Coexistence of obstructive sleep apnea worsens the overall outcome of intracranial aneurysm: a pioneer study

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OBJECTIVE Obstructive sleep apnea (OSA) is associated with the progression of abdominal and thoracic aortic aneurysms. However, the role of OSA in the overall outcome of intracranial aneurysms (IAs) has not yet been established. Authors of this report investigated the role of OSA in the overall outcome of IAs.

METHODS Radiological and clinical data on patients (from 2010 through 2015) with confirmed IA were retrospectively reviewed. Significant differences between the OSA and non-OSA groups were determined using a chi-square test. Logistic regression analysis was performed to identify the predictors of an unfavorable IA outcome.

RESULTS Among the 283 patients with confirmed IAs, 45 patients (16%) were positively screened for OSA, a proportion that was significantly higher than the prevalence of OSA in nonaneurysmal neurosurgical patients (4%, p = 0.008). The percentage of patients with hypertension (p = 0.018), a body mass index ≥ 30 kg/m² (p < 0.0001), hyperlipidemia (p = 0.034), diabetes mellitus (p = 0.005), chronic heart disease (CHD; p = 0.024), or prior stroke (p = 0.03) was significantly higher in the OSA group than in the non-OSA group. Similarly, the percentage of wide-necked aneurysms (p = 0.00001) and patients with a poor Hunt and Hess Grade IV–V (p = 0.01) was significantly higher in the OSA group than in the non-OSA group. In addition, the percentage of ruptured aneurysms (p = 0.03) and vasospasms (p = 0.03) was significantly higher in the OSA group. The percentage of patients with poor modified Rankin Scale (mRS) scores (3–6) was significantly higher in the OSA group (p = 0.03). A separate cohort of patients with ruptured IAs showed similar results. In both univariate (p = 0.01) and multivariate (p = 0.04) regression analyses, OSA was identified as an individual predictor of an unfavorable outcome. In addition, hypertension and prior stroke were revealed as predictors of a poor IA outcome.

CONCLUSIONS Complications of IA such as rupture and vasospasm are often the consequence of uncontrolled OSA. Overall outcome (mRS) of IAs is also affected by the co-occurrence of OSA. Therefore, the coexistence of OSA with IA affects the outcome of IAs. Obstructive sleep apnea is a risk factor for a poor outcome in IA patients.

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KEY WORDS obstructive sleep apnea; cerebral aneurysms; comorbidities; rupture; vasospasm; outcome; vascular disorders

The prevalence of intracranial aneurysm (IA) is 2%–10% in the general population. Although cerebral aneurysm is sometimes asymptomatic and an incidental finding, it can rupture and lead to life-threatening conditions such as subarachnoid hemorrhage and stroke. Several factors such as hypertension, smoking, obesity, aneurysm size, and hyperlipidemia can cause the progression and rupture of brain aneurysms. However, previous studies have shown that obstructive sleep apnea (OSA) significantly increases the risk of cardiovascular events such as myocardial infarction and stroke. Severe OSA is directly related to a high risk of cardiovascular events, and treatment of this disease using continuous positive airway pressure (CPAP) has a possible role in reducing the risk. In addition, recent studies have suggested that OSA is an individual risk factor for progression of abdominal and thoracic aortic aneurysms. It causes progression of an aortic aneurysm by provoking endothelial dysfunction via inducing oxidative stress, sympathetic activity, and vascular shear stress. Moreover, insulin resistance, metabolic...
disturbances, and hypercoagulability may be associated with OSA and thus may contribute to cardiovascular disease in these patients. \textsuperscript{39} In the existing literature, there are no data on a potential relationship between OSA and the progression or outcome of IA. In the present study, we addressed the matter by estimating the prevalence of OSA in patients with IA. We also investigated the association of OSA with aneurysm size, rupture rate, vasospasm, and outcome (modified Rankin Scale [mRS] score) in IA.

**Methods**

The present study was performed after obtaining approval from the institutional review board at the LSU Health Sciences Center in Shreveport, Louisiana. It is a retrospective review of the clinical records of patients with symptoms of IA who had presented to the neurology and neurosurgery services. Information related to clinical history, neuroimaging, treatment procedures, and outcomes of patients with confirmed IAs between January 2010 and December 2015 was collected retrospectively by reviewing the medical records and relevant imaging. In addition, information on age, sex, ethnicity, and major risk factors of cerebral aneurysm progression were obtained from the patient charts. Patients with incidental aneurysms were excluded from the study.

**Diagnosis of IA**

Intracranial aneurysm was initially suspected in patients presenting with clinical symptoms such as severe headache, neurological deficits, hemiparesis, ataxia, loss of consciousness, and altered mental status. Thereafter, we confirmed IA by performing either 4-vessel angiography or MR angiography (MRA).

**Diagnosis of OSA**

All patients were screened using the STOP-BANG Sleep Apnea Questionnaire over the telephone. In the questionnaire, patients were asked the following questions: 1) Do you snore loudly (louder than talking or loud enough to be heard through closed doors)? 2) Do you often feel tired, fatigued, or sleepy during the daytime? 3) Has anyone observed that you stop breathing during your sleep? 4) Do you have or are you being treated for high blood pressure? 5) Body mass index > 35 kg/m\(^2\)? 6) Age over 50 years old? 7) Neck circumference > 15.7 inches? and 8) Gender male? Patients scored 1 for each positive answer (possible total score of 8), and those with a score greater than 3 were considered to be at risk for OSA. \textsuperscript{10} Polysomnography (PSG) was used to confirm the diagnosis of OSA.

To determine the prevalence of OSA among nonaneurysmal neurosurgical patients, we reviewed 100 such cases and calculated the percentage of patients with OSA.

**Hunt and Hess Scale**

We graded the patients’ preoperative clinical symptoms using the Hunt and Hess (HH) Scale: Grade 0 = unruptured aneurysm, Grade 1 = asymptomatic or slight headache and neck stiffness, Grade II = moderate to severe headache and neck stiffness, Grade III = drowsy and minimal neurological deficit, Grade IV = stuporous and moderate to severe hemiparesis, and Grade V = coma. \textsuperscript{19,35}

**Modified Rankin Scale**

At the most recent follow-up, we evaluated the postoperative clinical outcome using the mRS: Score 0 = no symptoms, Score 1 = no significant disability, Score 2 = slight disability, Score 3 = moderate disability (needs some help), Score 4 = moderately severe disability (cannot walk without help), Score 5 = bedridden and needs continuous nursing care, and Score 6 = dead. \textsuperscript{38}

**Vasospasm**

Vasospasm was radiologically diagnosed using 4-vessel angiography.

**Follow-Up**

Four-vessel angiography was performed after treatment and annually thereafter. The average duration of clinical follow-up was 31 months (range 3–131 months).

**Statistical Analysis**

The statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) software, version 24.0 (IBM Corp.). A chi-square test was used to determine the significance between the 2 groups (OSA vs non-OSA). Univariate and multivariate regression analyses were performed to identify independent risk factors for an unfavorable outcome after treatment. A p value < 0.05 was considered significant.

**Results**

**Patient Demographics**

Among 283 patients with IA (Fig. 1), 73 (26%) were male and 210 (74%) were female. One hundred seventy patients (60%) were white and 113 (40%) were African American. The median patient age was 58 years (range 17–84 years). At the last follow-up, 45 cases (16%) were positively screened for OSA. Among these positively screened cases, 19 underwent PSG to confirm the diagnosis of OSA. There was no difference in age, sex, and race distribution between the IA patients with OSA and those without OSA (Table 1 and Fig. 2). There was a significant difference (p = 0.008) in the prevalence of OSA between the nonaneurysmal neurosurgical patient population and the patients with cerebral aneurysms (4% vs 15.9%, respectively). In the entire series, there were 20 patients with incidental aneurysms, and among these 20 patients were 2 with OSA. Therefore, among the 303 patients with IAs in the entire series, 47 (15.5%) had OSA. However, there was a similar significant difference in the prevalence of OSA, comorbidities, aneurysm neck size, HH Grade V, vasospasm, and poor outcome (mRS Scores 3–6) between the groups even after including the patients with incidental aneurysms (Supplemental Table 1). We divided the patients according to HH grade and found that 145 (51.2%), 43 (15.1%), 57 (20.1%), 12 (4.2%), 19 (6.7%), and 7 (2.5%) had HH Grade 0, I, II, III, IV, and V clinical symptoms,
respectively. There was a significant difference (p = 0.005) in the prevalence of severe (HH Grade V) cases between the OSA and non-OSA patients with brain aneurysms.

**Comorbidities**

**Hypertension**

Among the 283 patients with IAs, 201 (71%) had hypertension. In the OSA group of 45 patients, 38 (84.4%) had hypertension (Table 1 and Fig. 3B). In the non-OSA group, 163 patients (68%) had hypertension. There was a significant difference in the prevalence of hypertension between these 2 groups (p = 0.018).

**Obesity**

Among the 283 patients, 98 (34.6%) were obese (body mass index ≥ 30 kg/m²). In the OSA group, 37 patients (82.2%) were obese; in the non-OSA group, 61 (25.6%) were obese (Table 1 and Fig. 3A). There was a significant difference in the prevalence of obesity between these 2 groups (p < 0.0001).

**Hyperlipidemia**

Among the 283 patients, 45 (16%) had high lipid levels: 12 cases (26.7%) in the OSA group and 33 cases (14%) in the non-OSA group (Table 1). There was a significant difference in the presence of high lipid levels between these 2 groups (p = 0.034).

**Cardiac Events**

Thirty-eight patients (13.4%) experienced cardiac events: 11 cases (24.4%) in the OSA group and 27 (11.3%) in the non-OSA group (Table 1 and Fig. 3D). Similar to the above factors, there was a significant difference in cardiac events between these 2 groups (p = 0.024).

**Prior Stroke**

Among 283 cases, 56 (20%) cases had prior stroke: 14 cases (31.1%) in the OSA group and 42 cases (17.6%) in the non-OSA group (Table 1 and Fig. 3E). There was a significant difference in prior stroke between these 2 groups (p = 0.03).

**Diabetes Mellitus**

Among all the patients with IAs, 37 (13.1%) had diabetes mellitus (DM): 12 patients (26.7%) in the OSA group and 25 (10.5%) in the non-OSA group (Table 1 and Fig. 3C). There was a significant difference in the prevalence of DM between these 2 groups (p = 0.005).

**Aneurysm Characteristics**

The majority of patients with IAs had aneurysms in the anterior circulation (87%; Table 2 and Fig. 4). There was no significant difference in the distribution of primary locations (anterior vs posterior circulations); however, a significantly higher (p = 0.02) percentage of OSA patients had aneurysms in the anterior communicating artery. Among all the patients with IAs, 83 had multiple aneurysms. A total of 138 patients (48.8%) had ruptured IAs: 27 (60%) in the OSA group and 111 (46.6%) in the non-OSA group. There was a significant difference in the frequency of ruptured aneurysms between these 2 groups (p = 0.03).

**Wide-Necked Aneurysms**

A total of 102 patients (36%) had wide-necked IAs (> 4 mm): 27 (60%) in the OSA group and 75 (31.5%) in the non-OSA group. There was a significant difference in the percentage of wide-necked aneurysms between these 2 groups (p = 0.0001; Table 1 and Fig. 4D).
Overall, 145 patients (51.2%) underwent endovascular treatment for their aneurysms, and 120 (42.4%) underwent microsurgical clipping (Table 2). All of the patients with OSA underwent either coiling (60%) or clipping (40%) of aneurysms. In the non-OSA group, 49.6% and 42.8% of patients underwent coiling and clipping, respectively. The other 7.6% cases were under observation.

### Outcome After Treatment

#### mRS Score

At the last follow-up, the overall median mRS score was 0.00 (Table 3). In the OSA group, the median score was 1.00, and in the non-OSA group, the median score was 0.00. The median mRS score was significantly higher in the OSA group than in the non-OSA group (p = 0.01). Similarly, the percentage of poor mRS scores (3–6) was significantly greater in the OSA group (18%) than in the non-OSA group (8.6%; Fig. 5A), p = 0.03.

#### Residual Aneurysms

Among 195 patients with IAs, the percentage of complete occlusions and residual aneurysms was 88.7% and 11.3%, respectively (Table 3). The percentage of residual aneurysms was considerably higher in the OSA group (17%) than the non-OSA group (10%), but there was no significant difference between the two (p = 0.21; Fig. 5B).

#### Vasospasm

The overall occurrence of vasospasm in patients with ruptured IAs was 20% of the cases overall (Table 3). The occurrence of vasospasm among patients with ruptured IA was significantly higher in the OSA group (30%) than in the non-OSA group (18%, p = 0.03; Fig. 5C).
Ventriculoperitoneal Shunt

Thirty-three patients (12.5%) required placement of a ventriculoperitoneal (VP) shunt. This included 5 OSA cases (11.1%) and 28 non-OSA cases (13%). There was no significant difference in the requirement for a VP shunt between these 2 groups (p = 0.45; Table 3).

Symptomatic Changes and Complications After Treatment

Improvements in clinical symptoms are shown in Table 4. Headache (p < 0.0001) and confusion (p = 0.03) were significantly improved after treatment. Ataxia and loss of consciousness were resolved in all patients with these symptoms. Thirty-three patients (12.4%) developed new hydrocephalus, which was managed with the placement of VP shunts (Table 3). One patient (0.4%) experienced a stroke after treatment. Among 265 patients, 1 patient (0.4%) died after treatment, and this patient was from the OSA group. Eight patients (3%) developed new-onset third cranial nerve palsy, and there was no significant difference in the occurrence of this complication between the OSA and non-OSA groups.

Hospital Length of Stay After Treatment

Among all treated patients, the average length of stay (LOS) was 8.1 days. The mean LOS was 9.5 days in the OSA group and 7.7 days in the non-OSA group (Fig. 5D). There was a trend for an increased LOS in the OSA group, but no significant difference was observed between the groups (p = 0.09).

In this study, we investigated the comorbidities and outcome in ruptured-aneurysm patients with or without OSA (Table 5). The results were similar to those in the overall study population. The prevalence of obesity (OSA 81% vs non-OSA 27%, p < 0.0001), hypertension (OSA 85% vs non-OSA 62%, p = 0.0003), hyperlipidemia (OSA 26% vs non-OSA 12%, p = 0.018), chronic heart disease (CHD; OSA 26% vs non-OSA 9%, p = 0.002), and prior stroke (OSA 26% vs non-OSA 8%, p = 0.001) was significantly higher in the OSA group than in the non-OSA group among the patients with ruptured aneurysms. The percentage of severe clinical symptoms (HH Grade V) was significantly higher in the OSA group (14.8%) than in the non-OSA group (2.7%, p = 0.005). Similarly, the prevalence of an unfavorable clinical outcome (mRS Score 3–6) was significantly higher in the OSA group (33% vs 2.7%, p = 0.0001). The percentage of patients with vasospasm was also higher in the OSA group (30% vs 18%, p = 0.03).

Predictors of Poor Outcome

Logistic regression analysis was performed to identify predictors of a poor outcome in patients with IAs, and the results are shown in Table 6. The following covariates were included in the model: age (> 50 vs < 50 years), sex (male vs female), ethnicity (white vs African American),
number of aneurysms (single vs multiple), location of aneurysm (posterior vs anterior circulation), aneurysm neck size (> 4 vs < 4 mm), obesity (yes vs no), hyperlipidemia (yes vs no), hypertension (yes vs no), DM (yes vs no), CHD (yes vs no), prior stroke (yes vs no), drug abuse (yes vs no), smoking (yes vs no), OSA (yes vs no), HH grade (IV–V vs I–III), treatment type (clipping vs coiling), adjuvant therapy (yes vs no), ruptured aneurysm (yes vs no), and vasospasm (yes vs no). On univariate analysis, hypertension (p = 0.02), smoking (p = 0.002), CHD (p = 0.04), prior stroke (p = 0.02), COPD (p = 0.0001), and chronic obstructive pulmonary disease (COPD) (p = 0.0001) were found to be statistically significant.

### TABLE 2. Aneurysm characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>OSA Group (%)</th>
<th>Non-OSA Group (%)</th>
<th>Total (%)</th>
<th>p Value (OR, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aneurysm location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>40 (88.9%)</td>
<td>206 (86.6%)</td>
<td>246 (86.9%)</td>
<td>0.82 (1.2, 0.47–3.15)</td>
</tr>
<tr>
<td>ACoA</td>
<td>16 (35.6%)</td>
<td>50 (21%)</td>
<td>66 (23.3%)</td>
<td>0.02 (2.1, 1.1–4.20)</td>
</tr>
<tr>
<td>PCoA</td>
<td>6 (13.3%)</td>
<td>53 (22.3%)</td>
<td>59 (20.8%)</td>
<td>0.14 (1.8, 0.84–4.36)</td>
</tr>
<tr>
<td>MCA</td>
<td>8 (17.8%)</td>
<td>38 (16%)</td>
<td>46 (16.2%)</td>
<td>0.85 (1.1, 0.51–2.59)</td>
</tr>
<tr>
<td>ACA</td>
<td>3 (6.7%)</td>
<td>9 (3.8%)</td>
<td>12 (4.2%)</td>
<td>0.53 (1.8, 0.44–8.67)</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>5 (11%)</td>
<td>32 (13.4%)</td>
<td>37 (13.1%)</td>
<td>0.82 (0.82, 0.31–2.12)</td>
</tr>
<tr>
<td>Multiple aneurysms</td>
<td>10 (22%)</td>
<td>73 (30.7%)</td>
<td>83 (29.3%)</td>
<td>0.19 (1.6, 0.80–3.17)</td>
</tr>
<tr>
<td>Aneurysm status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unruptured</td>
<td>18 (40%)</td>
<td>127 (53.4%)</td>
<td>145 (51.2%)</td>
<td></td>
</tr>
<tr>
<td>Ruptured</td>
<td>27 (60%)</td>
<td>111 (46.6%)</td>
<td>138 (48.8%)</td>
<td>0.03 (1.8, CI 1.0–3.2)</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coiling</td>
<td>27 (60%)</td>
<td>118 (49.6%)</td>
<td>145 (51.2%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Clipping</td>
<td>18 (40%)</td>
<td>102 (42.8%)</td>
<td>120 (42.4%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Observation</td>
<td>0 (0%)</td>
<td>18 (7.6%)</td>
<td>18 (6.4%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

ACA = anterior cerebral artery; ACoA = anterior communicating artery; MCA = middle cerebral artery; PCoA = posterior communicating artery. Boldface type indicates statistical significance.
(p = 0.03), and OSA (p = 0.01) were identified as positive predictors of poor outcome. However, on multivariate analysis, hypertension (p = 0.03), smoking (p = 0.002), and OSA (p = 0.04) were identified as positive predictors of a poor outcome. In this series, all other factors did not show any significant relation to poor outcome. However, when we determined the predictors of a poor outcome in the ruptured aneurysm group separately, HH Grade IV and V, in addition to the above-mentioned predictors, was revealed as a predictor of a poor outcome on both univariate (p = 0.03, OR 2.9, 95% CI 1.1–8.52) and multivariate (p = 0.015, OR 4.7, 95% CI 1.35–16.24) analysis.

Discussion

This is the first study to investigate OSA in individuals with IA and determine its potential influence on the outcome of IA in these patients (see Fig. 6 for a schematic of this influence). Our findings revealed a higher prevalence of OSA among patients with IAs than among patients in the nonaneurysmal neurosurgical group. The percentage of patients with hypertension, DM, hyperlipidemia, cardiac events, cerebrovascular accidents, and obesity was significantly higher in the OSA group. Our results also demonstrated that wide-necked aneurysms, IA rupture, vasospasm, and poor outcome were significantly more prevalent in the patients with OSA. It is well established that OSA causes hypertension by stimulating the sympathetic nervous system and altering vascular function. Obstructive sleep apnea causes hyperlipidemia by increasing lipid synthesis and decreasing clearance of lipoproteins. An earlier report suggested a close association between OSA and cardiovascular disease. Research evidence has also suggested that OSA increases the incidence

FIG. 4. Bar graphs (A–C) representing the location of aneurysms in the OSA and non-OSA groups. Bar graphs demonstrating the distribution of wide-necked (D) and ruptured (E) aneurysms and HH Grade V patients (F) between these 2 groups. *p < 0.05 is considered significant. ACom = anterior communicating artery.
of stroke. Therefore, as hyperlipidemia, hypertension, cardiac disease, and cerebral events are comparatively high in patients with OSA, these confounders may have partially contributed to the overall outcome of this study.

**OSA and IA Size**

Recent studies have suggested that OSA plays an important role in the progression or expansion of abdominal and thoracic aortic aneurysms. This expansion of an aneurysm eventually results in aortic aneurysm rupture and poor outcome in patients with IA. In abdominal aortic aneurysms, it is well established that the size of the aneurysm influences rupture risk, mortality, and life expectancy. In addition, on serial MRA, Burns and colleagues observed that the larger brain aneurysms more frequently became enlarged. In the current study, the size of the aneurysm was greater in the OSA group, indicating that OSA may have contributed to enlarging the aneurysm diameter. Similarly, a large aneurysm neck diameter has been shown to enhance the chance of rupture. In the present study, the number of wide-necked aneurysms was higher in the OSA group, further indicating OSA’s role in the progression of IAs.

**OSA and Ruptured IA**

It has been shown that the prevalence of OSA is significantly higher in patients with ruptured IAs (60.4%) than in non-OSA patients (31.6%). Therefore, OSA may cause the rupture of these aneurysms. In the present study, 60% of the patients with OSA had ruptured IAs, whereas 46% of the patients without OSA had ruptured IAs. This finding is in agreement with results in previous studies.

**OSA and Severity of Clinical Symptoms**

The impact of OSA on the severity of clinical symptoms of aortic disease is not definitively proven. However, several studies have suggested that the more severe the OSA, the more grave the aortic aneurysm. In the present study, severe IA clinical symptoms (HH Grade V) occurred more frequently in the OSA group, indicating the role of OSA in the deterioration of patients with cerebral aneurysms. This deterioration could be explained by the increased aneurysm neck size described above as well as the increased aneurysm rupture in patients with OSA. In addition, a higher prevalence of hypertension, DM, CHD, and prior stroke in patients with OSA may have contributed to the deteriorating clinical symptoms.

**OSA and Vasospasms**

Research evidence suggests that OSA is associated with impaired endothelial function and reduced endothelial regeneration. An earlier study showed that there was a clear association between OSA and diminished cerebrovascular dilation. Nitric oxide (NO) levels and the number of endothelial progenitor cells (EPCs) are decreased in patients with OSA. Obstructive sleep apnea increases reactive oxygen species (for example, peroxynitrite) and systemic inflammatory markers (for example, NF-kB), which in

**TABLE 3. Follow-up results among patients with IAs**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OSA Group</th>
<th>Non-OSA Group</th>
<th>Total</th>
<th>p Value (OR, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median mRS score</td>
<td>1.00</td>
<td>0.00</td>
<td>0.00</td>
<td>0.01</td>
</tr>
<tr>
<td>Good (mRS 0–2)</td>
<td>37/45 (82%)</td>
<td>201/220 (91.4%)</td>
<td>238/265 (89.8%)</td>
<td></td>
</tr>
<tr>
<td>Poor (mRS 3–6)</td>
<td>8/45 (18%)</td>
<td>19/220 (8.6%)</td>
<td>27/265 (10%)</td>
<td>0.03 (2.5, 1.0–7.05)</td>
</tr>
<tr>
<td>Radiological FU</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete occlusion</td>
<td>30/36 (83.3%)</td>
<td>143/159 (99.9%)</td>
<td>173/195 (88.7%)</td>
<td></td>
</tr>
<tr>
<td>Residual</td>
<td>6/36 (16.7%)</td>
<td>16/159 (10.1%)</td>
<td>22/195 (11.3%)</td>
<td>0.21 (1.8, 0.74–4.76)</td>
</tr>
<tr>
<td>Vasospasm in patients w/ ruptured aneurysm</td>
<td>8/27 (30%)</td>
<td>20/111 (18%)</td>
<td>28/120 (20.2%)</td>
<td>0.03 (1.95, 0.95–4.04)</td>
</tr>
<tr>
<td>VP shunt</td>
<td>5/45 (11.1%)</td>
<td>28/220 (12.7%)</td>
<td>33/265 (12.4%)</td>
<td>0.45 (1.6, 0.55-5.22)</td>
</tr>
<tr>
<td>Mean LOS (range)</td>
<td>9.5 (1–30)</td>
<td>7.7 (1–29)</td>
<td>8.1 (1–30)</td>
<td>0.09</td>
</tr>
<tr>
<td>Complications</td>
<td>1/45 (2.2%)</td>
<td>0/220 (0%)</td>
<td>1/265 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>5/45 (11%)</td>
<td>28/220 (12.7%)</td>
<td>33/265 (12.4%)</td>
<td>0.72</td>
</tr>
<tr>
<td>New hydrocephalus</td>
<td>1/45 (2.2%)</td>
<td>0/220 (0%)</td>
<td>1/265 (0.4%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Stroke</td>
<td>2/45 (4.4%)</td>
<td>6/220 (2.7%)</td>
<td>8/265 (3%)</td>
<td></td>
</tr>
<tr>
<td>Third CN palsy</td>
<td>1/45 (2.2%)</td>
<td>0/220 (0%)</td>
<td>1/265 (0.4%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Death</td>
<td>1/45 (2.2%)</td>
<td>0/220 (0%)</td>
<td>1/265 (0.4%)</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 4. Preoperative and postoperative symptoms**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preop</th>
<th>Postop</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>283</td>
<td>265</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>221 (78.1%)</td>
<td>66 (24.9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Confusion</td>
<td>21 (7.4%)</td>
<td>3 (1.1%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Ataxia</td>
<td>5 (1.8%)</td>
<td>0 (0%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Hemiparesis</td>
<td>13 (4.6%)</td>
<td>10 (3.8%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Dizziness</td>
<td>21 (7.4%)</td>
<td>13 (4.9%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>5 (1.8%)</td>
<td>0 (0%)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

**Notes:**

- CN = cranial nerve; FU = follow-up; LOS = length of stay in hospital.
- Boldface type indicates statistical significance.
Association of obstructive sleep apnea and intracranial aneurysms

The level of endothelin-1, a vasoconstrictor, is increased in patients with OSA and causes vasospasm and hypertension. Obstructive sleep apnea provokes aneurysm rupture, and after the aneurysm ruptures, cerebral vessels can narrow erratically. It has been shown that treatment with CPAP in OSA reduces endothelin-1 levels and reverses vasoconstriction. In addition, CPAP therapy increases the serum levels of nitrite and nitrate as well as the number of EPCs. In the present study, the percentage of patients with a ruptured aneurysm and vasospasm was significantly higher in the OSA group, and this finding is in agreement with previous study results.

OSA and Clinical Outcome After Treatment in IA Patients

Previous studies have shown that patients with OSA and cerebrovascular disease have poor clinical outcomes including low survivability; however, CPAP treatment reduces the risk of death. Cerebral aneurysm rupture causes subarachnoid hemorrhage that results in a poor outcome in these patients and may require surgical intervention. These patients may need a longer hospital stay, which will increase health care costs. In addition, vasospasm after ruptured cerebral aneurysm can cause ischemic stroke. Results of the present study concur with the findings of previous studies showing a poor outcome in patients with OSA, possibly due to the higher number of ruptured aneurysms and vasospasms in this group.

Therefore, we investigated outcome separately in the patients with ruptured aneurysms. As expected, the percentage of comorbidities, severe clinical symptoms, vasospasm, and poor clinical outcomes significantly varied between the IA patients with and without OSA, but those in the patients with OSA were consistently higher than those in the patients without. These findings suggest the importance of prevention and treatment of uncontrolled OSA in the management of IAs.

Predictors of Poor Outcome

Several factors including age, sex, hypertension, smoking, and aneurysm size and location have been investigated as regards their association with a poor outcome in IAs. Our aim was to determine whether OSA is an individual risk factor for a poor outcome in patients with IA. In both univariate and multivariate analyses, we found for the first time that OSA is an individual risk factor for an unfavorable outcome in IA patients. In previous studies, an age above 50 years has been identified as an individual risk factor for a poor outcome of IA. In our study, although an age above 50 years was an individual risk factor for a ruptured aneurysm, it had no effect on overall outcome. Female sex is another risk factor for a poor outcome in.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OSA Group</th>
<th>Non-OSA Group</th>
<th>p Value (OR, 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases</td>
<td>27</td>
<td>111</td>
<td></td>
</tr>
<tr>
<td>Age in yrs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>57</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>39–70</td>
<td>17–84</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7 (26%)</td>
<td>30 (27%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>20 (74%)</td>
<td>81 (73%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>21 (47%)</td>
<td>57 (51.4%)</td>
<td>0.03 (1.9, 1.05–3.51)</td>
</tr>
<tr>
<td>African American</td>
<td>24 (53%)</td>
<td>54 (48.6%)</td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior circulation</td>
<td>24 (89%)</td>
<td>3 (11%)</td>
<td></td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>97 (87.4%)</td>
<td>14 (12.6%)</td>
<td></td>
</tr>
<tr>
<td>Mean aneurysm size in mm</td>
<td>7.5</td>
<td>6.7</td>
<td>Not significant</td>
</tr>
<tr>
<td>Wide-necked aneurysms (&gt;4 mm)</td>
<td>17 (63%)</td>
<td>28 (25%)</td>
<td>&lt;0.0001 (5.6, 2.95–11.16)</td>
</tr>
<tr>
<td>Severe clinical symptoms (HH Grade V)</td>
<td>4 (14.8%)</td>
<td>3 (2.7%)</td>
<td>0.005 (5.6, CI 1.52–31.55)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTN</td>
<td>23 (85%)</td>
<td>69 (62%)</td>
<td>0.0003 (4.9, 2.25–11.53)</td>
</tr>
<tr>
<td>Obesity</td>
<td>22 (81%)</td>
<td>30 (27%)</td>
<td>&lt;0.0001 (12.1, 5.97–25.68)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>7 (26%)</td>
<td>13 (12%)</td>
<td>0.018 (2.5, 1.15–5.98)</td>
</tr>
<tr>
<td>DM</td>
<td>4 (15%)</td>
<td>13 (12%)</td>
<td>0.67 (1.2, 0.52–3.21)</td>
</tr>
<tr>
<td>CHD</td>
<td>7 (26%)</td>
<td>10 (9%)</td>
<td>0.002 (3.5, 1.5–9.11)</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>7 (26%)</td>
<td>9 (8%)</td>
<td>0.001 (4, 1.64–10.88)</td>
</tr>
<tr>
<td>Poor clinical outcome (mRS Score 3–6)</td>
<td>9 (33%)</td>
<td>11 (9.9%)</td>
<td>0.0001 (4.4, 1.95–10.74)</td>
</tr>
<tr>
<td>Vasospasm</td>
<td>8 (30%)</td>
<td>20 (18%)</td>
<td>0.03 (1.95, 0.95–4.04)</td>
</tr>
</tbody>
</table>

Boldface type indicates statistical significance.
IA patients; however, we could not find any significant difference in sex distribution. Hypertension and smoking are major risk factors for an unfavorable outcome in IA patients. Our findings regarding hypertension and smoking are in complete agreement with the results of earlier studies.

Similarly, the coexistence of CHD and cerebral disease results in an increased likelihood of an unfavorable outcome. In our univariate regression analysis, CHD and prior stroke were identified as risk factors for a poor outcome; however, in our multivariate analysis, there was no significant difference. A larger aneurysm size and an aneurysm location in the posterior circulation also play a role in a poor outcome for IAs.

**Study Limitations**

The present study has several limitations. Firstly, it has an inherent limitation because of its retrospective design.
Secondly, it is a single-institution study with a relatively small volume of cases in the OSA group. Thirdly, although screening for OSA with the STOP-BANG questionnaire is 94%–97% sensitive, half of the patients with OSA in this series did not undergo a PSG study to confirm the OSA. This was a preliminary study, and we did not conduct it in a blinded fashion. Fourthly, as mentioned earlier in Discussion, confounders such as hypertension, obesity, and sex are associated with both IA and OSA (STOP-BANG scale). Therefore, it is possible that these factors may have individually contributed to the overall outcome of the study. Lastly, it is not appropriate to incorporate patients with incidental cerebral aneurysms and ruptured aneurysms in the same analysis, particularly the high percentage of ruptured aneurysms in the OSA group. Therefore, we excluded patients with incidental aneurysms from this study.

Conclusions

In summary, the prevalence of OSA is higher in patients with cerebral aneurysms. Obstructive sleep apnea can increase the prevalence of hypertension, CHD, and prior stroke in these patients. In the presence of OSA, the complications of IA as rupture and vasospasms are also increased. In addition, the overall outcome (mRS) of IAs is affected by the coexistence of OSA. Therefore, co-occurrence of OSA and IA affects the overall outcome of IA and serves as an individual risk factor for a poor outcome. Screening patients with IA for an initial diagnosis of OSA using the STOP-BANG questionnaire is useful. However, a randomized controlled trial in a large volume of patients is warranted to further investigate the effect of OSA in this specific population.

References


**Disclosures**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author Contributions**

Conception and design: Bir, Chernyshev. Acquisition of data: Bir. Analysis and interpretation of data: Bir, Chernyshev. Drafting the article: Bir, Chernyshev. Critically revising the article: Bir, Cuellar, Sun, Guthikonda, Liendo, Minagar, Chernyshev. Reviewed submitted version of manuscript: Nanda, Cuellar, Sun, Guthikonda, Liendo, Minagar, Chernyshev. Approved the final version of the manuscript on behalf of all authors: Nanda. Statistical analysis: Bir, Chernyshev. Administrative/technical/material support: Nanda, Minagar, Chernyshev. Study supervision: Nanda, Bir, Minagar, Chernyshev.

**Supplemental Information**

Online-Only Content

Supplemental material is available with the online version of the article.

Supplemental Table 1. [https://thejns.org/doi/suppl/10.3171/2016.10.JNS162316](https://thejns.org/doi/suppl/10.3171/2016.10.JNS162316)

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