Prevalence of symptoms and risk of sleep apnea in patients with ruptured cerebral aneurysm

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ABSTRACT

الأهداف: تحديد مدى انتشار أعراض ومخاطر انقطاع التنفس أثناء النوم بين المرضى اللذين يعانون من تمزق الأوعية الدموية في الدماغ.

الطريقة: في هذه الدراسة لحالات فردية مقترنة بحالات ضابطة، تم توزيع النسخة العربية لاستبيان برلين للمرضى في مدينة الملك فهد الطبية بالرياض، المملكة العربية السعودية لمصابين بتمزق الأوعية الدموية بين يناير2006م و يوليو 2011م (53 مريض). وتم توزيع استبيان برلين للحالات الضابطة في عيادات الصحة الأولية والتي كانت متطابقة مع الحالات الفردية من ناحية العمر، ومؤشر كتلة الجسم، والجنس (212 حالة).

النتائج: أظهرت الدراسة أن متوسط العمر للمرضى الذين يعانون من تمزق الأوعية الدموية في الدماغ 15.2 ± 50.7 عام، ومتوسط مؤشر كتلة الجسم كان 4.8 ± 27.9،وقد اشتكى 75.5% من الشخير مقارنة ب 46.7% من الحالات الضابطة (p=0.000). ارتفاع ضغط الدم في 67.9% من الحالات مقارنة مع 30.2% من الضابطة (p=0.000). استناداً لاستبيان برلين 60.4% من الحالات تعتبر معرضة بشكل كبير لانقطاع التنفس أثناء النوم مقارنة مع 31.6% من الحالات الضابطة (p=0.000) .

خاتمة: أن معدل انتشار انقطاع التنفس أثناء النوم عال بين المرضى الذين يعانون من تمزق الأوعية الدموية في الدماغ. تقريباً 60% مرضى مصابين بتمزق الأوعية الدموية في الدماغ معرضين بشكل كبير من انقطاع التنفس أثناء النوم وقد يستفيدون من التقييم السليم لعلاج انقطاع التنفس أثناء النوم.

Objectives: To determine the prevalence of symptoms and risk of obstructive sleep apnea (OSA) among patients with ruptured cerebral aneurysms.

Methods: In this case-control study, a validated Arabic version of the Berlin Questionnaire (BQ) was administered to patients admitted to King Fahd Medical City, Riyadh, Saudi Arabia with cerebral aneurysms between January 2006 and July 2011 (n=53). The same questionnaire was administered to a control group comprised of patients attending primary health care clinics who were matched for age, body mass index (BMI), and gender (n=212).

Results: The mean age of patients with ruptured cerebral aneurysms was 50.7 ± 15.2 years, and the mean BMI was 27.9 ± 4.8 kg/m^2. In this group, 75.5% complained of snoring compared with 46.7% of the controls (p=0.000). Hypertension was present in 67.9% of cases compared with 30.2% of the controls (p=0.000). Based on the BQ scores, 60.4% of the cases were considered to be at high risk for OSA compared with 31.6% of the controls (p=0.000).

Conclusion: The prevalence of OSA symptoms among patients with ruptured cerebral aneurysms is very high. Almost 60% of patients with ruptured cerebral aneurysms are at risk for OSA.

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Cerebral aneurysms are relatively common and can lead to significant rates of morbidity and mortality. The prevalence of these common lesions is approximately 2-3% in the adult population.[1,2] The rupture of a cerebral aneurysm with subsequent subarachnoid hemorrhage (SAH) is the most common clinical presentation of this pathology.[3] Increased age, excess weight, geographic location, female gender, smoking, hypertension, excessive use of alcohol, a family history of SAH and diseases such as polycystic kidney disease, and Ehlers-Danlos disease are all risk factors for cerebral aneurysms. A few of these factors are modifiable and can be managed easily in primary care settings.[4-6]

Obstructive sleep apnea (OSA) is a common clinical syndrome in general medical practice. Obstructive sleep apnea is described as cyclic attacks of occlusion or near occlusion of the pharynx during sleep, causing an intermittent hypoxia. Obstructive sleep apnea has been linked to several cardio- and cerebrovascular disorders, including hypertension, myocardial infarction, carotid stenosis, aortic dissection, abdominal aortic aneurysm, and ischemic stroke.[7-10] Moreover, OSA may accelerate atherosclerosis by aggravating key atherogenic factors.[7] Hypertension and atherosclerosis are possible theoretical links between cerebral aneurysms and OSA. Finding an association between OSA and cerebral aneurysms would justify further prospective studies to identify OSA as a modifiable risk factor. We hypothesize that OSA is prevalent among patients with ruptured cerebral aneurysms. Therefore, we designed this study to determine the prevalence of symptoms and risk of OSA among patients with ruptured cerebral aneurysms.

Methods.

Study population. This cross-sectional study included patients who underwent surgical treatment for ruptured cerebral aneurysms between January 2006 and July 2011 at King Fahd Medical City, Riyadh, Saudi Arabia, and who were living independently in the community after their discharge at the time of the study (n=91). Of those patients, 53 (62.2% males) agreed to participate and were included in the study. The control group comprised patients attending primary health care clinics in King Khalid University Hospital, Riyadh, Saudi Arabia who were matched to cases for age, body mass index (BMI), and gender (n=212). Trained doctors and medical students administered a validated Arabic version of the Berlin Questionnaire (BQ) to all participants. The institutional ethics committee approved the study, and informed consent was obtained from all participants.

Berlin Questionnaire. The BQ is a validated questionnaire that assesses the symptoms and features of OSA. The details of the questionnaire have been published previously.[11] The BQ classifies patients as being at high or low risk for OSA. The questionnaire is divided into 3 sections: the first examines the presence and severity of snoring and apnea, the second assesses daytime fatigue, and the third examines the patient's co-morbidities and demographics. Those with positive scores in 2 or 3 of the categories were considered to be at high risk, while a positive score in one or none of the categories was an indication of low risk.[11] The BQ has been reported to predict a respiratory disturbance index (RDI) score of >5/hour with a sensitivity of 0.86, a specificity of 0.77, a positive predictive value of 0.89, and a likelihood ratio of 3.79.[11] The Arabic version of the BQ has been validated previously.[12] The reliability of self-reporting was tested in 30 control subjects for the following factors: age, height, weight, the presence or absence of hypertension, and the calculation of BMI for risk grouping. The self-reported data were comparable to those from medical chart reports. Based on the responses, patients, and controls were assessed as being at high or low risk for OSA. The BQ was administered to the study group after their discharge, and answered by the patients themselves and their bed partners (n=53).

Statistical analysis. Continuous data are expressed as the mean ± SD, and categorical data are expressed in the text and tables as n (%). Continuous variables (age and BMI) were compared using the independent samples t-test, and categorical variables were compared using the chi-square (x^2) test. If the estimated count were less than 5, Fisher's exact test was used. A p-value ≤0.05 was considered to be significant. The Statistical Package for Social Sciences software (SPSS Inc., Chicago, IL, USA) version 16.0 was used for data analysis.

Results.

Table 1 shows the general characteristics of the case and control groups. The mean age of cases was 50.7 ± 15.2 years, and the mean BMI was 27.9 ± 4.8 kg/m^2. The control group had a mean age of 50.2 ± 8.3 years and a mean BMI of 27.8 ± 3.9 kg/m^2. **Table 2** shows the distribution of responses to the questionnaire in both the case and control groups. Among the cases, 75.5% (40 patients) complained of snoring compared with 46.7% (99 subjects) of the control group (p=0.000). Hypertension was present in 67.9% of the cases (36 patients) compared with 30.2% (64 subjects) in the control group (p=0.000). Based on the BQ stratification for risk of OSA, 60.4% of the cases (32 patients) were considered to be at high risk for OSA compared with 31.6% (67 subjects) of the controls (p=0.000).

Table 1 - General characteristics and risk stratification of patients with cerebral aneurysms (CA) and controls.

Characteristics	Patients with CA (n=53)	Controls (n=212)	*P*-value	OR (95% CI)
Age (Years)	50.7 ± 15.2	50.2 ± 8.3	0.766	1.005 (0.975-1.035)
BMI (kg/m^2)	27.9 ± 4.8	27.8 ± 3.9	0.833	1.010 (0.938-1.086)
Gender				
Male	33 (62.3)	131 (61.8)	0.950	1.020 (0.548-1.898)
Female	20 (37.7)	81 (38.2)		
Risk of sleep apnea (according to the Berlin Questionnaire)				
High risk	32 (60.4)	67 (31.6)	0.000	3.298 (1.771-6.142)
Low risk	21 (39.6)	145 (68.4)		

Data are presented as the mean ± SD or n (%), BMI - body mass index, OR - odds ratio, CI - confidence interval

Table 2 - Distribution of the responses to the Berlin Questionnaire in both patients with cerebral aneurysms (CA) and controls.

Responses	Patient with CA (n=53)	Controls (n=212)	*P*-value
Do you snore (yes)	40 (75.5)	99 (46.7)	0.001
Loudness of snoring			0.002
Loud as breathing	4 (10.0)	44 (44.4)	
Loud as talking	19 (47.5)	28 (28.3)	
Louder than talking	12 (30.0)	17 (17.2)	
Very loud	5 (12.5)	10 (10.1)	
Frequency of snoring			
Almost every day	15 (37.5)	31 (31.3)	
3 to 4 times per week	0 (0.0)	20 (20.2)	
1 to 2 times per week	24 (60.0)	25 (25.3)	
1 to 2 times per month	1 (2.5)	23 (23.2)	
Does snoring disturb others?	25 (62.5)	62 (62.6)	0.989
Frequency of apnea			
Never or almost never	45 (84.9)	158 (74.5)	
Almost every day	6 (11.3)	4 (1.9)	
3 to 4 times per week	0 (0.0)	8 (3.8)	
1 to 2 times per week	1 (1.9)	12 (5.7)	
1 to 2 times per month	1 (1.9)	30 (14.2)	
Fatigue upon waking up			
Never or almost never	25 (47.2)	94 (44.3)	
Almost every day	14 (26.4)	43 (20.4)	
3 to 4 times per week	0 (0.0)	17 (8.0)	
1 to 2 times per week	14 (26.4)	31 (14.6)	
1 to 2 times per month	0 (0.0)	27 (12.7)	
Daytime fatigue			
Never or almost never	28 (52.8)	92 (43.4)	
Almost every day	15 (28.3)	40 (18.9)	
3 to 4 times per week	0 (0.0)	15 (7.1)	
1 to 2 times per week	9 (17.0)	34 (16.0)	
1 to 2 times per month	1 (1.9)	31 (14.6)	
Falling asleep while driving/riding a car	13 (24.5)	65 (30.7)	0.381
Frequency of falling sleep during driving/riding a car*			
Almost Every Day	10 (76.9)	13 (20.0)	
3 to 4 times per week	1 (7.7)	8 (12.3)	
1 to 2 times per week	0 (0.0)	10 (15.4)	
1 to 2 times per month	2 (15.4)	34 (52.3)	
Hypertension (yes)	36 (67.9)	64 (30.2)	0.000

*Data presented as percentages n (%)

Discussion. This study explored the association between OSA and ruptured cerebral aneurysms. The study demonstrated a high prevalence of OSA symptoms among a non-obese sample of patients with ruptured cerebral aneurysms. Compared with controls, a significantly higher proportion of ruptured cerebral aneurysm patients were at a high risk for OSA.

The pathological mechanisms that cause cerebral aneurysms are not fully understood. Cigarette smoking, heavy alcohol consumption, family history, gender, age, and, most importantly, hypertension has been found to influence the formation of these lesions.[4,6] Increased blood pressure and hemodynamic stresses are possible mechanisms of aneurysm formation for some of these factors. Vascular remodeling and inflammation are also involved in cerebral aneurysm formation.[13] Obstructive sleep apnea is associated with other mechanisms that could potentially be related to aneurysm formation and increased rupture risk, including endothelial dysfunction,[14] and oxidative stress.[15] Obstructive sleep apnea is characterized by intermittent hypoxia. The short repetitive cycles of hypoxia and re-oxygenation activate different inflammatory processes and release adhesion molecules, pro-inflammatory cytokines, and chemokines, which may result in endothelial injury and dysfunction, leading to atherosclerosis.[16,17] Furthermore, hypertension is one of the serious consequences of OSA. Obstructive sleep apnea was accepted as

a secondary cause of hypertension by the Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.[18] Furthermore, OSA has been newly recognized as the most common condition associated with resistant hypertension.[9] In our study, co-existing hypertension was present in 67.9% of the cases compared with 30.2% of the controls. Previous studies have reported a high prevalence of hypertension among patients with cerebral aneurysms; with a mean prevalence of 43.5%.[19] Hypertension is thus, a strong link between OSA and cerebral aneurysms. Chronic hypertension has been reported to induce focal weakening of the vessel wall through intimal thickening and secondary necrosis of the tunica media.[19] These events could potentially be initiating factors in the development of aneurysms.

Although cerebral aneurysms and abdominal aortic aneurysms (AAAs) result from different pathological mechanisms, previous computational hemodynamics studies have shown that the 2 disorders share similar biomechanical characteristics.[17,20] Recently, a cohort study of 127 patients with AAA who underwent sleep studies,[8] reported that OSA was highly prevalent in this population. The investigators speculated that blood pressure changes in OSA lead to significant shear stresses on vessel walls, which can cause the development and expansion of the aneurysm. This mechanism can be theoretically applied to cases of cerebral aneurysms; however, there is limited evidence to support this explanation.

There are some limitations to our study, and the results must be interpreted within the context of these limitations. As this study was conducted after the condition (ruptured cerebral aneurysm) had been diagnosed, it was impossible to know whether OSA symptoms were present at the time of the diagnosis. Another limitation is the relatively small number of patients with ruptured cerebral aneurysms included in the study. Nevertheless, the primary value of this study is that it provides important information about sleep-disordered breathing in patients with cerebral aneurysms for the first time, and opens the door for further research in this field.

In summary, this study showed that the prevalence of OSA symptoms among patients with ruptured cerebral aneurysm is very high. Almost 60% of patients with ruptured cerebral aneurysms are at risk for OSA. Further prospective studies are needed to confirm the findings of this study. Moreover, as OSA is a risk factor for hypertension and atherosclerosis, future studies should prospectively assess the impact of early detection and treatment of OSA on the incidence of cerebral aneurysm.

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