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Obstructive Sleep Apnea and Ischemic Stroke Etiology: Is There a Link?

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Sleep Sci

Abstract

Objectives The objective of this study is to evaluate the presence of obstructive sleep apnea (OSA) and its potential association with subtypes of stroke according to the classification of the Trial of Org 10172 in Acute Stroke Treatment (TOAST).

Materials and Methods This cross-sectional study recruited 100 consecutive patients with a recent diagnosis of stroke or acute transient ischemic attack and evaluated the presence of OSA and its potential association with subtypes of TOAST.

Results The prevalence of OSA was 51%. The mean age was 68 ± 15 years. Patients with OSA ($n = 51$, 51%) presented higher frequency of diabetes and previous stroke/acute transient ischemic attack (39.2 versus 18.4%, $p = 0.018$) than patients without OSA. There was no association between the presence of OSA and the etiology of stroke/ acute transient ischemic attack according to the TOAST classification ($p = 0.698$).

Conclusions Despite the biological plausibility of a positive association between the presence of OSA and TOAST classification, this hypothesis was not confirmed. This underscores that the subtype of stroke should not influence decisions about OSA screening.

Keywords
- sleep apnea
- stroke
- ischemic stroke
- classification
- etiology

Introduction

The etiology of stroke is the key element for determining management strategies to reduce the risk of a new event and to optimize costs related to health care. The etiological subtypes of ischemic stroke are stratified into five categories, according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification: Large vessels atherosclerosis, small vessels occlusion, cardioembolic, other determined causes and undetermined etiology.[1,2] Obstructive sleep apnea (OSA) is linked to the occurrence of stroke.[3] Potential plausible mechanisms include endothelial dysfunction, inflammation,

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atherosclerosis progression, atrial remodeling and atrial fibrillation.[4] Considering that some TOAST subtypes are more related to these factors - such as the cardioembolic subtype and great vessels - it is reasonable to speculate that OSA could be more associated with a higher occurrence of some subtypes of ischemic stroke or acute transient ischemic attack (TIA).[3–5] The objective of this study is to evaluate the presence of OSA and its potential association with subtypes of stroke by TOAST classification.

Materials and Methods

This cross-sectional study recruited consecutive adult patients with a recent diagnosis of stroke or TIA admitted to the neurological emergency room of two tertiary hospitals between November 2019 and November 2020 in Recife, Brazil. We excluded patients with hemorrhagic stroke, cerebral venous infarction, National Institute of Health Stroke Scale (NIHSS) >25; severe impairment of the level of consciousness that could interfere with the sleep study; decompensated heart failure; continuous use of oxygen, mechanical ventilation or positive pressure ventilation and current treatment of OSA. The study was approved by the Human Research Ethics Committee (CAAE: 23526719.5.0000.5192) and the participants signed the informed consent form.

For all patients, we conducted a clinical evaluation including demographic and anthropometric data, functional assessment using the Rankin scale and Barthel independence, and complementary neurological tests following standard protocols. All patients were categorized according to the etiological subtypes of the TOAST classification during hospitalization. The sleep study was performed during hospitalization or within 30 days after the stroke, using a portable sleep monitor (ApneaLink™, ResMed, San Diego, CA, USA). OSA was defined by an apnea-hypopnea index ≥15 events/hour.[6,7] Mixed events were computed in addition to obstructive events to distinguish them from central events. The TOAST classification and OSA diagnosis were performed in a blinded fashion. Pearson's Chi-square, Fisher's exact and T-student tests or Mann-Whitney tests were used to compare variables between groups. A two-sided p value <0.05 was considered significant. Data were analyzed with Stata® statistical software.

Results

Of 190 screened patients, 100 patients were included the final analysis (stroke, 81; TIA, 19). The reasons for excluding 47% of the patients included refusals ($n = 36$), active pneumonia ($n = 5$), current OSA treatment ($n = 7$), current use of oxygen ($n = 15$), dementia syndrome with behavioral change with impossibility of performing polysomnography ($n = 19$) and severe neurological impairment with NIHSS >25 ($n = 8$). Our sample comprised predominantly females (54%). The mean age was 68 ± 15 years. A ►**Table 1** presents the baseline characteristics of the groups.

The sleep study was performed within 5.8 ± 5.0 days after hospital admission. Patients with OSA ($n = 51$, 51%) presented higher frequency of diabetes and previous stroke/TIA (39.2 versus 18.4%, $p = 0.018$) than patients without OSA. Only one patient had central sleep apnea episodes. However, obstructive events were predominant even in this

Table 1 Baseline characteristics of stroke patients categorized by the presence of obstructive sleep apnea (OSA).

Factors	No OSA (AHI < 15) n = 49	OSA (AHI ≥15) n = 51	*p*-value
Age, years	65.63 ± 14,73	70.07 ± 14,27	0.1285
Sex			0.052
Male	31 (63.27%)	23 (45.10%)	
Female	18 (36.73%)	28 (54.90%)	
Systolic blood pressure, mmHg	151.40 ± 31,00	159.60 ± 26,61	0.1585
Diastolic blood pressure, mmHg	84.51 ± 14,18	85.56 ± 13,24	0.7005
Neck circunference, cm	38 (34–46)	38 (33–43)	0.4433
Abdominal circunference, cm	106 (101–118)	108 (96–118)	0.9066
Body mass index, kg/m^2	27.22 ± 4,35	28.05 ± 3,87	0.3206
Comorbid disease			
Diabetes mellitus	19 (38.78%)	33 (64.71%)	0.008
Hypertension	35 (71.43%)	41 (80.39%)	0.208
Coronary artery disease	11 (22.45%)	11 (21,57%)	0.553
Dyslipidemia	11 (22.45%)	20 (39,22%)	0.055
Previous stroke	9 (18.37%)	20 (39,22%)	0.018
Presence of arrhythmias			0.543

Table 1 (*Continued*)

Factors	No OSA (AHI < 15) n = 49	OSA (AHI ≥15) n = 51	*p*-value
FA	8 (16.33%)	5 (9,80%)	
Other arrhythmias No-FA	3 (6.12%)	5 (9,80%)	
No arrhythmia	38 (77.55%)	41(80,39%)	
Sedentary lifestyle	39 (79.59%)	41 (80,39%)	0.559
Smoking	14 (28.57%)	14 (27,45%)	0.539
Alcoholism	6 (12.24%)	8 (15,69)	0.419
NIHSS	2 (1–4)	3 (1–5)	0.1469
Barthel Index			0.330
< 60 points	7 (14.29%)	10 (19,61%)	
≥60 points	42 (85.71%)	41 (88,39%)	
Modified Rankin Scale			0.559
0–2 Score	39 (79.59%)	41 (80.39)	
≥3 Score	10 (20.41%)	10 (19.61)	

Abbreviations: AHI, Apnea-hypopnea index; FA, Atrial fibrillation; NIHSS, National Institutes of Health Stroke Scale; OSA, obstructive sleep apnea.

case. There were no significant differences in other variables including age, obesity, hypertension, smoking, atrial fibrillation and several scales including NIH, Barthel and Rankin. As shown in ►**Fig. 1**, the prevalence of OSA was similar in all stroke subtypes.

Discussion

This study assessed the etiology of ischemic stroke according to the OSA status using a standard classification. Previous studies evaluated the association of OSA with specific stroke subtypes, such as the cardioembolic subtype. Very few studies addressed all subtypes of ischemic stroke using standard classifications. In a retrospective analysis of three medical centers in Shandong Province, China, OSA was associated with a higher incidence of lobar hemorrhage (5.3-fold) and small-vessel disease (80%).[5] However, according to the authors, only patients with common symptoms of OSA performed sleep studies. Our results are consistent with those provided by Brown and colleagues. In their study, the ischemic stroke subtype was not associated with the presence or severity of OSA.[4] Our study has strengths and limitations. The availability of objective sleep studies (and not just sleep questionnaires) is one strength. In addition, the inclusion of all TIA and stroke subtypes also reinforces the importance of our work. One limitation was the exclusion of a relatively large number of patients due to our stringent inclusion and exclusion criteria (beyond refusals to participate). However, this approach was important for excluding clear confounders such as current OSA treatment, active infection or oxygen use. Another limitation is the cross-sectional study design. In conclusion, the presence of OSA, evaluated after a stroke episode, is not associated with stroke subtype. Despite the potential biological plausibility for a positive association with some subtypes based on the TOAST classification, this hypothesis is not confirmed in our study underscoring that the subtype of stroke should not influence decisions about OSA screening.

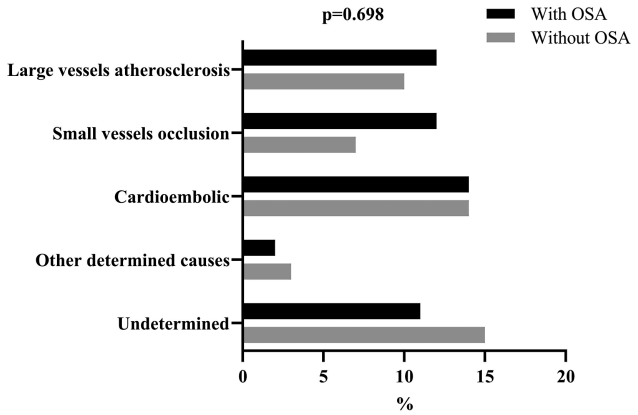

Fig. 1 Etiology of stroke/TIA according to the TOAST classification.

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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