the benefits of CPAP treatment, and instructions about CPAP machine use daily for 2 days, weekly for the first month, and then monthly. Research staff made visits to refit masks or to troubleshoot equipment as needed. Because polysomnography, and not auto-CPAP, is the gold standard method of diagnosing sleep apnea, intervention patients received unattended portable polysomnography at 90 days after TIA (Figure 1).

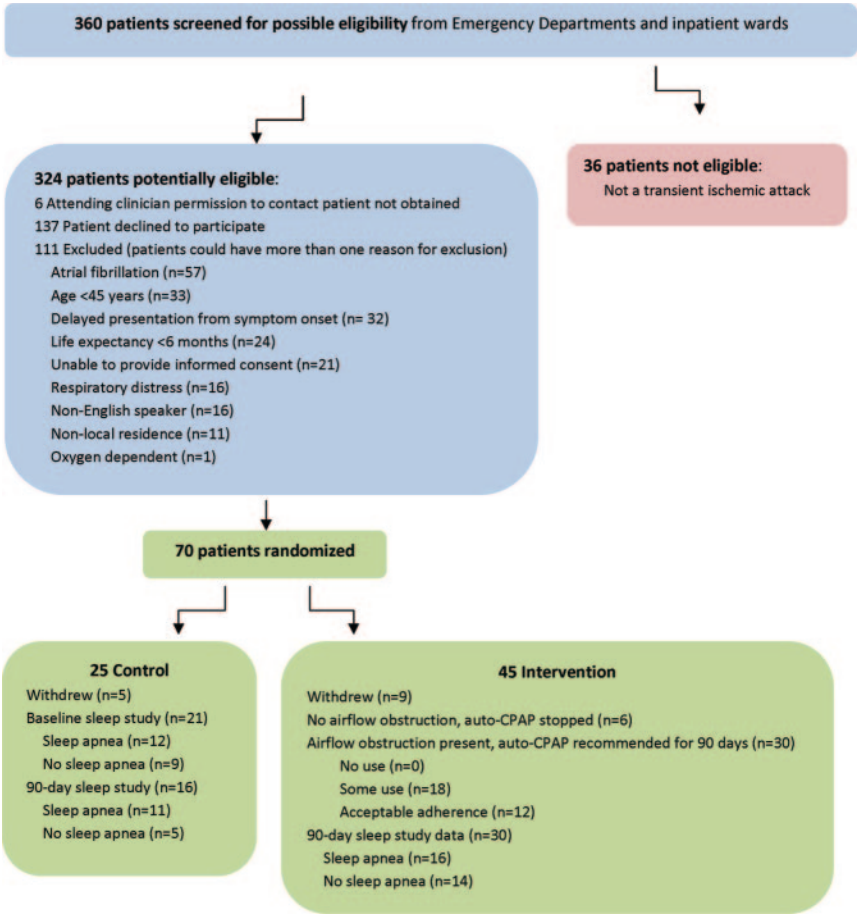

Figure 2. Patient screening and recruitment diagram.

Outcomes

The primary outcomes were sleep apnea prevalence at baseline (measured by polysomnography among control patients) and the proportion of TIA patients with sleep apnea with acceptable auto-CPAP adherence. The secondary outcome was the 90-day post-TIA recurrent vascular events rate. Recurrent vascular events included recurrent TIA, stroke, acute myocardial infarction, hospitalization for congestive heart failure, and death.[2]

Adverse Events

All adverse events were reviewed by a panel that included an internist, a neurologist, and a pulmonologist. The panel classified each adverse event as serious or nonserious and as related or unrelated to the study intervention.

Analysis Plan

Descriptive statistics (eg, mean with SDs, medians, and proportions) were used to describe the baseline characteristics and outcomes. To compare differences in the outcome rates between control and intervention patients and among sleep apnea patients with varying auto-CPAP use, χ^2 tests or Fisher exact tests were used for binary or ordinal variables and Student t tests or Wilcoxon rank sum tests for dimensional variables. Two-sided P values were used to evaluate differences between the intervention and control groups. A P value of 0.05 was used to determine statistical significance. An intention-to-treat analysis was performed comparing the recurrent vascular event rate among intervention patients compared with control patients. A secondary prespecified analysis of the recurrent vascular event rates was conducted among patients with sleep apnea according to the amount of auto-CPAP use.

This project was designed to enroll a sufficient number of subjects to ensure face validity for our feasibility assessments. It was not powered to identify differences in vascular events between patients in the intervention versus control groups. No imputations were made for missing data. All analyses were conducted using SAS 9.1. This study was registered with clinical trials.gov (NCT00251290) and was approved by all of the human subject committees of the participating center.

Results

A total of 360 patients were screened for possible eligibility; 36 did not have a TIA, 6 could not be contacted because permission to do so was not received by their attending clinician, 137 patients declined to participate, and 111 met ≥1 exclusion criterion (Figure 2). A total of 70 patients were enrolled: 45 intervention and 25 control. Among these, 9 of 45 (20%) were lost to follow-up in the intervention group, and 5 of 25 (20%) were lost in the control group. Among the 45 intervention patients, 36 used the auto-CPAP machine, 6 of whom had no evidence of airflow obstruction based on the AHI or the pressure recordings; therefore, they had the CPAP discontinued, leaving 30 intervention patients eligible for ongoing CPAP use. Incomplete sleep study data resulted either from poor quality electroencephalography data or from patient refusal to perform or complete the sleep study. Complete unattended polysomnography data were available in 21 of 25 (84%) control patients at baseline, 16 of 25 (64%) control patients at 90 days, and 30 of 45 (67%) intervention patients at 90 days (Figure 2).

Table 1 provides a comparison of baseline characteristics among the patients in the intervention versus control groups.

Table 1. Baseline Characteristics (n=70)

Characteristic	Intervention (n=45)	Control (n=25)	*P* Value*
Age range (y)	47–88	45–88	…
Mean±SD	66.3±11.9	67.4±12.8	0.73
White race: n (%)	35 (77.8)	16 (64.0)	0.21
Female gender: n (%)	22 (48.9)	13 (52.0)	0.80
Past medical history: n (%)			
Hypertension	33 (73.3)	16 (64.0)	0.41
Hyperlipidemia	26 (57.8)	10 (40.0)	0.15
Diabetes mellitus	15 (33.3)	6 (24.0)	0.41
Stroke	7 (15.6)	5 (20.0)	0.74
TIA	7 (15.6)	7 (28.0)	0.23
Atrial fibrillation	6 (13.3)	1 (4.0)	0.41
Myocardial infarction	5 (11.1)	1 (4.0)	0.41
Congestive heart failure	3 (6.7)	1 (4.0)	1.00
Chronic obstructive pulmonary disorder	2 (4.4)	0 (0)	0.53
Current tobacco smoking: n (%)	2 (8.0)	8 (17.8)	0.48
Blood pressure (mm Hg): mean±SD			
Systolic	140.3±21.8	142.0±16.9	0.75
Diastolic	78.3±12.5	82.1±11.5	0.21
Neck circumference (inches): mean±SD	15.6±1.2	15.3±1.4	0.40
Waist circumference (inches): mean±SD	41.2±3.4	40.3±5.5	0.48
Weight (pounds): mean±SD	179.5±27.5	178.7±42.8	0.94
Body mass index (kg/m^2): mean±SD	28.6±4.1	27.8±6.5	0.59
Excessive daytime sleepiness: n (%)	17 (37.8)	7 (28.0)	0.41
ABCD^2 score	1.67±1.0	1.72±0.94	0.96
Symptom duration: mean±SD	3.9±5.3	4.3±7.8	0.79
Time from symptom onset to CPAP or sleep study (hours)			
Mean±SD	39.4±23.7	45.0±37.1	0.50
<24 hours: n (%)	8 (18)	4 (16)	…
≥24 hours, <48 hours: n (%)	27 (60)	15 (60)	…
≥48 hours: n (%)	10 (22)	6 (24)	…
Concomitant care: n (%)			
Admission brain imaging received	45 (100)	25 (100)	1.00
Antithrombotic therapy	40 (89)	24 (96)	0.41
Smoking cessation counseling for smokers	4/5 (80)	0/2 (0)	0.14
Carotid imaging received	37 (82)	17 (68)	0.17
ACEI/ARB medication received	23 (51)	11 (44)	0.57
Statin medication received	23 (51)	10 (40)	0.46
Echocardiography received	42 (93)	19 (76)	0.06

*P values refer to 2-sided P values obtained from Student t tests, Wilcoxon tests, χ^2 tests, or Fisher exact tests.
The ABCD^2 score is used to predict short-term recurrent event rates among patients with TIA.
ACEI/ARB refers to an angiotensin converting enzyme inhibitor or receptor blocking medication.

There were no statistically significant differences in the baseline characteristics of the 2 groups, although the control patients had higher rates of previous stroke and previous TIA (Table 1). The majority of patients received auto-CPAP within 48 hours after the TIA symptom onset: <24 hours, 8 of 45 (18%); ≥24<48 hours, 27 of 45 (60%); and ≥48 hours, 10 of 45 (22%). The concomitant care rates were similar between the 2 groups, although the control patients received less echocardiography (Table 1).

Sleep Apnea Prevalence

The majority of TIA patients had sleep apnea, both at baseline (12 of 21 [57%] control patients) and at 90 days (27 of 46 [59%] control and intervention patients; Table 2). The control and intervention groups had similar rates of sleep apnea based on polysomnography at 90 days: control, 11 of 16 (69%) and intervention, 16 of 30 (53%; P=0.31).

Among control patients who had complete polysomnography data at both baseline and 90 days, 6 of 14 (43%) had

Table 2. Prevalence of Sleep Apnea*

Characteristic	Baseline (n=21)	90-Day (n=46)
AHI range	0–36.7	0–61.6
Mean±SD	11.1±11.7	11.0±13.2
Sleep apnea prevalence n (%)	12 of 21 (57)	27 of 46 (59)
Central event AHI: range	0–1.6	0–35.3†
Mean±SD	0.41±0.59	1.88±7.36
Total sleep time (hours:minutes): range	1:10–9:16	0:46–10:48
Mean±SD	5:51±2:33	5:60±1:54
Mean oxygenation (%): range	92–97	90–98
Mean±SD	94.4±1.6	94.7±1.6
Oxygen desaturation index ≥4%	0.2–16.8	0–54.8
Mean±SD	3.4±4.8	3.5±8.1

*The prevalence of sleep apnea is based on polysomnography data. The diagnosis of sleep apnea was made if the AHI was ≥5.

†We observed frequent central events in only 1 intervention patient with severe sleep apnea (AHI 61.6) who also had frequent obstructive events.

sleep apnea at both time points, 2 of 14 (14%) did not have sleep apnea at both time points, 4 of 14 (29%) had no sleep apnea in the acute TIA period but sleep apnea present after 90 days, and 2 of 14 (14%) had sleep apnea in the acute TIA period but not after 90 days. Therefore, in 8 of 14 (57%) patients, their diagnostic categorization was stable, but in 6 of 14 (43%) patients, their diagnostic categorization changed from the acute TIA period to 90 days after TIA. The AHI from the acute TIA period ranged from 0.5 to 36.7 among patients with stable diagnoses and from 0.0 to 7.5 among patients with a change in diagnosis. Therefore, an AHI of >7.5 could be used to identify patients who are unlikely to change their diagnostic category.

Among the 30 intervention patients with complete polysomnography and auto-CPAP data, the diagnostic agreement was agreement in 15 of 27 (55%) patients, with a positive predictive value of 55% and a negative predictive value of 57%.

Auto-CPAP Use

Among the 30 intervention patients who had evidence of airflow obstruction based on data from the auto-CPAP machine, acceptable adherence was observed in 12 (40%), some use in 18 (60%), and none with no use (Table 3).

Recurrent Vascular Events

When examining the effect of auto-CPAP on the recurrent vascular event rate according to an intention-to-treat analysis (including both patients with and without sleep apnea and including patients in the intervention group who did not use CPAP), we observed that 3 of 25 (12%) of control patients had a recurrent vascular event compared with 1 of 45 (2%) of intervention patients (P=0.13; Table 4). Among patients with sleep apnea at baseline, the recurrent vascular event rate was highest among patients with no CPAP use: no use, 1 of 12 (8%); some use, 1 of 18 (6%); acceptable adherence, 0 of 12 (0%; P=0.34; Table 4). Among patients with any evidence of sleep apnea, either from the auto-CPAP machine or from unattended polysomnography at baseline or at 90 days after TIA (this approach allows for the classification of the most number of patients because it uses all possible data), the recurrent vascular event rate was highest among patients with no CPAP use: no use, 3 of 19 (16%); some use, 1 of 21 (5%); acceptable adherence, 0 of 13 (0%; P=0.08).

Table 3. Auto-CPAP Use

Auto-CPAP Use Category	Eligible Intervention Patients* (n=30)
Proportion of nights used: range	0.02–0.88
Mean±SD	0.47±0.33
No. of hours/night CPAP used: range (hours)	1.5–8.5
Mean±SD	5.6±1.9
CPAP use: n (%)	…
None: 0 nights or 0 hours/night	0 (0)
Some: <70% nights for <4 hours/night	18 (60)
Excellent: ≥70% nights for ≥4 hours/night	12 (40)

*Eligible intervention patients included the 30 patients who had evidence of sleep apnea from the auto-CPAP machine.

Adverse Events

Serious adverse events were observed among 4 of 25 (16.0%) control patients and 7 of 45 (15.6%) intervention patients (P=1.0). The 4 serious events among the control group included a new stroke in 2 patients and recurrent TIAs in 2 patients. The serious events among the 7 intervention patients included a new stroke in 2 patients, a hospitalization for atrial fibrillation complicated by hypotension in 1 patient, a hospitalization for hyperglycemia in 1 patient, a hospitalization for hypoglycemic in 1 patient, 1 patient who was hospitalized once for congestive heart failure and once with dehydration, and 1 patient who was hospitalized for acute renal failure and also for radiotherapy for cancer. No serious adverse events were related to the intervention.

Nonserious adverse events were observed among 1 of 25 (4.0%) control patients and 5 of 45 (11.1%) intervention patients (P=0.41). The nonserious adverse events related to the study intervention included skin irritation from the mask (n=2) and sneezing/nasal irritation because of the CPAP (n=2).

Discussion

Our findings indicate that sleep apnea is common among this selected group of acute TIA patients, and that it is feasible to implement a strategy of using auto-CPAP in the acute TIA period to diagnose and treat sleep apnea. The recurrent vascular event rate seen in this cohort of TIA patients (12% among the controls) was lower than the expected 25% event rate.[2–4] This study was designed to assess the feasibility of diagnosing and treating sleep apnea among patients with acute TIA. The study was designed to have adequate sample size and therefore adequate statistical power to address the feasibility aims; it was not designed to have adequate power to evaluate the efficacy of auto-CPAP in the prevention of recurrent vascular events among post-TIA patients. Although the recurrent event rate was lower among intervention patients in this study, this difference did not reach statistical

Table 4. Recurrent Vascular Events

	Overall (Intention-to-Treat) n=70			Sleep Apnea† (by Auto-CPAP Use Category) n=42		
Outcome	Control (n=25)	Intervention (n=45)	*P* Value	None (n=12)	Some (n=18)	Acceptable (n=12)
Vascular events	3 (12)	1 (2)	0.13	1 (8)	1 (6)	0 (0)

Vascular events included recurrent TIAs, stroke, myocardial infarction, hospitalization for congestive heart failure, or any death.
†The adherence analysis only included sleep apnea patients, including 12 control patients in the "none" group.

significance, perhaps because this study was not powered to detect this difference.

The prevalence of sleep apnea observed in this study is similar to rates observed in previous studies.[6,7] For example, Parra et al studied 39 TIA patients and found that 62% had sleep apnea based on an AHI of >10.[6] Moreover, we found that although the overall prevalence remains fairly stable over the first 3 months after TIA (acute, 57% versus 90 days, 59%), the diagnostic categorization of an individual patient may shift from the acute TIA period to the 90-day period. Our results indicate that an AHI of >7.5 can identify patients with sleep apnea in the acute TIA period who will continue to have sleep apnea after 90 days.

The auto-CPAP use observed in this study was similar to some previous reports in non-TIA patients but higher than those several reported studies of CPAP use among patients with stroke.[7,18,19] It may be that TIA patients have higher adherence than stroke patients because TIA patients do not have neurological impairments that could interfere with regular CPAP use. We might also have observed a higher adherence because our study staff visited with patients to encourage auto-CPAP use and to help patients overcome any difficulties they may have experienced with the equipment. The auto-CPAP use analysis excluded patients who did not have sleep apnea and patients who withdrew from the study; this approach increases the relative adherence rate but is the standard analytic practice.[7] The 20% withdrawal rate among intervention patients serves to potentially bias our results in favor of reporting a relatively higher auto-CPAP adherence. Despite this limitation, the adherence that was observed was better than expected given that a small minority of patients were symptomatic with excessive daytime sleepiness.

Despite a lower-than-expected recurrent vascular event rate, our finding that increasing auto-CPAP use was associated with a lowered recurrent vascular event rate (albeit not statistically significantly so) is consistent with the findings of Martinez-Garcia et al, who found among patients distant from a stroke or TIA that the recurrent vascular event rate was 7% among CPAP users (n=15) and 36% among patients without CPAP use (n=36; $P=0.03$).[19] The mechanisms by which CPAP may reduce recurrent vascular events after TIA are unknown but may include lowering blood pressure, improving oxygenation, decreasing platelet activation, improved left-ventricular ejection fraction, which may contribute to improve cerebral perfusion, or lowering fibrinogen.[20–22] Future studies should confirm the effectiveness of CPAP in the acute TIA period and should also be directed at examining the mechanism by which CPAP may improve outcomes. Future trials that evaluate post-TIA interventions should design their sample size with the 12% event rate we observed (as opposed to the 25% event rate described in cohort studies).[2–4]

One noteworthy aspect of this research design is the application of an intervention not based on patient symptoms but rather based on estimated disease prevalence within a group. Specifically, we did not provide the intervention strategy only to patients with daytime sleepiness or other symptoms consistent with sleep apnea, but rather provided the intervention to all stroke patients randomized to the intervention group. The rationale for this approach was based on the previous literature[6,7] that has demonstrated that sleep apnea is common among TIA patients, the safety profile of the intervention in routine clinical practice, and the need to provide treatment as early as possible in the acute TIA period to achieve maximal benefit. Our findings suggest that this approach is feasible and may improve patient outcomes. An alternative research design would have been to use sham CPAP for patients randomized to the control arm. Sham CPAP was not used in this study because the "usual care" control arm approach provided a scientifically sound comparison while enhancing the feasibility of conducting the study and ensuring patient safety.

Future studies are needed to answer several key questions that relate to the implementation of this strategy within routine clinical practice: is there a group of patients for whom the auto-CPAP intervention is most beneficial and a group for whom it is unlikely to be helpful? how long should the auto-CPAP be continued? at what point, if ever, should a formal polysomnography be performed? and for TIA patients who nap during the day and sleep at night, should the auto-CPAP be used both during the day and at night?

The primary strength of the design of this study was that it was a randomized controlled comparison of usual care versus a strategy of diagnosing and treating sleep apnea in the acute TIA period. We sought to include a broad range of patients to enhance the generalizability of these findings. Despite these strengths, the following limitations require attention. First, although the patients were recruited from a Department of Veterans Affairs medical center, a large tertiary care center, a moderately large community hospital, and physician offices in one county, these findings should be replicated in a larger multisite study that is powered to detect differences in the recurrent vascular event rate.

Second, we used an approach using auto-CPAP early post-TIA without first using diagnostic polysomnography. We found relatively poor diagnostic agreement between the auto-CPAP machine and the polysomnography (55% agreement). This strategy provides for the earliest possible administration of auto-CPAP therapy. Given the safety of auto-

CPAP and the relatively high prevalence of sleep apnea, this approach is likely to provide the earliest treatment to the largest number of patients with low risk of harm. Future studies will have to address the issue of whether auto-CPAP is beneficial to patients despite this diagnostic inaccuracy.

Third, although the losses to follow-up were equal in both groups, 20% losses in each arm was higher than we expected. Any conclusions drawn from this study must be made in the context of this withdrawal rate.

Despite these limitations, these research findings suggest that the strategy of diagnosis and treating sleep apnea among selected acute TIA patients may be a novel therapeutic strategy to improve patient outcomes. Future studies are needed to confirm these findings. Given that no specialized systems are needed to implement CPAP therapy, this intervention may have the potential to be applicable to most TIA patients regardless of the size or complexity of the facility where they receive their care.

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Disclosures

The authors had full access to all of the data and take responsibility for the integrity and accuracy of the analyses.

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Auto-Titrating Continuous Positive Airway Pressure for Patients With Acute Transient Ischemic Attack: A Randomized Feasibility Trial

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Abstract

应用自动调节连续气道正压通气治疗急性短暂性脑缺血发作患者
一项随机对照可行性试验

Auto-Titrating Continuous Positive Airway Pressure for Patients With Acute Transient Ischemic Attack

A Randomized Feasibility Trial

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背景和目的：短暂性脑缺血发作 (TIA) 患者存在再发血管事件的风险。本研究主要观察目标是评价 TIA 患者中睡眠呼吸暂停的患病率，以及睡眠呼吸暂停患者进行自动调节连续气道正压通气 (auto-CPAP) 治疗的依从性。次要观察目标是描述在具有睡眠呼吸暂停的 TIA 患者中，应用 auto-CPAP 治疗的亚组再发血管事件的比率。

方法：所有入选的 TIA 患者被随机分为干预组及对照组。干预组患者均接受两晚的 auto-CPAP 治疗，对其中存在睡眠呼吸暂停的亚组患者延续治疗至 90 天。所有干预组患者在 TIA 后 90 天行多导睡眠描记仪检测。对照组患者则仅在基线和 TIA 后 90 天时进行多导睡眠描记仪检测，并不接受 auto-CPAP 治疗。良好依从 auto-CPAP 治疗的定义为总监测时间内至少有 75% 的夜间使用了 auto-CPAP 治疗，并且每晚至少使用 4 小时。血管事件包括再发 TIA、卒中、需住院治疗 (或死亡) 的充血性心力衰竭、心肌梗死。

结果：本研究共纳入 70 例急性 TIA 患者：45 例干预组和 25 例对照组。大多数患者存在睡眠呼吸暂停：基线为 57%，TIA 后 90 天为 59%。在 30 例具有气流阻塞的干预组亚组患者中，12 例患者 (40%) 良好依从了 auto-CPAP 治疗，18 例患者 (60%) 为部分使用，并无患者从未使用过。对照组及干预组分别有 3 例 (12%) 和 1 例 (2%，*P*=0.13) 患者再发了血管性事件。存在睡眠呼吸暂停并且未接受 auto-CPAP 治疗的患者，血管事件再发率最高：从未使用、部分使用及良好依从 auto-CPAP 治疗的患者血管事件再发率分别为 16%、5% 和 0% (*P*=0.08)。

结论：急性 TIA 患者常存在睡眠呼吸暂停现象。在 TIA 的急性期给予 auto-CPAP 治疗是可行的。仍需要大样本研究进一步评价睡眠呼吸暂停的诊治是否可减少 TIA 后再发血管事件。

关键词：睡眠障碍，短暂性脑缺血发作，治疗

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表 3　Auto-CPAP 的使用情况

Auto-CPAP 的使用情况分类	符合干预标准的患者 * (n=30)
夜间使用比率：范围	0.02-0.88
均数 ± 标准差	0.47 ± 0.33
使用 CPAP 治疗的小时数 / 晚：范围 (小时)	1.5-8.5
均数 ± 标准差	5.6 ± 1.9
使用 CPAP：例数 (%)	…
从未使用过：0 次夜间使用或 0 小时 / 晚	0 (0%)
部分使用：<70% 夜间使用，<4 小时 / 晚	18 (60%)
良好依从：≥ 70% 夜间使用，≥ 4 小时 / 晚	12 (40%)

* 符合干预标准的 30 例患者为使用 auto-CPAP 治疗并存在明确的睡眠呼吸暂停者。