Neck circumference, a bedside clinical feature related to mortality of acute ischemic stroke

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Summary

Objective: The aim of this study was to evaluate clinical/demographic factors, sleep alterations and one year mortality in acute ischemic stroke. **Methods:** This was a prospective study of 89 consecutive patients (mean age 64.39 ± 8.51 years) with acute ischemic stroke. High risk of obstructive sleep apnea (OSA) was evaluated by the Berlin questionnaire, daytime somnolence by the Epworth Sleepiness Scale (> 10) and subjective sleep quality by the Pittsburgh Sleep Quality Index (> 5). Clinical and anthropometric data including body mass index, hip-waist ratio, neck circumference (NC) were obtained. Increased NC was defined if > 43 cm in men and > 38 cm in women. Stroke severity was estimated by the Barthel Index and the modified Rankin Scale. The end-point was death after 12 months follow-up. **Results:** One-year mortality was 8.9%. Non-survivors were older (p = 0.006) and had larger NC (p = 0.02). Among all cases, large NC was related to high risk of OSA, diabetes and hypertension (Fisher's exact test). Compared to men, women showed relatively larger NC. Overall, family history of stroke (74.2 %), diabetes (33.7%) and hypertension (78.6%) were frequent; obesity (11.2%) was uncommon. Daytime sleepiness (34.8 %), poor sleep quality (65.2%) and risk of OSA (58.42%) were frequently found. **Conclusion:** Poor sleep quality, excessive daytime sleepiness and high risk of OSA are frequent in this sample with acute ischemic stroke. One-year mortality was related to older age and large NC. As obesity is uncommon in acute stroke patients, a large NC should be taken as a significant clinical sign related to mortality.

Keywords: Sleep; stroke; sleep apnea; neck circumference; mortality.

Resumo

Perímetro cervical, uma medida à beira do leito relacionada com a mortalidade no acidente vascular cerebral isquêmico

Objetivo: O objetivo do estudo é avaliar em pacientes com acidente vascular cerebral (AVC) isquêmico, os fatores clínico/demográficos, alterações do sono e a mortalidade após um ano. **Métodos:** Trata-se de estudo prospectivo envolvendo 89 pacientes consecutivos (64,39 ± 8,51 anos) com AVC isquêmico agudo. Foram avaliados o risco elevado de apneia obstrutiva do sono (AOS) (questionário de Berlin), a sonolência diurna (Escala de Sonolência Epworth > 10) e a qualidade subjetiva do sono (Índice de Qualidade de Sono Pittsburgh > 5). O índice de massa corpórea, a relação cintura-quadril e o perímetro cervical (PC) foram estudados: PC aumentado foi definido se > 43 cm (homens) e > 38 cm (mulheres). Estimou-se a gravidade da doença pelo Índice de Barthel e pela Escala de Rankin modificada. O desfecho final foi o óbito após 12 meses. **Resultados:** A mortalidade após um ano foi de 8,9%. Os pacientes que foram a óbito eram mais idosos (p = 0,006) e apresentavam PC aumentado (p = 0,02). O PC aumentado relacionou-se com a presença de diabetes, hipertensão arterial e risco elevado de AOS (teste exato de Fisher). As mulheres apresentavam, relativamente, maior PC. Entre todos, história familiar de doença cerebrovascular (74,2%), diabetes (33,7%) e hipertensão (78,6%) foram frequentes; obesidade (11,2%) foi incomum. Sonolência diurna (34,8%), má qualidade do sono (65,2%) e risco de AOS (58,42%) foram frequentes. **Conclusão:** Alterações do sono são frequentes no AVC isquêmico agudo. Mortalidade foi mais comum em pacientes mais idosos e com maior PC. No AVC isquêmico, o PC aumentado relaciona-se com a mortalidade e provavelmente constitui-se uma medida clínica importante a ser considerada.

Unitermos: Sono; acidente vascular cerebral; apneia do sono; perímetro cervical; mortalidade.

Study conducted at Hospital Fernandes Távora, Fortaleza, CE, Brazil

Submitted on: 04/13/2011
Approved on: 07/19/2011

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Conflict of interest: None.

Introduction

Identifying factors associated with stroke mortality is of great clinical importance. Some clinical characteristics such as age, gender, diabetes and systemic arterial hypertension are known to influence stroke risk[1-4]; however, their ability to predict outcome is limited. Previously, it has been demonstrated that obstructive sleep apnea (OSA) is associated with increased mortality in stroke[5]. Obesity and the distribution of body fat are of utmost importance for the risk OSA[6]. It has been said that "obesity increases the risk of OSA by approximately 10-fold from a range of 2 to 4% in the general adult population, to up to 20 to 40% in those with a body mass index (BMI) > 30"[7]. Traditionally, the BMI was used as a measure to diagnose obesity. Other types of measures have been shown to predict the distribution of body fat: waist circumference, hip circumference, waist to hip ratio and neck circumference (NC) have all been associated with increased body fat. Recently, NC has been associated with the severity of OSA independently of visceral obesity, especially in non-obese patients[8].

Obstructive sleep apnea is associated with increased cardiovascular risk and systemic hypertension and has been confirmed as an independent risk factor for stroke[5,9-11]. A cohort study involving a large number of patients showed that OSA significantly increases the combined risk of stroke or death from any cause, and this increase is independent of other risk factors, including hypertension[5]. Therefore, although OSA and stroke-related death have been previously related, the mechanisms of OSA on stroke-related death remain unclear.

Other factors such as hypertension, diabetes, in addition to OSA severity might play differential roles on death rates reported so far. Moreover, other important aspects regarding the relationship between sleep abnormalities and stroke still need to be addressed. For instance, excessive daytime sleepiness has been shown to influence mortality in a large population of elderly patients[12]. This brings up the question whether OSA or other sleep disturbances are on the basis of excessive daytime sleepiness in these cases. It should be noted that in many centers, stroke patients do not routinely undergo sleep studies and although polysomnography has been increasingly more available, OSA has not been sufficiently evaluated.

Evaluating the association between measures such as the BMI and larger NC with mortality in stroke may be clinically useful. The aim of this study was to investigate clinical/demographic factors, sleep disturbances and mortality one-year after ischemic stroke.

Methods

Study design and participants

This is a prospective study of consecutive patients of both genders with diagnosis of acute stroke admitted for in-hospital care. All cases were recruited from a tertiary general hospital in Fortaleza – CE over a period of one year (January to December, 2009). Inclusion criteria were clinical diagnosis of ischemic stroke and age from 45 to 80 years. Exclusion criteria were dementia, loss of the ability to communicate, stupor or coma, cancer, severe lung, hepatic or renal diseases, and/or unwillingness to participate in the study. None of the included patients refused to participate in the initial evaluation. Among 96 stroke patients, seven were lost to follow-up: 89 individuals completed the study. All cases were examined within the first 15 days after stroke. The main outcome was death from any cause during 12 months of follow-up. The protocol was approved by the local research ethics committee and subjects gave informed consent (COMEPE 002.02.07).

Procedures

A purpose-built questionnaire was used to obtain demographic data, habits, relevant family medical history and comorbidities, such as type 2 diabetes and systemic arterial hypertension. Special emphasis was put on the use of alcohol drinking and smoking. Heavy alcohol consumption was considered present if, on a daily basis, more than 4 drinks for men and 3 drinks for women were reported, or on a weekly basis, more than 14 drinks for men and more than 7 for women were consumed[13]. The definition of smoking used in this research was "smoked during one or more days in the last 30 days" prior to the questionnaires, without taking into account the degree of nicotine dependence. Full medical examination was performed on all subjects. Anthropometric measures including the waist-hip ratio, NC (cm) and BMI were obtained. Neck circumference was obtained at a point just below the larynx (Adam's Apple) and perpendicular to the long axis of the neck: it was considered large if > 43 cm in men and > 38 cm in women[14,15]. Body mass index was calculated as the ratio between weight (kg) and squared height (m^2). Ancillary test results were obtained from medical chart review.

High risk of OSA was evaluated by the Berlin questionnaire[16]. Daytime somnolence was assessed by the Epworth Sleepiness Scale (ESS), a questionnaire containing eight items that ask for expectation of dozing in eight hypothetical situations[17]. Epworth Sleepiness Scale score greater than 10 indicates excessive daytime somnolence. Subjective sleep quality was evaluated by the Pittsburgh Sleep Quality Index (PSQI)[18]. Pittsburgh Sleep Quality Index has seven components, each one dealing with a major aspect of sleep: 1) subjective quality of sleep; 2) sleep onset latency; 3) sleep duration; 4) sleep efficiency; 5) presence of sleep disturbances; 6) use of hypnotic-sedative medication; and 7) presence of daytime disturbances, as an indication of daytime alertness. Individuals with total PSQI score of six or more were considered poor sleepers. The Berlin questionnaire, PSQI and Epworth Sleepiness Scale

were directed to symptoms present or not before the stroke event. Head computerized tomography was performed within 7 days of the onset of the stroke in all cases. Stroke outcome was estimated by the Barthel Index (BI)[19] and the modified Rankin Scale (mRS)[20-22] during hospital stay. Stroke outcome, mortality, and occurrence of new vascular events were assessed by a structured telephone interview 12 months later.

Statistical analysis

Data are expressed as absolute values, frequency, mean and standard deviation (SD) values. Student's *t*-test was used to analyze continuous variables and the Mann-Whitney U test to analyze discontinuous variables. Categorical variables were analyzed by Fisher exact test. A forward stepwise multiple regression analysis evaluated how variables were associated with stroke mortality. Variables with $p < 0.2$ and variables historically associated with stroke mortality, such as diabetes and hypertension, were all included as potential predictor variables; a $p < 0.05$ was required for a variable to be retained in the final model. Statistical analysis was performed with the Statistic Package for Social Sciences (SPSS-16) software for Windows. Statistical significance was assumed at $p < 0.05$.

Results

The study group consisted of 89 consecutive patients (mean age = 64.39±8.5), predominantly male (n = 57). Overall, the majority of patients reported family history of cerebrovascular disease (74.2%). Obesity (BMI > 30) was present in only 10 patients (11.2%). Thirty patients had diabetes (33.7%) and 70 had systemic arterial hypertension (78.6%). Hypertension was not related to the presence of diabetes (Fisher's exact test, p = 0.58). Also, hypertension was not related to stroke severity (BI, p = 0.14 and mRS, p = 0.10, Mann-Whitney test). Thirty-one cases were found to have excessive daytime sleepiness (34.8%) and 45 presented poor sleep quality (65.2%). Risk of OSA was present in 52 cases (58.4%). Thirty-one patients were smokers (34.8%) and heavy drinking was detected in 17 (19.1%). Large NC was more frequent in women than in men (Table 1). In women, large NC was present in 23 subjects (71.8%); in men large NC was found in 12 cases (21.0%). Among all cases, large NC was related to high risk of OSA, diabetes and hypertension and reduced smoking (Table 2).

One-year mortality was 8.9 %. Table 3 depicts characteristics of patients according to survival after one year follow-up. Cases that did not survive were older (p = 0.006) and had higher NC (p = 0.02). Other features such as BMI, presence of hypertension or diabetes, quality of sleep, excessive daytime sleepiness and risk of OSA were not significantly different between survivors and non-survivors (Table 3). Multivariate logistic regression analysis, in a model that included hypertension, diabetes and BI, showed that age (p = 0.005) and NC (p = 0.01) were independently associated with one-year mortality.

Discussion

This study shows that among patients with ischemic stroke, NC is an important clinical measure related to the presence of diabetes, hypertension and high risk of OSA. Older age and larger NC were more frequent in non-survivors. In accordance with a previous study, obesity was uncommon in these patients[23]. Also, increased NC was more common in women. In this sample study, smoking was inversely related to larger NC. Based on these findings, it is suggested that future studies should consider between gender differences [24].

The current data confirm the association between OSA and large NC[8, 25]. Recent studies also show that measurement of NC is associated independently with cardiovascular risk[26]. This evidence is of clinical utility considering that NC can be easily obtained in patients with acute stroke. Currently, routine sleep studies of patients with acute stroke are not recommended: however, OSA has been shown an independent predictor of mortality in ischemic stroke[5, 27]. In this study, the Berlin questionnaire was used. It should be noticed that the Berlin questionnaire shows low sensitivity for detecting OSA[28].

It is suggestive that recently, in ischemic stroke, long-term continuous positive airway pressure (CPAP) treatment was associated with a reduction in excess risk of mortality only in cases with moderate to severe OSA[29].

Table 1 – Demographic and clinical characteristics of 89 patients with acute ischemic stroke

Variables	Patients with stroke (n = 89)
Mean age (years)	64.39 (8.51)
Gender (male/female)	57/32 (64%/36%)
Body mass index (kg/m^2)	25.36 (4.05)
Neck circumference (cm)	40.33 (3.72)
History of diabetes	30 (33.7%)
History of hypertension	70 (78.65%)
Smoking	31 (34.83%)
History of drinking	17 (19.1%)
Risk of apnea (Berlin questionnaire)	52 (58.42%)
PSQI, mean (SD)	7.99 (3.7)
ESS, mean (SD)	8.55 (5.85)
Modified Rankin Scale, mean (SD)	2.92 (1.42)
Barthel index, mean (SD)	65.85 (30.1)

PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale.

Table 2 – Demographic and clinical characteristics of 89 patients with ischemic stroke according to the presence of average or increased neck circumference (male > 43 cm and female> 38 cm)

Variables	Average neck circumference n = 54	Increased neck circumference n = 35	p-value
Mean age (years)	64.12 (8.76)	64.79 (8.44)	[a] 0.73
Gender (male/female) (% values)	45/9 (83.3/16.7)	12/23 (34.2/65.8)	[b] 0.000*
Body mass index (kg/m^2)	24.68 (3.45)	26.60 (4.90)	[a] 0.06
Hemoglobin (g/dL)	13.49 (1.34)	13.31 (1.09)	[a] 0.58
Glucose (mg/dL)	142.88 (68.61)	169.90 (80.0)	[a] 0.14
Urea (mg/dL)	39.03 (16.23)	44.65 (20.61)	[a] 0.22
Creatinine (mg/dL)	1.00 (0.45)	1.15 (0.72)	[a] 0.30
History of diabetes	13 (24.07%)	17 (48.57%)	[b] 0.03*
History of hypertension	39 (72.22%)	31 (88.57%)	[b] 0.04*
Smoking	25 (46.29%)	6 (17.14%)	[b] 0.01*
History of drinking	16 (29.62%)	5 (14.28%)	[b] 0.34
High risk of apnea	26 (50.0%)	26 (74.28%)	[b] 0.01*
PSQI, mean (SD)	7.66 (3.93)	8.58 (3.33)	[c] 0.26
ESS, mean (SD)	8.26 (5.65)	9.15 (6.22)	[c] 0.52
Modified Rankin Scale, mean (SD)	2.78 (1.36)	3.15 (1.5)	[c] 0.20
Barthel index, mean (SD)	68.75 (29.17)	57.07 (29.68)	[c] 0.12

PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale. [a] Student's *t*-test; [b] Fisher`s exact test; [c] Mann Whitney; *p < 0.05%.

Table 3 – Clinical and demographic characteristics of patients with ischemic stroke according to survival/non survival after one year (n = 89)

	Survivors n = 81	Non-survivors n = 8	F; p-value
Mean age (years)	63.62 (8.50)	72.25 (2.71)	[a] 8.09; 0.006*
Gender (male/female)	53/28	4/4	[b] 0.74; 0.39
Body mass index (kg/m^2)	25.40 (3.98)	24.94 (5.15)	[a] 0.07; 0.79
Neck circumference (cm)	40.05 (3.62)	43.28 (3.81)	[a] 5.04; 0.02*
History of diabetes	27 (33.3%)	3 (37.5%)	[b] 0.05; 0.81
History of hypertension	64 (79.0%)	6 (75.0%)	[b] 0.05; 0.80
Smoking	28 (34.5%)	3 (37.5%)	[b] 0.03;0.85
History of drinking	15 (18.5%)	2 (25%)	[b] 0.18; 0.83
Risk of apnea (Berlin questionnaire)	48 (59.2%)	5 (62.5)%	[b] 0.009; 0.92
PSQI, mean (SD)	8.03 (3.71)	7.50 (3.88)	[c] 0.11; 0.73
ESS, mean (SD)	8.40 (5.78)	10.0 (6.74)	[c] 0.54;0.46
Modified Rankin Scale, mean (SD)	2.90 (1.41)	3.14 (1.67)	[c] 0.18; 0.66
Barthel index, mean (SD)	65.35 (29.2)	48.57 (37.16)	[c] 2.00; 0.16

PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale. [a] Student's *t*-test; [b] Fisher`s exact test; [c] Mann Whitney; *p < 0.05%.

Neck circumference is considered a marker of central obesity and has been associated not only with sleep apnea but also with increased cardiovascular risk and insulin levels[30]. Future studies using positive pressure therapy might take into account this anthropometric measure in comparison to OSA severity. It is a fact that currently patients with stroke are not routinely screened for OSA. Taken this evidence, we suggest that NC should be considered a relevant measure, in daily clinical practice, in all acute and chronic stroke patients. It is an easily obtainable measure that can guide the need for polysomnography, which is currently considered the gold standard method for diagnosing OSA.

Several studies have shown that associated risk factors such as BMI, hip waist measure, snoring and NC are to be taken as indicative of OSA[31]. In consequence, flow diagrams using anthropometric measures and evaluation of sleepiness have been suggested to improve diagnostic accuracy of OSA[32]. Anthropometric measures such as NC and BMI have been identified as the most important predictors of OSA[8,31]. However, some controversy remains: it has been shown that NC is not associated with OSA[33]. Despite the recognized association between increasing BMI and the severity of OSA, in this small group of ischemic stroke patients increased BMI was present in less than 20% of cases. According to our findings, a previous study has recognized obesity and hypersomnolence to be dissociated from OSA severity in stroke patients[23].

A previous study shows age was an important determinant of mortality in stroke patients [34]. In this sample, the lack of association with usual comorbidities such as hypertension and diabetes can be explained by the fact that this was a small sample. Failure to demonstrate an association between risk of OSA and mortality may be explained by the fact that the Berlin questionnaire identifies the entire severity spectrum of OSA, not separating mild and moderate-severe cases. This makes the NC as an important factor to be considered.

Until recently, the diagnosis of OSA has not been usually included in the evaluation of stroke patients. To this moment, the influence of OSA severity and overnight desaturation in acute cerebral ischemic lesions remains to be determined. Several limitations of this study must be acknowledged. For instance, polysomnography, the gold standard measure for the diagnosis of OSA, was not evaluated. Other aspects are the reduced number of patients in the study which may have led to a failure to associate hypertension with stroke severity. We suggest that in stroke patients, while obesity is frequently absent and not indicative of OSA, a large NC should be more investigated as a potential clinical sign of OSA.

Conclusion

This study shows that sleep abnormalities are frequent in patients with acute ischemic stroke. Obesity is uncommon in these patients. Large NC is related to the presence of sleep apnea, diabetes and hypertension. Also, older age and larger NC were independently associated with one-year mortality.

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