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Original Article

Using a modified version of the "STOP-BANG" questionnaire and nocturnal oxygen desaturation to predict obstructive sleep apnea after stroke or TIA

Mark I. Boulos [a, b, c, *, 1], David R. Colelli [a, 1], Sophie R. Vaccarino [a, 1], Maneesha Kamra [a], Brian J. Murray [a, b, c], Richard H. Swartz [a, b]

[a] L.C. Campbell Cognitive Neurology Research Unit, Heart and Stroke Foundation Canadian Partnership for Stroke Recovery, University of Toronto Stroke Program, Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada
[b] Department of Medicine, Division of Neurology, University of Toronto, Toronto, ON, Canada
[c] Sleep Laboratory, Sunnybrook Health Sciences Centre, Toronto, ON, Canada

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ABSTRACT

Purpose: Obstructive sleep apnea (OSA) is a risk factor and common morbidity for stroke and transient ischemic attack (TIA). However, screening for OSA in patients with stroke or TIA is uncommonly performed, due in part to difficulties associated with conducting polysomnography (PSG) and Home Sleep Apnea Tests (HSATs). The 8-point "STOP-BANG" questionnaire has been shown to have high methodological quality in screening for OSA. This study examined the clinical utility of a modified version of the "STOP-BANG" questionnaire, which removed neck circumference and included nocturnal oxygen desaturation in diagnosing OSA (ie, the "STOP-BAG-O" tool), with the goal of improving uptake and accuracy in diagnosing OSA.

Methods: In total, 231 participants completed both the STOP-BAG questionnaire and PSG or HSAT within 12 months of stroke/TIA. Using receiver-operating curves, scores on the "STOP-BAG-O" and "STOP-BAG" questionnaires were assessed for their ability to predict a diagnosis of OSA and classify at least 50% of the study population.

Results: Compared to an OSA diagnosis of AHI$\geq$10, the STOP-BAG (using cut-offs of $\leq$3 and $\geq$4) had a sensitivity and specificity of 83.5% and 67.2%, respectively. The STOP-BAG-O (using cut-offs of $\leq$3 and $\geq$5) had a sensitivity and specificity of 95.9% and 78.4%, respectively. For all AHI cut-offs used, the area under the curve for the STOP-BAG-O was greater and statistically different ($p < 0.001$) than that for the STOP-BAG.

Conclusions: The STOP-BAG-O is a valid tool for identifying risk of OSA post-stroke/TIA. The simplicity of this tool and ease of assessing nocturnal oxygen desaturation makes it a feasible option for widespread use.

1. Introduction

Obstructive sleep apnea (OSA) is a common disorder characterized by reduced pharyngeal dilator muscle tone during sleep, which causes intermittent interruptions in airflow [1]. OSA exposes the brain and body to cycles of awakening and hypoxia, promotes systemic inflammation and oxidative stress, activates platelets, and disrupts vascular endothelial function [1]. OSA is both a risk factor [2] and common comorbidity after stroke and transient ischemic attack (TIA) [3], affecting 61% of stroke survivors and 52% of patients post-TIA [4]. Overall, after adjusting for other vascular risk factors, sleep apnea increases stroke risk by approximately four times [2], and increases mortality nearly 3-fold when left untreated [5]. After stroke, sleep apnea is an independent predictor of worse functional outcomes [6], greater functional impairment, and longer hospitalizations [7]. The small randomized trials that have investigated early treatment of OSA post-stroke using nasal continuous

* Corresponding author. Sunnybrook Health Sciences Centre, Room A442 - 2075 Bayview Avenue, Toronto, Ontario, M4N 3M5, Canada. Fax: + 416 480 5753.
E-mail address: mark.boulos@sunnybrook.ca (M.I. Boulos).
[1] Co-first authors contributed equally to this work.

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positive airway pressure (CPAP) have shown mixed results and a definitive trial has not yet been completed [8–12].

The 2014 stroke prevention guidelines from the American Heart Association state that consideration may be given to screening for sleep disorders such as OSA [13]. However, screening for OSA in patients with stroke or TIA is uncommon [14]. There are many factors limiting routine screening and assessment [15]; one key factor contributing to the under-diagnosis of OSA post-stroke/TIA is the difficulty associated with conducting polysomnography (PSG) in a sleep laboratory [14]. PSG has limited access and is costly and time-consuming, and many patients are unwilling to sleep overnight in a laboratory setting [16]. Home sleep apnea tests (HSATs) have been found to be feasible for unattended use after stroke/TIA [17]. However, HSATs are unavailable in many institutions and may be too costly for routine use in some stroke clinics [16]. For these reasons, simple screening questionnaires have been developed to identify those patients at high or low-risk for OSA.

The "STOP-BANG" questionnaire has been shown to have high methodological quality in screening for OSA [18]. This questionnaire is an 8-point scale consisting of yes/no questions related to snoring, tiredness during daytime, observed apneas, high blood pressure, body mass index (BMI), age, neck circumference, and gender [19]. By using this concise and simple screening tool, those at low-risk for OSA can be identified, thereby saving time and costs on PSGs and/or HSATs. Neck circumference is often not obtained, and has been shown to not significantly improve model performance in patients with cerebrovascular disease [20]. Therefore, the "STOP-BAG" questionnaire, without neck circumference, has been suggested as an equally valid screening tool [20].

Although OSA is a major predictor of recovery and quality of life in stroke/TIA survivors, there has been limited work examining the use of the STOP-BANG questionnaire in this patient population [16,20–22]. Prior studies that used the STOP-BANG questionnaire, or any variant of it, are summarized in Table 1 [16,20–22]. There are significant differences between OSA patients with and without stroke/TIA: post-stroke OSA patients tend to be less sleepy [2] and be older [16] than those without stroke. Furthermore, over 50% of stroke patients without sleep apnea do snore [4], suggesting that snoring may not be a strong predictor of OSA in stroke patients. These differences indicate that the STOP-BANG questionnaire originally designed for use in the general population may not be fully valid for use in patients with stroke/TIA. In addition, previous research has demonstrated that oximetry may be helpful in assessing for OSA [23–25], however, guidelines from the American Academy of Sleep Medicine (AASM) do not support use of oximetry alone in predicting sleep apnea [26]. This suggests the potential value of investigating whether the combination of the STOP-BAG questionnaire with nocturnal oxygen desaturation may serve as a useful tool in predicting OSA in stroke/TIA patients.

Our primary objective was to examine whether adding nocturnal oxygen desaturation to the STOP-BAG score improved the discriminative ability and usefulness of this screening tool in predicting OSA in a population of stroke/TIA patients. In order to maximize the utility of our screening tool, we selected cut-offs which classified $\geq$50% of our sample and categorized patients as being low- or high-risk for OSA. We secondarily investigated the relationship between individual STOP-BAG variables and nocturnal oxygen desaturation in predicting a diagnosis of OSA, as assessed by PSG or a HSAT.

2. Methods

2.1. Study population

Between April 11, 2012 and July 21, 2017, 231 participants were recruited from two studies: "Post-stroke Triage "DOC": Simple Screening for Depression, Obstructive Sleep Apnea and Cognitive Impairment" (DOC, N = 58; https://clinicaltrials.gov/ct2/show/NCT02007265) and a single-centre randomized controlled trial entitled "SLEep APnea Screening using Mobile Ambulatory Recorders after TIA/stroke" (SLEAP SMART, N = 173; https://clinicaltrials.gov/ct2/show/NCT02454023). These studies were reviewed and approved by the local Research Ethics Board, and all study participants provided written informed consent. We included patients who participated in these studies and completed the STOP-BAG questionnaire, as well as PSG or HSAT within 12 months of the index stroke/TIA. PSGs were conducted at our hospital sleep laboratory for all DOC study patients (N = 58) and for 38.7% of the SLEAP SMART study patients (N = 67); the remainder of the SLEAP SMART patients underwent HSAT (N = 106). For this manuscript, inclusion criteria included a diagnosis of ischemic stroke or stroke-specialist diagnosed TIA occurring within 365 days of the study testing and English speaking (including English as a Second Language, or able to communicate through translator). Patients were excluded if they could not complete the study requirements due to significant physical or cognitive impairment (eg, aphasia), or if their sleep testing demonstrated predominantly central sleep apnea (N = 5). For the SLEAP SMART study, patient exclusion criteria also included: (1) previous diagnosis of OSA; (2) current CPAP use; (3) less than 12 months life expectancy at the time of recruitment; (4) respiratory or cardiac problems that could affect the accuracy of HSAT screening results; (5) use of medical devices that would affect placement of the HSAT screening devices and/or CPAP; (6) pregnancy; and (7) no provincially funded medical coverage. The STOP-BANG questionnaire assesses obstructive sleep-disordered breathing; as a result, patients who predominantly had central sleep apnea were not included in our analyses.

2.2. Sleep screening

Eligible participants completed overnight OSA screening via laboratory PSG or using a HSAT. The HSAT used in this study was the ApneaLink Air and it was completed at home or in the patient's hospital room. The ApneaLink HSAT records respiratory movements, oxygen saturation and airflow and has been validated against PSG for the detection of OSA [27,28]. Use of this HSAT has been demonstrated to be feasible in the stroke/TIA population [17].

Scoring for both PSG and HSAT was completed according to the standards of the AASM [29]. As has been previously described [30], apneas were defined as a decline in peak signal excursion for at least 10 s and hypopneas were defined as a decline in peak signal excursion by 30% for at least 10 s, with an oxygen desaturation of $\geq$4%. The scoring of the ApneaLink Air was automated and reviewed by a sleep specialist; where concerns arose, a sleep technologist also reviewed the raw tracings. The AHI was calculated from PSG or HSAT data as the total number of apneic and hypopneic events detected per hour during the night of recorded sleep.

2.3. Outcome measures

Following a diagnosis of ischemic stroke or TIA, patients completed the STOP-BANG questionnaire [19]. The questionnaire was completed post-stroke/TIA and patients responded in reference to the post-stroke/TIA period. We used the STOP-BANG questionnaire as originally described [19] except that we excluded neck circumference, which gave rise to the "STOP-BAG" questionnaire.

In addition, oximetry data was recorded from PSG and HSAT data and included in the analysis. An oxygen desaturation event was noted if the saturation level decreased by 4% for at least 5 s. If the patient had a lowest oxygen desaturation value $\leq$ 88%, they

Table 1
Summary of prior studies that have used the STOP-BANG questionnaire, or any of its variants, to predict OSA risk after stroke/TIA.

Publication	Sample Size (N)	Time between stroke/TIA and sleep test	AHI cut-off	Results	Cut-off score used	Sensitivity, Specificity
Boulos et al., 2016 [16]	N = 69 - 46 (66.7%) ischemic stroke - 7 (10.1%) hemorrhagic stroke - 16 (23.2%) TIA	Within 180 days	≥10	• STOP-BAG significantly detected OSA • STOP-BAG scores were significantly correlated with AHI • Male sex and BMI were independent predictors of OSA	2	0.94 0.14
Katzan et al., 2016 [20]	N = 208 - 99 (47.6%) ischemic stroke - 12 (5.8%) hemorrhagic stroke - 59 (28.4%) other cerebrovascular disease - 38 (18.3%) other	Within 1 year	≥10	• STOP-BAG model can be used to identify cerebrovascular patients at increased risk for OSA • Addition of neck circumference and other variables did not significantly improve the models	3	0.93 0.54
Swartz et al., 2017 [21]	N = 88 - 39 (44.3%) TIA - 37 (42.1%) stroke - 12 (13.6%) other	No restriction	≥15	• The area under receiver operating curve was 0.660 when comparing gold-standard PSG with the STOP questionnaire • When logistic regression was applied to ROC curve analysis controlling for age, sex and BMI, AUC was 0.798	One cut-point cut-off: 2 Low-risk cut-off: 0 High-risk cut-off: 4	One cut-point: 0.59, 0.65 Two cut-points: 0.95, 0.96 but 83% remained intermediate risk
Sico et al., 2017 [22]	N = 194 - 107 (55.2%) ischemic stroke - 57 (29.4%) TIA - 30 (15.5%) TIA or ischemic stroke	Cohort 1: within 30 days of ischemic stroke or any time after TIA Cohort 2: within 1 week	≥5	• STOP-BANG Questionnaire did not strongly predict the presence of OSA on a formal PSG in an exclusively post-ischemic stroke or TIA population	0.654	0.35 0.73

Abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; OSA = obstructive sleep apnea; PSG = polysomnography; ROC = receiver operating curve; TIA = transient ischemic attack.

were given one additional point to the total STOP-BAG score, which created the "STOP-BAG-O" score.

The primary definition of OSA used for this study was an AHI cut-off ≥10 events per hour. Additional AHI cut-offs were also assessed (eg AHI ≥5, AHI ≥15, AHI ≥30) to evaluate the sensitivities and specificities of the STOP-BAG and STOP-BAG-O screening tools in predicting OSA.

2.4. Statistical analysis

Descriptive statistics were computed for recorded variables. Normally distributed continuous variables were reported as means and standard deviations. Non-normally distributed continuous variables were reported as median and interquartile range (IQR). Categorical variables were reported as frequency counts.

To investigate our primary objective of whether adding nocturnal oxygen desaturation to the STOP-BAG score would improve the clinical utility of this tool, for both the STOP-BAG and the STOP-BAG-O screening tools, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each AHI cut-off score. Cut-off scores were selected to classify ≥50% of the sample; in order to maximize sensitivity and specificity, cut-off scores were chosen as low- and high-risk scores. Additionally, Receiver Operating Characteristic (ROC) curves were prepared for each AHI cut-off for the STOP-BAG and the STOP-BAG-O screening tools, and the areas under the curve (AUC) at each level were also computed. Since the STOP-BAG and STOP-BAG-O were nested models, we compared the addition of oximetry using the roc.test function in "R", which permitted statistical comparison with bootstrapping of the AUCs for each model.

To evaluate independent predictors of an OSA diagnosis, logistic regression analyses were conducted with the eight STOP-BAG-O variables. OSA diagnosis was the dependent variable for the model and the definition used was an AHI ≥10. For each predictor, the odds ratio (OR), 95% confidence interval (CI) and their respective p-value was reported. In addition, we ran Spearman correlation coefficients to assess whether total scores on the STOP-BAG-O and STOP-BAG screening tools would be correlated with AHI. Furthermore, model validation was completed with bootstrapping where resampling was performed 100 times with replacement to assess for model overfitting. For all analyses, a p-value <0.05 was considered to be statistically significant. Analyses were performed with the statistics software "R", version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria) or with the Statistical Package for the Social Sciences 24.0 (IBM Corp., Armonk, NY).

3. Results

Two hundred and thirty-one patients from the SLEAP-SMART and DOC studies who were diagnosed with an ischemic stroke or TIA completed PSG or HSAT testing and the STOP-BAG questionnaire within one year of their stroke/TIA event. As mentioned in the methods, patients diagnosed with central sleep apnea (N = 5) were not included in analyses. Of these 231 patients, 58.0% (N = 134) were not diagnosed with OSA, having an AHI < 10. The remaining 97 patients were diagnosed with OSA: 42.0% (N = 97) had an AHI ≥ 10, 28.6% (N = 66) had an AHI ≥15, and 10.8% (N = 25) had an AHI ≥ 30. The mean (±SD) age was 64.41 ± 15.27, the median BMI was 26.36 kg/m^2. In our patient population, 74.9% (N = 173) suffered a stroke as opposed to a TIA. The median time between the index

cerebrovascular event and recruitment/baseline testing was eight days, and the median time between the index cerebrovascular event and sleep testing was 99 days. The clinical characteristics of our study population are outlined in Table 2.

The sensitivities, specificities, PPV and NPV values for the STOP-BAG and STOP-BAG-O cut-offs are presented in Tables 3 and 4, respectively. For the STOP-BAG questionnaire, a cut-off of ≤3 allowed us to maximize sensitivity, while a cut-off of ≥4 permitted maximizing specificity; these cut-offs were used to distinguish those at low- or high-risk, respectively, for a diagnosis of OSA (AHI ≥10), as has been previously described [19], as well as classify ≥50% of the sample. These cut-offs yielded a sensitivity of 83.5% and specificity of 67.2%. For the STOP-BAG-O screening tool, cut-offs of ≤3 and ≥5 were selected to maximize sensitivity and specificity and classify ≥50% of the sample. These cut-offs yielded a sensitivity of 95.9% and specificity of 78.4%.

Values for the area under the receiver-operating curve were calculated for each AHI cut-off for both the STOP-BAG and STOP-BAG-O and are presented in Table 5; the receiver-operating curves are displayed in Fig. 1. Using our primary definition for OSA (ie, an AHI of ≥10), the STOP-BAG questionnaire yielded an AUC of 0.682 while the STOP-BAG-O yielded an AUC of 0.751. For all the AHI cut-offs examined, the AUC was greater for the STOP-BAG-O compared to the STOP-BAG. To determine if there was a significant difference between the two models, a statistical comparison was performed using bootstrapping. Results are presented in Table 5; for each AHI cut-off, there was a statistically significant difference between the two models ($p < 0.001$).

Logistic regression analyses were completed to assess which variables of the STOP-BAG-O were independent predictors of OSA, and the results are reported in Table 6. Using an AHI cut-off of ≥10, the variables that significantly independently predicted an OSA diagnosis were BMI (OR: 4.42, 95% CI: 1.09–11.80, $p = 0.035$), age (OR: 6.29, 95% CI: 1.32–9.68, $p = 0.012$), male sex (OR: 8.98, 95% CI: 1.44–5.77, $p = 0.003$), and nocturnal oxygen desaturation (OR: 31.56, 95% CI: 6.61–50.09, $p < 0.001$). Internal model validation indicated there was no concern of overfitting. Moreover, the model had a C-index value of 0.828 indicating a strong model with good discrimination. In addition, total scores on the STOP-BAG and STOP-BAG-O screening tools were significantly correlated with AHI ($p < 0.001$).

4. Discussion

In our study, the "STOP-BAG-O" screening tool, a modified version of the "STOP-BAG" questionnaire that included oximetry data, demonstrated enhanced clinical utility compared to the STOP-BAG questionnaire in predicting a diagnosis of OSA in stroke/TIA patients. For all AHI cut-offs used, the area under the curve for the STOP-BAG-O was greater and statistically different than that for the STOP-BAG questionnaire. Regression analysis of the STOP-BAG-O variables demonstrated that BMI, age, male sex, and nocturnal oxygen desaturation significantly predicted a diagnosis of OSA.

The cohort in this study is the largest to date that has assessed the STOP-BAG questionnaire in stroke and TIA patients. The STOP-BAG questionnaire is easily and quickly administered, making this questionnaire highly feasible for in-clinic use. However, the model performance of the STOP-BAG questionnaire in our study, which did not include oxygen desaturation, was relatively poor with an AUC of 0.682. Providing patients with a pulse oximeter to take home for one night or use for one night in-hospital, can allow for efficient detection of nocturnal oxygen desaturation and can provide added value when included into the total STOP-BAG-O score to assess for OSA risk. By identifying those at low-risk for OSA, high costs and lengthy wait-times associated with PSG may be decreased. Furthermore, by using the screen to classify those at high-risk, patients in more serious and immediate need of further testing can be identified. Use of an oximeter would be cheaper than HSAT; and, prior work has demonstrated that completion rates were

Table 2
Clinical characteristics of study population (N = 231).

Variable	Total Population N = 231	OSA (AHI≥10) N = 97	No OSA (AHI<10) N = 134
	Mean (SD)		
Age	64.4 (15.3)	69.0 (13.5)	61.1 (15.7)
	Median (IQR)		
BMI	26.4 (5.4)	27.2 (6.1)	25.9 (5.3)
Days between event and recruitment/baseline testing	8 (68)	6 (78)	10 (64.3)
Days between event and HSAT/PSG testing	99 (137)	100 (128.5)	94.5 (140.5)
Days between recruitment/baseline testing and HSAT/PSG testing	54 (117)	65 (136.5)	47.5 (115.3)
AHI	7 (15)	20 (17)	3 (5)
OAI	0.9 (3.6)	4.4 (7.5)	0.1 (0.9)
CAI	0.1 (0.6)	0.6 (3.4)	0 (0.2)
Hypopnea Index	4 (8.2)	11 (10.7)	1.6 (3.5)
Sleep Under 90 min	4 (25)	12 (36.5)	1 (11.3)
	N (%)		
Male	138 (59.7%)	69 (71.1%)	69 (51.5)
Stroke	173 (74.9%)	74 (76.3%)	99 (73.9)
Completed PSG	125 (54.1%)	53 (54.6%)	72 (53.7)
STOP variables			
Snore	107 (46.3%)	52 (53.6%)	55 (41.0%)
Tired	116 (50.2%)	50 (51.5%)	66 (49.3%)
Observed apnea	47 (20.3%)	25 (25.8%)	22 (16.4%)
High blood pressure	136 (58.9%)	69 (71.1%)	67 (50%)
AHI			
0–4.9	85 (36.8%)		
5–9.9	49 (21.2%)		
10–14.9	31 (13.4%)		
15–29.9	41 (17.7%)		
30+	25 (10.8%)		

Abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; CAI = central apnea index; HSAT = home sleep apnea test; IQR = interquartile range; OAI = obstructive apnea index; PSG = polysomnography; SD = standard deviation.

Table 3
Sensitivity, specificity, and cumulative percent for STOP-BAG cut-off scores (N = 231).

Cut-off score		0	1	2	3	4	5	6	7
Cumulative %		1.3	7.8	29.0	56.3	82.7	95.7	99.6	100
AHI≥5	Sens.	1.000	1.000	0.959	0.808	0.555	0.240	0.062	0.007
	Spec.	0.000	0.035	0.141	0.459	0.765	0.941	0.988	1.000
	PPV	0.632	0.640	0.657	0.720	0.802	0.875	0.900	1.000
	NPV	1.000	1.000	0.667	0.582	0.500	0.419	0.380	0.370
AHI≥10	Sens.	1.000	1.000	0.979	0.835	0.588	0.289	0.082	0.01
	Spec.	0.000	0.022	0.119	0.381	0.672	0.910	0.985	1.000
	PPV	0.420	0.425	0.446	0.494	0.564	0.700	0.800	1.000
	NPV	1.000	1.000	0.889	0.761	0.692	0.639	0.738	0.583
AHI≥15	Sens.	1.000	1.000	1.000	0.864	0.606	0.333	0.121	0.015
	Spec.	0.000	0.018	0.109	0.352	0.630	0.891	0.988	1.000
	PPV	0.286	0.289	0.310	0.348	0.396	0.550	0.800	1.000
	NPV	1.000	1.000	1.000	0.866	0.800	0.770	0.738	0.717
AHI≥30	Sens.	1.000	1.000	1.000	0.920	0.800	0.360	0.120	0.04
	Spec.	0.000	0.015	0.087	0.316	0.607	0.850	0.966	1.000
	PPV	0.108	0.110	0.117	0.140	0.198	0.225	0.300	1.000
	NPV	1.000	1.000	1.000	0.970	0.962	0.916	0.900	0.896

Abbreviations: AHI = apnea-hypopnea index; NPV = negative predictive value; PPV = positive predictive value; Sens = sensitivity; Spec = specificity.

Table 4
Sensitivity, specificity, and cumulative percent for STOP-BAG-O cut-off scores (N = 231).

Cut-off score		0	1	2	3	4	5	6	7	8
Cumulative %		1.3	4.3	16.9	37.2	63.2	84.8	96.5	99.6	100
AHI≥5	Sens.	1.000	1.000	1.000	0.938	0.795	0.514	0.219	0.055	0.007
	Spec.	0.000	0.035	0.118	0.353	0.659	0.882	0.965	1.000	1.000
	PPV	0.632	0.640	0.661	0.714	0.800	0.882	0.914	1.000	1.000
	NPV	1.000	1.000	1.000	0.769	0.651	0.514	0.418	0.381	0.370
AHI≥10	Sens.	1.000	1.000	1.000	0.959	0.835	0.577	0.268	0.082	0.01
	Spec.	0.000	0.022	0.075	0.261	0.522	0.784	0.933	1.000	1.000
	PPV	0.420	0.425	0.439	0.484	0.559	0.659	0.743	1.000	1.000
	NPV	1.000	1.000	1.000	0.897	0.814	0.719	0.638	0.901	0.583
AHI≥15	Sens.	1.000	1.000	1.000	0.985	0.864	0.591	0.303	0.121	0.015
	Spec.	0.000	0.018	0.061	0.230	0.467	0.721	0.909	1.000	1.000
	PPV	0.286	0.289	0.299	0.339	0.393	0.459	0.571	1.000	1.000
	NPV	1.000	1.000	1.000	0.974	0.895	0.815	0.765	0.740	0.717
AHI≥30	Sens.	1.000	1.000	1.000	1.000	0.920	0.800	0.360	0.120	0.040
	Spec.	0.000	0.015	0.049	0.189	0.408	0.684	0.874	0.976	1.000
	PPV	0.108	0.111	0.113	0.130	0.159	0.235	0.257	0.375	1.000
	NPV	1.000	1.000	1.000	1.000	0.977	0.966	0.918	0.901	0.896

Abbreviations: AHI = apnea-hypopnea index; NPV = negative predictive value; PPV = positive predictive value; Sens = sensitivity; Spec = specificity.

substantially higher in older adults who used a wrist-worn oximeter (100%) compared to those who used HSAT (54%) [31].

We modified the original STOP-BANG questionnaire in two ways. First, we removed neck circumference, as this has been shown to have little impact on the STOP-BANG's performance in patients with cerebrovascular disease [20], and is not routinely obtained in clinical settings. Finally, we included oxygen desaturation as recent research has suggested that oxygen desaturation may play a role in OSA severity and may be a useful metric for predicting OSA [23–25]. Inclusion of this variable proved effective, as this variable was significantly and independently correlated with OSA diagnosis.

Table 5
Area under the receiver operating curves (AUC) values for different AHI cut-offs.

AHI cut-off	Area Under the Receiver Operating Curve		p-value
	STOP-BAG	STOP-BAG-O	
≥5	0.706	0.792	<0.001*
≥10	0.682	0.751	<0.001*
≥15	0.685	0.736	<0.001*
≥30	0.728	0.773	<0.001*

Abbreviations: AHI = apnea-hypopnea index.
*Indicates P < 0.05.

When individual STOP-BAG-O variables were compared with AHI using logistic regression, it was found that four variables were significantly predictive of an OSA diagnosis (defined as an AHI ≥ 10): BMI, age, male sex, and nocturnal oxygen desaturation. Previous research findings have demonstrated that BMI [16], age and male sex [16] and low nocturnal oxygen desaturation [23] are associated with increased risk of OSA. Using these four variables to create a new screening tool, the area under the curve was 0.777 for an AHI cut-off of ≥10; this finding warrants further investigation into the role these variables may play in screening for OSA. Of note, internal model validation using bootstrapping was completed and there was no concern of overfitting present in this 4-variable model.

When comparing AUCs for different cut-offs of STOP-BAG-O, the greatest AUC was achieved with a cut-off of 5 (AUC = 0.792). This value was comparable to previous literature [20,21] and superior to other studies [16,22]. The value obtained suggests that this screening tool had good accuracy in identifying mild cases of OSA (AHI ≥5).

In exploratory analyses, we assessed whether the area under the curves for the STOP-BAG and STOP-BAG-O differed for various sub-groups. Using the primary definition of an AHI ≥10 for a diagnosis of OSA, the models were compared to see if results differed whether: (i) PSG/HSAT was administered early versus late after stroke/TIA (ie less than versus greater than three-months

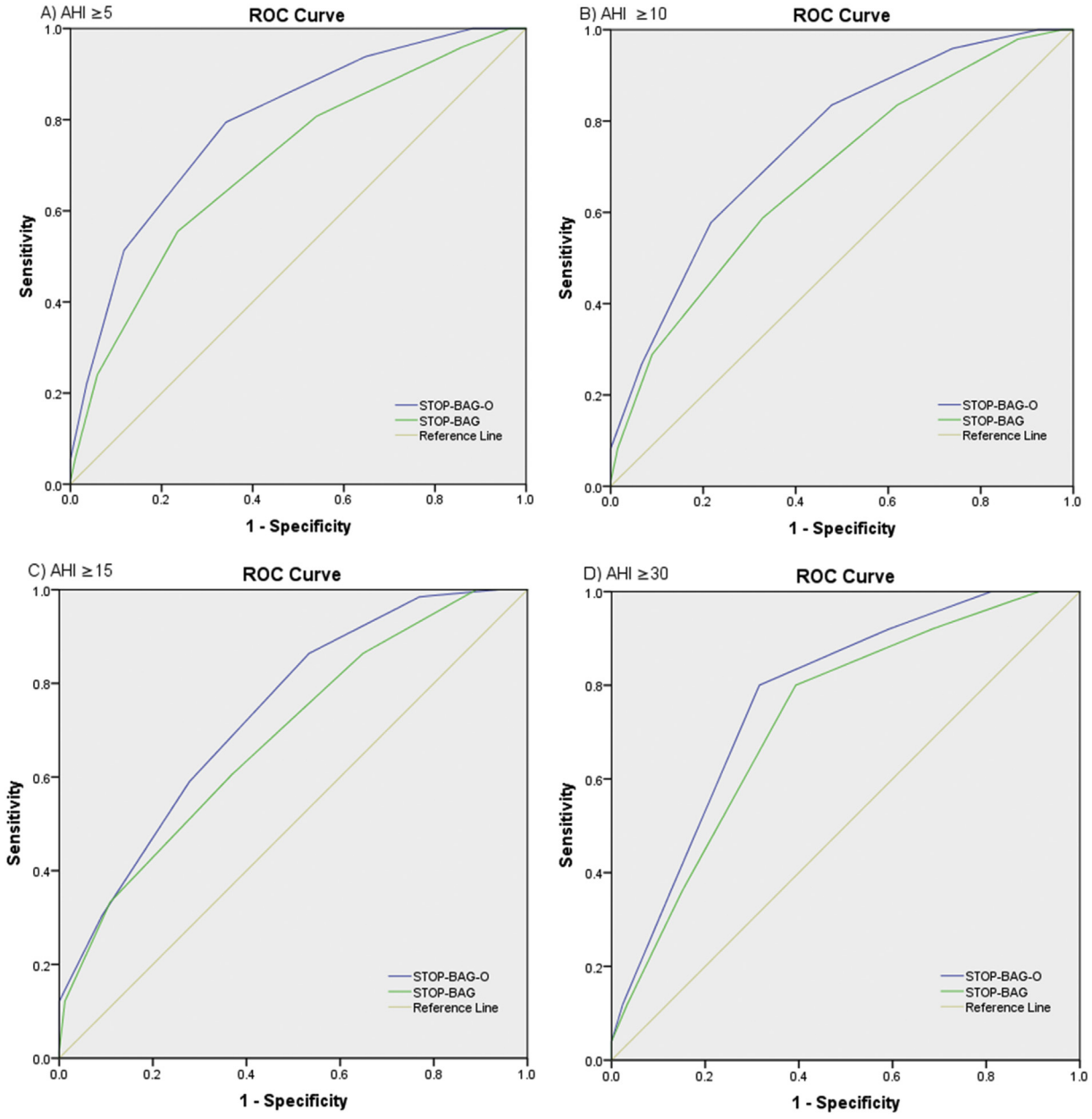

Fig. 1. Receiver operating characteristic curve for STOP-BAG-O and STOP-BAG at various AHI cut-off values. A) AHI ≥ 5 B) AHI ≥ 10 C) AHI ≥ 15 D) AHI ≥ 30.

post-stroke/TIA); (ii) there was a difference between modality used to diagnose OSA (ie, PSG versus HSAT); and (iii) patients presented with stroke or TIA. We found no significant differences in these analyses.

Table 6
Logistic regression analysis for independent predictors of OSA (AHI ≥ 10).

	OR	95% CI	p-value
Snoring	2.06	0.83–3.29	0.151
Tired	0.01	0.53–2.01	0.932
Observed apnea	0.60	0.61–0.12	0.437
Hypertension	1.87	0.82–3.15	0.171
BMI	4.42	1.09–11.80	0.035*
Age	6.29	1.32–9.68	0.012*
Gender (Male)	8.98	1.44–5.77	0.003*
Oxygen Desaturation	31.56	6.61–50.09	<0.001*

Abbreviations: BMI = body mass index; CI = confidence interval; OR = odds ratio.
*Indicates P < 0.05.

The present study has several limitations. First, although the HSAT (ApneaLink) used by some participants of this study has been shown to be highly sensitive (97%) and specific (100%) [32] compared to PSG, PSG remains the gold standard. Moreover, our results did not significantly differ whether HSAT or PSG was used. Second, patients with significant physical impairment and/or aphasia were excluded from this study (as they were unable to complete the STOP-BAG questionnaire, PSG and/or HSAT), therefore our results may not be applicable to patients with more severe strokes. Third, all our patients were recruited from a single centre and all participants were part of clinical trials, which may also limit generalizability. Fourth, by excluding neck circumference the performance of the STOP-BAG questionnaire may have decreased, in comparison to the STOP-BANG. However, neck circumference is not routinely measured in stroke clinics, and excluding this variable may therefore make our approach more feasible for broad application; also, prior work in the stroke population has demonstrated

that the addition of neck circumference to the STOP-BANG did not significantly improve model accuracy [20]. Additionally, the predictor oxygen desaturation is a component of the outcome as it is used in the definition of a hypopnea, and was derived from the PSG/HSAT devices used to diagnose OSA. Therefore, it may have artificially raised model performance. Finally, the oxygen desaturation parameter used in this study was derived from PSG or HSAT, and not from overnight pulse oximetry. However, overnight pulse oximetry is simple to obtain, and the purpose of our study was to demonstrate that the addition of nocturnal oxygen desaturation to the STOP-BAG score would enhance the ability of this screening tool to predict a diagnosis of OSA.

In conclusion, we report on the largest cohort to-date that has assessed the STOP-BAG questionnaire in stroke and TIA patients. We demonstrate that the STOP-BAG-O questionnaire is a valid and statistically superior tool compared to the STOP-BAG questionnaire for identifying those at low- or high-risk for post-stroke/TIA OSA. The simplicity and brevity of this screening tool makes it a feasible option for clinic or hospital use.

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Disclosures

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.12.019.

References

[1] Bradley TD, Floras JS. Obstructive sleep apnoea and its cardiovascular consequences. Lancet 2009;373:82–93.
[2] Arzt M, Young T, Finn L, et al. Association of sleep-disordered breathing and the occurrence of stroke. Am J Respir Crit Care Med 2005;172:1447–51.
[3] Bassetti C, Aldrich MS, Chervin RD, et al. Sleep apnea in patients with transient ischemic attack and stroke: a prospective study of 59 patients. Neurology 1996;47:1167–73.
[4] Johnson KG, Johnson DC. Frequency of sleep apnea in stroke and tia patients: a meta-analysis. J Clin Sleep Med JCSM – Offic Publ Am Acad Sleep Med 2010;6:131–7.
[5] Martinez-Garcia MA, Soler-Cataluna JJ, Ejarque-Martinez L, et al. Continuous positive airway pressure treatment reduces mortality in patients with ischemic stroke and obstructive sleep apnea: a 5-year follow-up study. Am J Respir Crit Care Med 2009;180:36–41.
[6] Mansukhani MP, Bellolio MF, Kolla BP, et al. Worse outcome after stroke in patients with obstructive sleep apnea: an observational cohort study. J Stroke Cerebrovasc Dis – Offic J Natl Stroke Assoc 2011;20:401–5.
[7] Kaneko Y, Hajek VE, Zivanovic V, et al. Relationship of sleep apnea to functional capacity and length of hospitalization following stroke. Sleep 2003;26:293–7.
[8] Parra O, Sanchez-Armengol A, Bonnin M, et al. Early treatment of obstructive apnoea and stroke outcome: a randomised controlled trial. Eur Respir J – Offic J Eur Soc Clin Respir Physiol 2011;37:1128–36.
[9] Ryan CM, Bayley M, Green R, et al. Influence of continuous positive airway pressure on outcomes of rehabilitation in stroke patients with obstructive sleep apnea. Stroke J Cereb Circ 2011;42:1062–7.
[10] Sandberg O, Franklin KA, Bucht G, et al. Nasal continuous positive airway pressure in stroke patients with sleep apnoea: a randomized treatment study. Eur Respir J – Offic J Eur Soc Clin Respir Physiol 2001;18:630–4.
[11] Wessendorf TE, Wang YM, Thilmann AF, et al. Treatment of obstructive sleep apnoea with nasal continuous positive airway pressure in stroke. Eur Respir J – Offic J Eur Soc Clin Respir Physiol 2001;18:623–9.
[12] Bravata DM, Sico J, Vaz Fragoso CA, et al. Diagnosing and treating sleep apnea in patients with acute cerebrovascular disease. J Am Heart Assoc 2018;7:e008841.
[13] Kernan WN, Ovbiagele B, Black HR, et al. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the american heart association/american stroke association. Stroke J Cereb Circ 2014;45:2160–236.
[14] Bravata DM, Ferguson J, Miech EJ, et al. Diagnosis and treatment of sleep apnea in patients' homes: the rationale and methods of the "gotosleep" randomized-controlled trial. J Clin Sleep Med JCSM – Offic Publ Am Acad Sleep Med 2012;8:27–35.
[15] Swartz RH, Bayley M, Lanctot KL, et al. Post-stroke depression, obstructive sleep apnea, and cognitive impairment: rationale for, and barriers to, routine screening. Int J Stroke – Offic J Int Stroke Soc 2016;11:509–18.
[16] Boulos MI, Wan A, Im J, et al. Identifying obstructive sleep apnea after stroke/tia: evaluating four simple screening tools. Sleep Med 2016;21:133–9.
[17] Boulos MI, Elias S, Wan A, et al. Unattended hospital and home sleep apnea testing following cerebrovascular events. J Stroke Cerebrovasc Dis – Offic J Natl Stroke Assoc 2017;26:143–9.
[18] Abrishami A, Khajehdehi A, Chung F. A systematic review of screening questionnaires for obstructive sleep apnea. Can J Anaesth J canadien d'anesthesie 2010;57:423–38.
[19] Chung F, Yegneswaran B, Liao P, et al. Stop questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology 2008;108:812–21.
[20] Katzan IL, Thompson NR, Uchino K, et al. A screening tool for obstructive sleep apnea in cerebrovascular patients. Sleep Med 2016;21:70–6.
[21] Swartz RH, Cayley ML, Lanctot KL, et al. The "doc" screen: feasible and valid screening for depression, obstructive sleep apnea (osa) and cognitive impairment in stroke prevention clinics. PLoS One 2017;12:e0174451.
[22] Sico JJ, Yaggi HK, Ofner S, et al. Development, validation, and assessment of an ischemic stroke or transient ischemic attack-specific prediction tool for obstructive sleep apnea. J Stroke Cerebrovasc Dis – Offic J Natl Stroke Assoc 2017;26:1745–54.
[23] Chung F, Liao P, Elsaid H, et al. Oxygen desaturation index from nocturnal oximetry: a sensitive and specific tool to detect sleep-disordered breathing in surgical patients. Anesth Analg 2012;114:993–1000.
[24] Magalang UJ, Dmochowski J, Veeramachaneni S, et al. Prediction of the apnea-hypopnea index from overnight pulse oximetry. Chest 2003;124:1694–701.
[25] Teramoto S, Matsuse T, Fukuchi Y. Clinical significance of nocturnal oximeter monitoring for detection of sleep apnea syndrome in the elderly. Sleep Med 2002;3:67–71.
[26] Collop NA, Anderson WM, Boehlecke B, et al. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. Portable monitoring task force of the american academy of sleep medicine. J Clin Sleep Med JCSM – Offic Publ Am Acad Sleep Med 2007;3:737–47.
[27] Erman MK, Stewart D, Einhorn D, et al. Validation of the apnealink for the screening of sleep apnea: a novel and simple single-channel recording device. J Clin Sleep Med JCSM – Offic Publ Am Acad Sleep Med 2007;3:387–92.
[28] Nigro CA, Dibur E, Malnis S, et al. Validation of apnealink ox for the diagnosis of obstructive sleep apnea. Sleep Breath Schlaf Atmung 2013;17:259–66.
[29] Iber C, Ancoli-Israel S, Chesson A, et al. The aasm manual for the scoring of sleep and associated events: rules, terminology and technical specifications. 2007. p. 17–49.
[30] Patel N, Raissi A, Elias S, et al. A modified definition for obstructive sleep apnea in home sleep apnea testing after stroke or transient ischemic attack. J Stroke Cerebrovasc Dis – Offic J Natl Stroke Assoc 2018;27:1524–32.
[31] Vaughan L, Redline S, Stone K, et al. Feasibility of self-administered sleep assessment in older women in the women's health initiative (whi). Sleep Breath Schlaf Atmung 2016;20:1079–91.
[32] Ng SS, Chan TO, To KW, et al. Validation of a portable recording device (apnealink) for identifying patients with suspected obstructive sleep apnoea syndrome. Intern Med J 2009;39:757–62.