

# Influence of Continuous Positive Airway Pressure on Outcomes of Rehabilitation in Stroke Patients With Obstructive Sleep Apnea

Clodagh M. Ryan, MD; Mark Bayley, MD; Robin Green, PhD;  
Brian J. Murray, MD; T. Douglas Bradley, MD

**Background and Purpose**—In stroke patients, obstructive sleep apnea (OSA) is associated with poorer functional outcomes than in those without OSA. We hypothesized that treatment of OSA by continuous positive airway pressure (CPAP) in stroke patients would enhance motor, functional, and neurocognitive recovery.

**Methods**—This was a randomized, open label, parallel group trial with blind assessment of outcomes performed in stroke patients with OSA in a stroke rehabilitation unit. Patients were assigned to standard rehabilitation alone (control group) or to CPAP (CPAP group). The primary outcomes were the Canadian Neurological scale, the 6-minute walk test distance, sustained attention response test, and the digit or spatial span-backward. Secondary outcomes included Epworth Sleepiness scale, Stanford Sleepiness scale, Functional Independence measure, Chedoke McMaster Stroke assessment, neurocognitive function, and Beck depression inventory. Tests were performed at baseline and 1 month later.

**Results**—Patients assigned to CPAP (n=22) experienced no adverse events. Regarding primary outcomes, compared to the control group (n=22), the CPAP group experienced improvement in stroke-related impairment (Canadian Neurological scale score,  $P<0.001$ ) but not in 6-minute walk test distance, sustained attention response test, or digit or spatial span-backward. Regarding secondary outcomes, the CPAP group experienced improvements in the Epworth Sleepiness scale ( $P<0.001$ ), motor component of the Functional Independence measure ( $P=0.05$ ), Chedoke-McMaster Stroke assessment of upper and lower limb motor recovery test of the leg ( $P=0.001$ ), and the affective component of depression ( $P=0.006$ ), but not neurocognitive function.

**Conclusions**—Treatment of OSA by CPAP in stroke patients undergoing rehabilitation improved functional and motor, but not neurocognitive outcomes.

**Clinical Trial Registration Information**—URL: <http://www.clinicaltrials.gov>. Unique identifier: NCT00221065. (*Stroke*. 2011;42:1062-1067.)

**Key Words:** continuous positive airway pressure ■ functional outcomes ■ neurocognitive outcomes  
■ obstructive sleep apnea ■ stroke

The incidence of stroke and its consequent burden of morbidity and mortality remain unacceptably high. If outcomes from stroke are to improve, then the underlying mechanisms of functional impairment will need to be addressed. One contributing factor may be obstructive sleep apnea (OSA).

Cross-sectional and prospective epidemiological data indicate that OSA is associated with increased risk of having a stroke independently of other risk factors.<sup>1-3</sup> Compared to the general population,<sup>4</sup> stroke patients have a 4- to 6-fold higher prevalence of OSA.<sup>5,6</sup> In the poststroke period, patients with OSA have greater functional impairment and higher mortality than patients without OSA.<sup>6,7</sup> These data suggest that OSA both increases the risk of stroke and, in the poststroke period, exacerbates the degree of disability as well as the risk of

death. It is therefore possible that treatment of coexisting OSA might improve recovery from stroke. Accordingly, we performed a randomized controlled trial in stroke patients with OSA during their inpatient stroke rehabilitation to determine if treatment with continuous positive airway pressure (CPAP) would improve functional, motor, and neuropsychological outcomes over a 4-week period.

## Subjects and Methods

### Study Design

This was a randomized, open label, parallel group trial with blind assessment of outcomes performed at the stroke rehabilitation unit of the Toronto Rehabilitation Institute.

Received August 12, 2010; accepted November 23, 2010.

From the Toronto Rehabilitation Institute (C.M.R., M.B., R.G., B.J.M., T.D.B.) and the Centre for Sleep Medicine and Circadian Biology (C.M.R., B.J.M., T.D.B.), University of Toronto, Ontario, Canada; the Department of Medicine (C.M.R., T.D.B.), Toronto General Hospital of the University Health Network and Sunnybrook Health Sciences Centre (B.J.M.), Toronto, Ontario, Canada.

The online-only Data Supplement is available at <http://stroke.ahajournals.org/cgi/content/full/STROKEAHA.110.597468/DC1>.

Correspondence to Clodagh M. Ryan, MD, 9N-967, Toronto General Hospital, 585 University Avenue, Toronto, Ontario, M5G 2N2. E-mail [clodagh.ryan@uhn.on.ca](mailto:clodagh.ryan@uhn.on.ca)

© 2011 American Heart Association, Inc.

*Stroke* is available at <http://stroke.ahajournals.org>

DOI: 10.1161/STROKEAHA.110.597468

## Subjects

Eligible patients were those admitted from acute care facilities to the stroke rehabilitation unit within 3 weeks of stroke onset with the following inclusion criteria: (1) 18 to 89 years of age; (2) completed ischemic or hemorrhagic stroke confirmed by a neurologist based on history of sudden onset of a neurological deficit lasting >24 hours, neurological deficit on physical examination, and brain lesion compatible with the neurological deficit on computerized tomography or MRI; (3) ability to follow simple commands in English; (4) competency to provide informed consent; and (5) OSA on an overnight attended polysomnogram (PSG) as described. Exclusion criteria were: (1) brain stem strokes that could increase aspiration risk while using CPAP; (2) previously diagnosed OSA on therapy; (3) concomitant central nervous system diseases such as dementia; (4) history of psychosis; (5) traumatic brain injury; and (6) anosagnosia, global, or Wernicke aphasia.

The study was approved by the Research Ethics Board of the Toronto Rehabilitation Institute and all subjects provided written consent before participation.

## Baseline Assessments

Clinical classification of strokes was performed according to the Oxfordshire Community Stroke Project criteria.<sup>8</sup> Eligible patients underwent a clinical assessment followed by an overnight PSG. PSG were performed using standard techniques and scoring criteria for sleep stages and arousals from sleep.<sup>9,10</sup>

The frequency of apneas and hypopneas per hour of sleep was expressed as the apnea–hypopnea index. Patients with an apnea–hypopnea index of  $\geq 15$  were classified as having sleep apnea for the purpose of this study. OSA was diagnosed when at least 80% of the respiratory events were obstructive.

Subjects with OSA then completed the functional, motor, and neuropsychological assessments between 2:00 and 5:00 PM administered by individuals blinded to subject randomization. To take the heterogeneity of stroke-related impairment into account, we evaluated several domains as our primary outcomes, including stroke severity by the Canadian Neurological scale, motor function by the 6-minute walk test, neurocognitive function by sustained attention to response test (a measure of vigilance), and the digit or spatial span-backward (a measure of executive function). Secondary outcomes included the Functional Independence measure (FIM), Chedoke-McMaster Stroke assessment of upper and lower limb motor recovery test, hand-grip strength, Berg Balance scale, Epworth Sleepiness scale (ESS), Stanford Sleepiness scale (SSS), the Purdue Pegboard test and the Beck depression inventory-1 (BDI). Please see <http://stroke.ahajournals.org> for additional information.

## Randomization

Eligible patients were randomly assigned by a computer-generated randomization schedule in random blocks of 2 and 4, with allocation concealment by opaque, sequentially numbered, sealed envelopes to either a control group that received standard stroke occupational and physiotherapy for the duration of the trial or a treatment group that, in addition, received CPAP for OSA.

CPAP was titrated during PSG to reduce the apnea–hypopnea index to <5 or to the highest pressure tolerated. Patients were then provided with a CPAP machine (Goodknight 420G; Tyco Healthcare) and were instructed to use it for at least 6 hours per night until the end of the trial. CPAP compliance was assessed by recording mask-on time.

Throughout the 4-week trial, time spent, and level of participation in physiotherapy were recorded 5 days per week by a physiotherapist blind to treatment allocation. Four weeks after randomization, baseline measurements were repeated, including a PSG performed either with or without CPAP as per treatment allocation (Figure 1).

## Statistical Analyses

We estimated that with a sample size of 22 in each group, the study would have a 90% power to detect 1 SD difference between the groups for the primary outcomes at a 2-tailed  $\alpha$  of 0.05. Baseline data

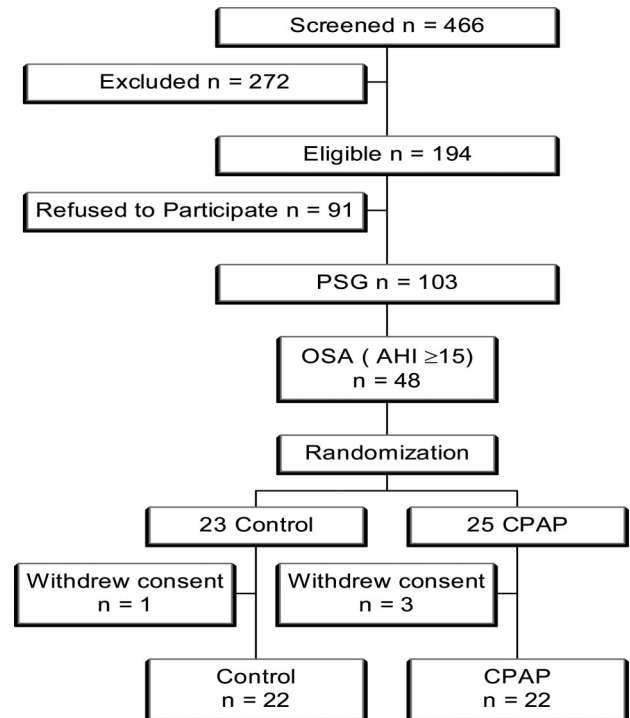


Figure. Progress of patients through the trial.

of the 2 groups were compared with *t* tests for continuous variables and Fisher exact test for categorical data. Outcomes were analyzed by the original assigned groups. Differences in the outcome variables, from baseline to follow-up, were compared within and between groups by analysis of covariance with post hoc analyses as appropriate. Test scores on psychometric data were transformed to a common metric (*z* scores) and aggregate scores were created.<sup>11</sup>  $P < 0.05$  was considered statistically significant. Continuous data are expressed as means  $\pm$  SD unless otherwise indicated.

## Results

### Characteristics of the Subjects

Progress of subjects through the trial is illustrated in Figure 1. Between June 2005 and March 2008, 466 patients with strokes admitted to the stroke rehabilitation unit were screened. Exclusions were mainly attributable to language barriers. One-hundred ninety-four met initial inclusion criteria, and 103 agreed to PSG. Of these, 48 (47%) had OSA with an apnea–hypopnea index  $\geq 15$ . One patient in the control group and 3 in the CPAP group left the study before trial completion; thus, outcome data were available for 22 patients in each group for analysis by originally assigned group. Stroke location and type (Table 1) and time from occurrence of the stroke to entry into the study were similar in the control and CPAP groups ( $19.7 \pm 16.8$  days versus  $21.5 \pm 8.7$  days;  $P = 0.41$ ).

Baseline data were similar in the control and CPAP groups, except more subjects in the control group had a history of smoking (Table 1). The Canadian Neurological scale and FIM scores were also similar in the 2 groups, indicating comparable functional impairment (Table 3). The ESS and SSS were similar in the 2 groups and were within normal limits, indicating a lack of subjective sleepiness (Table 2).

**Table 1. Baseline Characteristics of the Subjects**

	Control (n=22)	CPAP (n=22)
Age, years	60.7±10.3	62.8±12.8
Sex (M/F)	19/3	16/6
Body mass index, kg/m <sup>2</sup>	27.3±5.8	28.8±5.3
History of smoking, n (%)	11 (50)	7 (32)
Hypertension, n (%)	15 (68.2)	18 (81.8)
Hyperlipidemia, n (%)	17 (77.3)	16 (72.7)
Diabetes mellitus, n (%)	7 (31.8)	10 (45.5)
Ischemic heart disease, n (%)	2 (9.1)	6 (27.3)
Heart failure, n (%)	1 (4.6)	1 (4.6)
Atrial fibrillation, n (%)	4 (18.2)	3 (13.6)
Total hemorrhagic strokes, n	4	1
Total ischemic strokes, n	18	21
PACI	9	11
LACI	3	6
TACI	5	4
POCI	1	0
Right/left brain, n	6/16	9/13
Right/ left handedness, n	18/4	22/0

Values are mean±SD or % as indicated.

CPAP indicates continuous positive airway pressure; LACI, lacunar infarction; PACI, partial anterior circulation infarct; POCI, posterior circulation infarct; TACI, total anterior circulation infarct.

Sleep variables were similar in both groups. No adverse events were recorded during the study.

### Effects of CPAP on Sleep Variables

Among those randomized to CPAP who completed the trial, CPAP usage averaged 4.96±2.25 hours per day at a mean pressure of 8.1±0.5 cm H<sub>2</sub>O. There were no adverse effects of CPAP. Compared to the control group, the CPAP-treated group experienced a significant reduction in the apnea–

hypopnea index, as well as an increase in minimum sleep oxyhemoglobin saturation. Mean oxyhemoglobin saturation also improved within the CPAP group (Table 2). However, there were no improvements in sleep structure in either group.

### Physiotherapy

Time per day spent in physiotherapy and participation scores did not differ between the control and CPAP groups (control: 45±13 versus 45±9 minutes per day and  $P=0.97$ ; CPAP: 5.2±0.8 versus 5.4±0.7 and  $P=0.30$ ).

### Primary Outcomes

The CPAP group experienced significant improvements in the total Canadian Neurological scale score and its cognitive and motor components that were greater than in the control group (Table 3). There was a significant increase in the 6-minute walk distance (113 meters) in the CPAP group, but not in the control group (46 meters). However, the between-group difference was not significant. The CPAP group did not experience a significant improvement in sustained attention/vigilance on the sustained attention to response test but did show a significant improvement in digit span and visual spatial span-backward, not seen in the control group, although the between-group difference was not significant (Table 4).

### Secondary Outcomes

There were significant reductions in the ESS and SSS in the CPAP compared to the control group (Table 2). There were also significant improvements in the FIM and Berg Balance scale within both groups; however, these did not differ significantly between them. Separate analysis of the motor and cognitive components of the FIM revealed a significantly greater improvement in the motor, but not the cognitive, component in the CPAP than in the control group. The Chedoke-McMaster Stroke Assessment scale demonstrated significant improvements in the arm, hand, leg, and foot

**Table 2. Sleep Outcomes**

	Control (N=22)			CPAP (N=22)			<i>P</i> *
	Baseline	Follow-Up	<i>P</i>	Baseline	Follow-Up	<i>P</i>	
ESS	4.5±2.1	4.5±2.2	0.94	4.4±1.8	1.8±1.0	0.0001	<0.0001
SSS	2.5±1.3	2.0±1.0	0.06	2.2±1.1	1.3±0.6	0.005	0.05
AHI, n/hr	33.3±16.4	30.3±17.5	0.60	38.5±18.1	7.6±8.5	0.0001	<0.0001
TST, hr	6.30±0.90	5.82±1.77	0.27	5.66±1.15	5.83±1.01	0.63	0.89
S1, %	9.5±5.4	9.3±4.8	0.92	8.6±5.6	8.2±6.5	0.84	0.70
S2, %	61.3±9.1	54.4±12.4	0.06	60.3±8.7	59.7±9.9	0.84	0.17
SWS, %	12.2±6.6	17.1±13.0	0.13	14.1±9.5	14.8±7.6	0.80	0.36
REM, %	16.9±8.9	19.2±7.2	0.40	17.4±6.3	17.3±7.4	0.97	0.53
Arl, n/hr	25.5±12.8	26.2±14.4	0.87	28.6±22.0	18.8±13.4	0.09	0.10
Mean sleep SaO <sub>2</sub> , %	95.5±1.8	95.5±1.4	0.94	94.4±1.6	96.0±1.6	0.003	0.26
Minimum sleep SaO <sub>2</sub> , %	79.6±11.3	79.4±15.7	0.97	80.7±5.7	90.9±3.4	0.0001	0.005

Values are mean±SD.

AHI indicates apnea–hypopnea index; ArI, arousal index; CPAP, continuous positive airway pressure; ESS, Epworth Sleepiness scale; REM, rapid eye movement sleep; S1, stage 1 sleep; S2, stage 2 sleep; SaO<sub>2</sub>, oxyhemoglobin saturation; SSS, Stanford Sleepiness scale; SWS, slow wave sleep; TST, total sleep time.

\*Between-group differences by analysis of covariance adjusted for age and sex.

**Table 3. Functional and Motor Outcomes**

	Control (N=22)			CPAP (N=22)			P*
	Baseline	1 Month	P	Baseline	1 Month	P	
Canadian Neurological scale, total	7.7±1.9	8.4±1.5	0.16	7.3±1.9	9.6±1.7	<0.001	<0.001
Canadian Neurological scale, cognitive	4.6±0.2	4.6±0.2	0.72	4.4±0.5	4.8±0.3	0.01	<0.001
Canadian Neurological scale, motor	3.1±1.9	3.8±1.5	0.15	2.7±1.6	4.8±1.6	<0.001	<0.001
Functional Independence measure, total	85.8±17.7	105.8±13.9	<0.001	78.3±20.8	105.6±16.8	<0.001	0.07
Functional Independence measure, cognitive	23.4±7.1	26.6±7.4	0.14	23.5±6.0	27.4±5.4	0.03	0.76
Functional Independence measure, motor	62.5±15.1	79.2±13.8	<0.001	54.8±18.7	78.2±14.6	<0.001	0.05
Chedoke-McMaster Stroke Assessment scale							
Arm	4.3±1.9	4.8±1.9	0.02	3.8±1.7	4.9±1.6	<0.001	0.08
Hand	4.0±1.7	4.7±1.6	<0.001	4.0±1.7	4.7±1.7	<0.001	0.92
Leg	4.1±1.0	4.5±1.1	0.027	4.2±1.1	5.0±1.2	<0.001	0.001
Foot	3.8±1.3	4.3±1.3	0.007	3.6±0.9	4.3±1.2	<0.001	0.19
Berg Balance scale	28.2±17.5	44.3±11.3	0.001	29.5±19.2	43.7±14.6	0.01	0.64
6-minute walk distance, m†	270±236	316±178	0.29	190±176	303±157	0.02	0.75
Hand-grip affected/nonaffected ratio	0.48±0.46	0.61±0.58	0.09	0.39±0.41	0.45±0.5	0.29	0.36

Scale ranges: Canadian Neurological scale total, 1.5–11.5; Functional Independence measure total, 18–126; Chedoke-McMaster Stroke Assessment scale, 1–7; Berg Balance scale, 0–56.

CPAP indicates continuous positive airway pressure.

\*Between-group differences by analysis of covariance.

†n=16 control and n=16 CPAP.

scores within both groups, and a significantly greater improvement in the leg score in the CPAP than in the control group. There was no within-group or between-group difference in the ratio of hand-grip strength between the affected and nonaffected hand in either group (Table 3). CPAP had no significant effect on visuo-motor speed and hand dexterity as assessed by the Purdue Pegboard score or in mental efficiency on the digit and visual spatial span-forward (Table 4). There was no significant reduction in the total BDI in either the control group (13.3±9.8 to 10.4±8.7; *P*=0.35) or the CPAP group (12.6±11.8 to 8.8±9.0; *P*=0.76). The same was true for the somatic component of the BDI. However, there was a significant reduction in the affective component of the BDI in the CPAP compared to the control group (7.0±7.4 to 4.3±5.7 versus 7.6±7.2 to 6.2±7.0; *P*=0.006).

**Discussion**

This randomized trial involving stroke patients with OSA undergoing inpatient rehabilitation has demonstrated that,

compared to the control group, CPAP usage was associated with improvement in the overall severity of stroke-related impairment manifest by a greater improvement in one of the primary outcomes, the Canadian Neurological Scale score. Although there were improvements in some of the other primary outcomes within the CPAP group, including mobility assessed by 6-minute walk test distance and neurocognitive capacity assessed by the digit/spatial span-backward, these were not statistically significant compared to the control group. There was no within-group or between-group improvement in vigilance assessed by the sustained attention to response test score. CPAP usage was also associated with improvements in 5 of the secondary outcomes compared to the control group, including the motor component of the FIM, Chedoke-McMaster Stroke Assessment leg score, ESS, SSS, and the affective component of the BDI. Taken together, these results indicate a significant, although modest, beneficial effect of CPAP on stroke-related outcomes.

**Table 4. Neuropsychological Outcomes**

	Control (n=20)			CPAP (n=17)			P*
	Baseline	Follow-Up	P	Baseline	Follow-Up	P	
SART, total n of false-positive errors	12±7	11±7	0.21	13±5	15±6	0.32	0.26
SART, mean RT in the 4 trials just before a false press	484±121	433±141	0.24	491±120	503±148	0.53	0.26
Purdue Pegboard, dominant hand score	30±12	36±15	0.29	32±8	35±9	0.39	0.88
Purdue Pegboard, nondominant hand score	35±15	40±15	0.36	29±12	33±12	0.34	0.37
Purdue Pegboard, affected hand score	30±12	37±16	0.35	28±12	32±13	0.80	0.62
Digit+visual spatial span-forward	44±33	41±30	0.54	32±26	35±29	0.08	0.27
Digit+visual spatial span-backward	40±36	45±36	0.08	24±32	34±30	0.03	0.32

CPAP indicates continuous positive airway pressure; RT, reaction time; SART, sustained attention response time.

\*Analysis of covariance adjusted for age and sex.

The most prominent beneficial effects of CPAP therapy involved motor and functional outcomes. These included improvements in the motor components of the Canadian Neurological scale, FIM, and the leg motor component of the Chedoke-McMaster Impairment scale. These improvements were greater than those observed in the control group and were accompanied by a significant increase in 6-minute walking distance within the CPAP group. Since impaired motor function of the leg is a major limitation to stroke recovery because it limits functional independence,<sup>12</sup> these findings suggest that treatment of coexisting OSA by CPAP in stroke patients could improve functional independence and hasten return to community living.

ESS and SSS scores were within normal limits at baseline, indicating that patients were not hypersomnolent, consistent with the study by Arzt et al.<sup>13</sup> Nevertheless, treatment of OSA by CPAP caused reductions in ESS and SSS scores, even though it did not improve sleep structure, vigilance as assessed by the sustained attention to response test, or participation in physiotherapy. Thus, CPAP-related improvements in functional and motor outcomes could not be attributed to a reduction in hypersomnolence, because subjects were not hypersomnolent at onset of rehabilitation, or to increased physiotherapy participation.

CPAP had marginal, if any, effects on the cognitive outcomes that were assessed. For example, although there was a significant improvement in digit and visual span-backward within the CPAP group, suggesting improvement in executive functioning,<sup>14,15</sup> there were no improvements in sustained vigilance, attention span, and visuo-motor speed and dexterity, as tested by the sustained attention to response test, digit and visual span-forward, and Purdue Pegboard, respectively.

With respect to depression, compared to the control group, the CPAP group experienced a significant improvement in the affective, but not the somatic, component of the BDI. The former is a better index of mood after stroke, because the somatic component of the BDI is confounded by items that are also sensitive to the direct physiological effects of stroke (eg, loss of appetite). After a stroke, 25% to 40% of patients experience depression,<sup>16</sup> which is associated with worse neurological recovery<sup>17</sup> and increased mortality.<sup>18</sup> Therefore, reductions in poststroke depression may contribute to neurological recovery.

An important aspect of our trial was that only 3 (12%) patients randomized to CPAP left the study. For the remaining 22 people who completed the trial, CPAP compliance was excellent, with average daily use of 4.96 hours (considering total sleep times were  $\approx$ 5.60 hours). This excellent compliance is most likely because our subjects were inpatients during the entire trial period, and because nurses were trained to administer CPAP to study subjects.

The mechanisms by which CPAP achieved beneficial effects on motor and functional, but not neurocognitive, outcomes are not clear. CPAP-induced abolition of intermittent hypoxia and negative intrathoracic pressure swings should increase cerebral blood flow and oxygen delivery.<sup>19</sup> Accordingly, functional and motor improvements in the CPAP-treated group may have been attributable to alleviation

of the adverse cerebrovascular effects of OSA, possibly through enhanced neuroplasticity.

Two other randomized trials evaluated the response of stroke patients with OSA to CPAP. Sandberg et al<sup>20</sup> studied inpatients over a 1-month period. Subjects had good fixed-pressure CPAP compliance of 4.1 hours per night. However, the only improvement in the CPAP-treated group was a reduction in severity of depression.<sup>20</sup> Several differences between that study and ours could account for apparent differences in outcomes. For instance, their patients were 18 years older, 50% had heart failure, sleep apnea was predominantly central, and there were no evaluations of sleep structure, alertness, or motor and neuropsychological functions.

The study by Hsu et al<sup>21</sup> was similar to ours in that subjects predominantly had OSA and underwent assessments of subjective sleepiness, functional, and stroke severity outcomes. Their study differed from ours in that subjects were 14 years older, had more severe OSA, and did not undergo assessment of sleep structure by PSG or assessment of alertness, motor, or neuropsychological function. Subjects were studied over a longer period (6 months) and auto-titrating CPAP was used, with very poor compliance (1.4 hours per night). The negative results of that study therefore were likely attributable to poor CPAP compliance.

The heterogenous nature of neurological damage and stroke etiology makes evaluation of clinical interventions difficult.<sup>22</sup> We took this into account by assessing the effects of treating OSA on various aspects of stroke outcome in different domains. Nevertheless, the present trial was subject to some limitations. Forty-two percent of patients were not eligible for the study, primarily because of lack of fluency in English. This, coupled with the small sample size, and inability to evaluate the effect of stroke subtype, affected vessel size, and lateralization make it difficult to know whether the results apply to the general stroke population. Recovery from stroke may evolve over several months and the 1-month follow-up may not have been sufficient to evaluate the extent and duration of stroke recovery while using CPAP or to assess its effects once subjects left the hospital.<sup>22</sup>

## Conclusions

In conclusion, this randomized trial demonstrated that treatment of OSA by CPAP in stroke patients undergoing rehabilitation was associated with significant improvements in functional and motor outcomes as well as mood. Functional and motor impairments are often the most disabling features of stroke because they limit mobility and activities of daily living. Although our findings suggest that treating OSA in stroke patients improves these outcomes, larger longer-term trials are needed to determine whether such improvements can persist or evolve further over longer periods.

## Acknowledgments

The authors thank Dr William McIlroy for his expert opinion and access to facilities for the performance of motor tests.

## Sources of Funding

Supported by an operating grant from the Physicians Service Incorporated Foundation, Ontario, Canada.

## Disclosures

Tyco Health Care provided CPAP devices for the trial. Provision of ASV devices for investigator-initiated trial with Canadian Institutes of Health Research (to D.B. and C.R.).

## References

- Arzt M, Young T, Finn L, Skatrud JB, Bradley TD. Association of sleep-disordered breathing and the occurrence of stroke. *Am J Respir Crit Care Med*. 2005;172:1447–1451.
- Redline S, Yenokyan G, Gottlieb DJ, Shahar E, O'Connor GT, Resnick HE, Diener-West M, Sanders MH, Wolf PA, Geraghty EM, Ali T, Lebowitz M, Punjabi NM. Obstructive sleep apnea-hypopnea and incident stroke: The sleep heart health study. *Am J Respir Crit Care Med*. 2010;182:269–277.
- Yaggi H, Mohsenin V. Obstructive sleep apnoea and stroke. *Lancet Neurol*. 2004;3:333–342.
- Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med*. 1993;328:1230–1235.
- Johnson KG, Johnson DC. Frequency of sleep apnea in stroke and TIA patients: A meta-analysis. *J Clin Sleep Med*. 2010;6:131–137.
- Kaneko Y, Hajek VE, Zivanovic V, Raboud J, Bradley TD. Relationship of sleep apnea to functional capacity and length of hospitalization following stroke. *Sleep*. 2003;26:293–297.
- Sahlin C, Sandberg O, Gustafson Y, Bucht G, Carlberg B, Stenlund H, Franklin KA. Obstructive sleep apnea is a risk factor for death in patients with stroke: A 10-year follow-up. *Arch Intern Med*. 2008;168:297–301.
- Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet*. 1991;337:1521–1526.
- Iber CAIS, Chesson A, Quan SF, American Academy of Sleep Medicine. *The AASM manual for the scoring of sleep and associated events: Rules, terminology and technical specifications*. Westchester, IL: American Academy of Sleep Medicine; 2007.
- Rechtschaffen A, Kales A. *A manual of standardized terminology, techniques and scoring systems for sleep stages of human subjects*. Los Angeles, CA: UCLA Brain Information Service/Brain Research Institute; 1968.
- Spreen OSE. *A compendium of neuropsychological tests*. New York, NY: Oxford Press; 1991.
- Langhorne P, Coupar F, Pollock A. Motor recovery after stroke: A systematic review. *Lancet Neurol*. 2009;8:741–754.
- Arzt M, Young T, Peppard PE, Finn L, Ryan CM, Bayley M, Bradley TD. Dissociation of obstructive sleep apnea from hypersomnolence and obesity in patients with stroke. *Stroke*. 2010;41:e129–e134.
- Saunamäki T, Jehkonen M. A review of executive functions in obstructive sleep apnea syndrome. *Acta Neurol Scand*. 2007;115:1–11.
- Skidmore ER, Whyte EM, Holm MB, Becker JT, Butters MA, Dew MA, Munin MC, Lenze EJ. Cognitive and affective predictors of rehabilitation participation after stroke. *Arch Phys Med Rehabil*. 2010;91:203–207.
- Toso V, Gandolfo C, Paolucci S, Provinciali L, Torta R, Grassivaro N, DESTRO Study Group. Post-stroke depression: Research methodology of a large multicentre observational study (DESTRO). *Neurol Sci*. 2004;25:138–144.
- Kauhanen M, Korpelainen JT, Hiltunen P, Brusin E, Mononen H, Määttä R, Nieminen P, Sotaniemi KA, Myllylä VV. Poststroke depression correlates with cognitive impairment and neurological deficits. *Stroke*. 1999;30:1875–1880.
- Williams LS, Ghose SS, Swindle RW. Depression and other mental health diagnoses increase mortality risk after ischemic stroke. *Am J Psychiatry*. 2004;161:1090–1095.
- Diomedes M, Placidi F, Cupini LM, Bernardi G, Silvestrini M. Cerebral hemodynamic changes in sleep apnea syndrome and effect of continuous positive airway pressure treatment. *Neurology*. 1998;51:1051–1056.
- Sandberg O, Franklin KA, Bucht G, Eriksson S, Gustafson Y. Nasal continuous positive airway pressure in stroke patients with sleep apnoea: A randomized treatment study. *Eur Respir J*. 2001;18:630–634.
- Hsu CY, Vennelle M, Li HY, Engleman HM, Dennis MS, Douglas NJ. Sleep-disordered breathing after stroke: A randomised controlled trial of continuous positive airway pressure. *J Neurol Neurosurg Psychiatry*. 2006;77:1143–1149.
- Feigin VL, Barker-Collo S, McNaughton H, Brown P, Kerse N. Long-term neuropsychological and functional outcomes in stroke survivors: Current evidence and perspectives for new research. *Int J Stroke*. 2008;3:33–40.