Carotid Artery Wall Thickness in Patients With Obstructive Sleep Apnea Syndrome

Mauro Silvestrini, MD; Barbara Rizzato, MD; Fabio Placidi, PhD; Roberto Baruffaldi, MD; Alberto Bianconi, MD; Marina Diomedi, PhD

Background and Purpose—Epidemiological studies have suggested a pathophysiological link between sleep apnea syndrome and cerebrovascular diseases. The mechanism by which sleep disturbance can affect the predisposition to developing stroke is not clear. The aim of this study was to investigate whether patients with obstructive sleep apnea syndrome have an increase in atherosclerosis indicators at the carotid artery level.

Methods—We included 23 male patients with severe obstructive sleep apnea syndrome (respiratory disturbance index >30). Intima-media thickness and the presence of steno-occlusive lesions in the common carotid arteries were investigated with B-mode high-resolution ultrasonography. Results of the ultrasonographic examination were compared with those of a group of 23 subjects without obstructive sleep apnea syndrome who were matched for age and comorbid factors.

Results—The intima-media thickness of the common carotid arteries of patients with obstructive sleep apnea syndrome was significantly higher ($P<0.0001$) than that of control subjects (1.429±0.34 versus 0.976±0.17 mm).

Conclusions—Results of the present study show that carotid wall thickness is increased in patients with severe sleep apnea syndrome. There is strong evidence that an increase in the thickness of the carotid artery wall is a valid marker of the risk of stroke. For this reason, our finding seems to further strengthen the hypothesis that patients with obstructive sleep apnea syndrome are at risk of developing cerebrovascular diseases regardless of the association with other vascular risk factors. (Stroke. 2002;33:1782-1785.)

Key Words: atherosclerosis ■ carotid arteries ■ risk factors ■ sleep apnea, obstructive ■ ultrasonography, Doppler, duplex

Several studies have demonstrated that a large number of stroke patients suffer from sleep-disordered breathing, and very frequently they present the typical pattern of obstructive sleep apnea syndrome (OSAS).1-3 These findings have suggested that OSAS can be a risk factor for stroke.4 The possible pathophysiological link between OSAS and stroke has not been unequivocally established.5 Stroke could also be interpreted as a cause and not as a consequence of the sleep disorder. The high frequency of the association could be caused by the fact that patients with OSAS very often have conditions predisposing them to vascular diseases. The interpretation of stroke and OSAS as comorbidities is highly probable because OSAS patients very frequently suffer from cardiopathies, obesity, and hypertension, and in some cases they are smokers and alcohol abusers.6-10 Apnea episodes can induce cardiovascular, cerebral hemodynamic, and hemorheologic changes potentially able to trigger stroke in predisposed patients.11,12 Experimental studies have demonstrated that oxygen desaturation accompanying apneic events can promote degenerative changes at the level of the arterial walls.13 This fact suggests that the link between OSAS and stroke could be due, at least in part, to an increase in the progression of the atherosclerosis process at the level of the cerebral arteries. High-resolution B-mode ultrasonography provides a noninvasive method for quantifying subclinical arterial wall thickening and atherosclerosis progression.14,15 Our aim in this study was to compare the results of ultrasonographic examination at the level of the carotid arteries in 2 groups of subjects with and without OSAS who were matched for age and comorbid factors.

Subjects and Methods
During a 12-month period between 2000 and 2001, we included all consecutive male patients fulfilling the criteria for severe OSAS (respiratory disturbance index >30) referred to the outpatient clinic for evaluation of snoring and daytime somnolence. We identified 23 male patients who underwent careful neurological examination and brain CT that gave normal results. In addition, cardiological evaluation, including ECG and transthoracic echocardiography, complete blood work, and a clinical history were obtained from each patient; particular attention was paid to the major vascular risk factors.
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TABLE 1. Polysomnographic Characteristics of Subjects With OSAS and Control Subjects

<table>
<thead>
<tr>
<th></th>
<th>OSAS Subjects</th>
<th>Control Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>ODI</td>
<td>61.87±16.74</td>
<td>5.35±2.64</td>
</tr>
<tr>
<td>RDI</td>
<td>60.87±15.87</td>
<td>4.91±2.31</td>
</tr>
<tr>
<td>Average of lowest SaO2, %</td>
<td>82.78±4.88</td>
<td>92.58±2.31</td>
</tr>
<tr>
<td>Lowest SaO2 point, %</td>
<td>68.49±9.45</td>
<td>91.74±1.54</td>
</tr>
<tr>
<td>Time spent with SaO2 &lt;90%, %</td>
<td>50.35±25.56</td>
<td>0.26±0.45</td>
</tr>
</tbody>
</table>

ODI indicates oxygen desaturation index (number of >4% dips in SaO2 per hour); RDI, respiratory disturbance index (number of apneas and hypopneas per hour of sleep). Values are mean±SD.

IMT was measured at the thickest point, not including plaques, on the near and far walls with a specially designed computer program. CCA wall thickness was defined as the mean of the maximum wall thickness for the near and far walls on both the left and right sides. The subjects were examined by the same sonographer. The possibility of reproducing IMT measurements had previously been checked. The experiment was single blinded because the investigator was kept blind about the clinical characteristics of the recorded subject.

Statistical analysis of polysomnographic parameters was performed by means of a 1-way analysis of variance with group (ie, subjects with and without OSAS) as the between factor. Significance level was accepted at P<0.05.

To compare the ultrasonographic parameters of the 2 groups, a 1-way analysis of variance was used with the groups (ie, subjects with and without OSAS) as the between factor and IMT and plaque index as the dependent factors.

Results

The mean±SD ages of subjects with and without OSAS were 61.65±9.22 and 62.77±5.13 years, respectively. The percentage of risk factors present in both groups was as follows: 22% for smoking (3 subjects in both groups were slight smokers; 2 were heavy smokers), 65% for hypertension (10 subjects in both groups had mild hypertension; 5 had moderate hypertension), 17% for diabetes (3 subjects in both groups had uncomplicated diabetes; 1 had complicated diabetes), and 35% for hyperlipidemia (5 subjects in both groups had mild hyperlipidemia; 3 had severe hyperlipidemia). The mean±SD BMI was 31.25±5.35 kg/m² for subjects with OSAS and 31.67±5.13 kg/m² for subjects without OSAS; 13 subjects in both groups were obese (BMI >30 kg/m²), 5 were overweight (BMI, 25 to 30 kg/m²), and 5 were normal weight (BMI <25 kg/m²). The 2 groups were similar regarding the use of insulin, oral antidiabetic treatment, statins, and different classes of antihypertensive drugs. No patients or control subjects were taking antiplatelet or antithrombotic drugs. At the moment of our observation, the control of hypertension, diabetes, and hyperlipidemia was satisfactory in all subjects.

Table 1 shows mean and SD values of polysomnographic parameters. Total sleep time reported by subjects with and without OSAS was never <6 hours. The percentage of sleep in the supine position was ≈40%. All subjects without OSAS reported good quality of sleep. With regard to polysomnographic parameters, oxygen desaturation index, respiratory disturbance index, average of lowest SaO2 point, lowest SaO2 point, and percentage of time spent with SaO2 <90% were statistically different between groups (F=255.7, P<0.0001, df=1,44; F=279.9, P<0.0001, df=1,44; F=87.8, P<0.0001,
TABLE 2. Individual and Mean Values of CCA IMT and Plaque Index in Subjects With OSAS and Control Subjects

<table>
<thead>
<tr>
<th></th>
<th>IMT</th>
<th>PI</th>
<th>IMT</th>
<th>PI</th>
</tr>
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<tbody>
<tr>
<td>OSAS Subjects</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.993</td>
<td>0</td>
<td>0.972</td>
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<tr>
<td>2</td>
<td>0.778</td>
<td>0</td>
<td>0.881</td>
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<tr>
<td>3</td>
<td>0.969</td>
<td>0</td>
<td>1.151</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>0.947</td>
<td>0</td>
<td>1.032</td>
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</tr>
<tr>
<td>5</td>
<td>1.064</td>
<td>0</td>
<td>0.825</td>
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</tr>
<tr>
<td>6</td>
<td>1.226</td>
<td>1</td>
<td>1.075</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>1.106</td>
<td>0</td>
<td>1.090</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>1.425</td>
<td>0</td>
<td>0.549</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>1.725</td>
<td>1</td>
<td>1.204</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>1.458</td>
<td>0</td>
<td>1.113</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
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<td>0.923</td>
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<td>1.152</td>
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<td>14</td>
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<td>1</td>
<td>0.813</td>
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<tr>
<td>15</td>
<td>2.256</td>
<td>1</td>
<td>0.852</td>
<td>1</td>
</tr>
<tr>
<td>16</td>
<td>1.591</td>
<td>0</td>
<td>1.228</td>
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<td>17</td>
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<tr>
<td>18</td>
<td>1.657</td>
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<tr>
<td>19</td>
<td>1.753</td>
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<tr>
<td>20</td>
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<tr>
<td>21</td>
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<tr>
<td>22</td>
<td>1.534</td>
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<td>0.857</td>
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<tr>
<td>23</td>
<td>1.456</td>
<td>0</td>
<td>0.902</td>
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</tbody>
</table>

Mean ± SD: 1.429 ± 0.34, 0.30 ± 0.56, 0.976 ± 0.17, 0.22 ± 0.42

PI indicates plaque index.

Discussion

The findings of the present study suggest that patients with severe OSAS have an increased predisposition to developing atherosclerotic degeneration at the level of the carotid arteries. This predisposition seems to be independent of the coexistence of classic vascular risk factors. This last aspect is demonstrated by the comparison of the CCA IMT of subjects with and without OSAS who shared a similar vascular risk profile. It should be emphasized that the severity and duration of exposure to some vascular risk factors are very difficult to define exactly. For this reason, we cannot completely rule out the possibility that the difference in CCA IMT can be explained, at least in part, by an imperfect comparison of risk factor severity between OSAS patients and control subjects. However, we were very careful in the recruitment of control subjects to try to obtain a group very similar to that of the patients with OSAS for the vascular risk profile. Thus, particular attention was paid, in subjects with and without OSAS, to clinical histories and medical documentation, including recordings of duration and type of treatment, to obtain the best definition of the severity of each risk factor.

There are many unresolved questions regarding the association between OSAS and cerebrovascular diseases. A matter of controversy is the possibility that the high prevalence of OSAS described in stroke patients can be interpreted as evidence not only that sleep disturbance may increase the risk of stroke but also that cerebrovascular lesions can trigger breathing pattern abnormalities during sleep. This interpretative problem seems to be overcome, at least partially, by the results of prospective investigations showing a direct relationship between an increase in sleep duration and diurnal somnolence, which can be considered markers of OSAS, and the probability of suffering from stroke. Another problem concerns the possibility that the high frequency of the association between stroke and OSAS can be based simply on the fact that both conditions frequently occur in patients with similar cardiovascular risk factors.

An increased IMT at the level of the carotid arteries is a marker of generalized atherosclerosis, and it has been associated with a high risk of myocardial infarction and stroke. An increased IMT at the level of the carotid arteries can promote atherosclerotic changes at the level of the carotid arteries. The mechanism by which OSAS can promote atherosclerosis is not clear. Experimental studies have shown a direct relationship between oxygen desaturation and degenerative changes in the arterial walls. Cardiovascular instability leading to rapid and repeated changes in arterial blood pressure and the continuous changes in blood viscosity that have been described in patients with OSAS possibly constitute a marker of generalized atherosclerosis and it has been associated with a high risk of myocardial infarction and stroke. An increased IMT at the level of the carotid arteries is a marker of generalized atherosclerosis, and it has been associated with a high risk of myocardial infarction and stroke. A matter of controversy is the possibility that the high prevalence of OSAS described in stroke patients can be interpreted as evidence not only that sleep disturbance may increase the risk of stroke but also that cerebrovascular lesions can trigger breathing pattern abnormalities during sleep. This interpretative problem seems to be overcome, at least partially, by the results of prospective investigations showing a direct relationship between an increase in sleep duration and diurnal somnolence, which can be considered markers of OSAS, and the probability of suffering from stroke. Another problem concerns the possibility that the high frequency of the association between stroke and OSAS can be based simply on the fact that both conditions frequently occur in patients with similar cardiovascular risk factors. An increased IMT at the level of the carotid arteries is a marker of generalized atherosclerosis, and it has been associated with a high risk of myocardial infarction and stroke.
explained by the relatively young age of our study population. The presence of steno-occlusive lesions in the carotid arteries is significantly related to older age and to more advanced stages of atherosclerosis. IMT evaluation can be considered more specific for detecting early stages of atherosclerosis. In this study, we included subjects without any symptoms of cardiovascular and cerebrovascular disease. This fact could have contributed to the exclusion of subjects with more advanced atherosclerosis.

In this study, we investigated a group of patients with severe OSAS and without any specific treatment. Moreover, our patients had several associated vascular risk factors. For these reasons, it is not certain that the results of the present investigation can be generalized for subjects with mild OSAS or with a different vascular risk profile. This is probably the major limitation of our study. Further investigations are needed to evaluate the possible link between OSAS severity and the atherosclerosis process and to assess prospectively whether the treatment of OSAS in association with the control of other vascular risk factors positively influences the progression of vessel wall degenerative changes. The ultrasonographic evaluation of CCA IMT is a simple, noninvasive method of investigation that deserves further consideration because it permits definition of the current status of atherosclerosis and, most importantly, is particularly suitable for monitoring its progression.

References

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Stroke. 2002;33:1782-1785
doi: 10.1161/01.STR.000019123.47840.2D
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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