Cigarette smoking as a risk factor for recurrence of aneurysms treated by endosaccular occlusion

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Object. Aneurysms treated by endovascular coil embolization have been associated with coil compaction, and the rate of recanalization has been reported to be as high as 40%. The authors report the first published evidence of a correlation between aneurysm recanalization correlated with a history of cigarette smoking.

Methods. The authors conducted a retrospective chart review of all cases involving patients admitted to their institution from January 1, 2003, to December 31, 2003, for treatment of a cerebral aneurysm. Cases in which patients were treated with coil embolization were reviewed for inclusion. Coil compaction was defined as change in the shape of the coil mass. Aneurysm recanalization was defined as an increase in inflow to the aneurysm in comparison with baseline. The incidence of coil compaction and the relationship with cigarette smoking history were compared in patients with and without recurrence.

Results. A total of 110 patients qualified for inclusion. The odds ratio (OR) for aneurysm recanalization after endosaccular occlusion with respect to history of cigarette smoking was significant for the entire cohort (OR 4.53, 95% confidence interval [CI] 1.95–10.52) and especially for the female cohort (OR 3.72, 95% CI 1.45–9.54). The male cohort demonstrated a trend toward a direct correlation, but the sample size was not large enough for statistical significance (OR 7.50, 95% CI 1.02–55.00).

Conclusions. There was an increased risk of recanalization especially in patients with low-grade subarachnoid hemorrhage who had a history of cigarette smoking. These data suggest a correlation between cigarette smoking and aneurysm recurrence. (DOI: 10.3171/JNS/2008/108/4/0672)

KEY WORDS • aneurysm • coil embolization • recurrence • smoking

Aneurysmal SAH is a devastating disease, with an annual incidence in the US of 1 case per 10,000 people.1,4,10,12,13,15,18,22,23 Published case series have demonstrated a significant association between smoking and increased risk of SAH in the order of a 3- to 6-fold increase in comparison with the nonsmoking population.4,18 The quantity of cigarettes smoked has also been found to have a positive correlation with increased risk of SAH.15 Multiple cases of de novo saccular aneurysm formation in patients followed up for previously treated aneurysms have been correlated with a history of cigarette smoking.16,17

Aneurysms treated by endovascular means with coil embolization have been associated with coil compaction and recanalization requiring retreatment in some patients. The incidence of recanalization has been documented to be anywhere from 12 to 40% in different centers where coil embolization is routinely performed.3,12,15,27 The immediate angiographic results influenced by catheter stability, aneurysm geometry, and neck diameter have been determined to be critical in predicting complete and successful endovascular occlusion.14 To our knowledge, no study documenting a correlation between aneurysm recanalization and history of cigarette smoking history has previously been reported in the literature.

Clinical Materials and Methods

Patient Population and Data Collection

We conducted a retrospective chart review of all the cases involving patients admitted to our institution from January 1, 2003, to December 31, 2003, for treatment of a cerebral aneurysm. After identifying the patients treated by endosaccular occlusion we reviewed their records for data pertaining to their age, their sex, Hunt and Hess grade at presentation (I–IV, because patients assessed as Grade V are not routinely treated at our institution), location of the aneurysm, history of cigarette smoking, and evidence of recanalization or coil compaction on follow-up digital subtraction angiography, computed tomography angiography, and/or magnetic resonance angiography studies. Coil compaction was defined as change in the shape of the coil mass. Aneurysm recanalization was defined as an increase in inflow to the aneurysm in comparison with baseline. The incidence of coil compaction and the relationship with history of cigarette smoking in patients who suffered recurrence

Abbreviations used in this paper: CI = confidence interval; ISAT = International Subarachnoid Aneurysm Trial; OR = odds ratio; SAH = subarachnoid hemorrhage.
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were compared with corresponding data obtained in the control group of patients without recurrence. The correlation between incidence of coil compaction and the correlation with clinical grade at the time of treatment were assessed. We finally looked at the correlation between coil compaction and aneurysm recanalization, aneurysm location, and history of cigarette smoking.

Patients whose charts did not include information about smoking history, patients with fusiform aneurysms and flow-related or nidal arteriovenous malformation aneurysms, patients treated with balloon occlusion, and patients who did not return for follow-up examinations were excluded from the study.

Statistical Analysis

Odds ratios with 95% CIs were calculated to compare the odds of aneurysm recanalization in relation to smoking history. A Mann–Whitney U-test was used to rank the rates of aneurysm recanalization based on the Hunt and Hess grade (I–IV); patients with unruptured aneurysms were considered to have a grade of 0). A t-test was then performed to compare the rates of aneurysm recanalization and the Hunt and Hess grade. Logistic regression analysis was used to control for possible confounding effects of variables related to smoking history and the rate of aneurysm recanalization. All of the probability values reported are two-tailed; probability values ≤ 0.05 were considered to indicate statistical significance. All analyses were performed with the use of SPSS software version 13.0 (SPSS, Inc.).

Results

A total of 110 patients met the criteria for inclusion in the study. Twenty-three (20.9%) of these patients were men and 87 (79.1%) were women. The mean duration of follow-up was 24 months (range 18–30 months). Of the men, 16 (69.6%) had a history of smoking and 7 (30.4%) were nonsmokers. Of the women, 45 (51.7%) had a history of smoking and 42 (48.3%) were nonsmokers.

In the male cohort, 14 patients (60.9%) had evidence of coil compaction and recanalization at follow-up. Twelve of the men with evidence of coil compaction had a previous history of smoking while 2 of the nonsmokers had coil compaction at follow-up imaging.

In the female cohort, 32 women (36.8%) of the 87 had evidence of coil compaction and recanalization during follow-up. Twenty-three women with coil compaction had a history of cigarette smoking; the remaining 9 women with aneurysm regrowth did not have a history of smoking. Two of the women with a history of cigarette smoking who had been lost to follow-up suffered fatal SAH.

Table 1 demonstrates the cohort characteristics and grades at presentation. Table 2 presents the calculated ORs and 95% CIs for comparison of the odds of aneurysm recanalization in relation to history of cigarette smoking, as well as the summary data related to patient classification. The OR for aneurysm recanalization after endovascular occlusion with respect to history of cigarette smoking was significant for the entire cohort (OR 4.53, CI 1.95–10.52) and especially for the female cohort (OR 3.72, CI 1.45–9.54). The male cohort demonstrated a trend toward direct correlation but the sample size was not large enough for statistical significance (OR 7.50, CI 1.02–55.00).

Aneurysm recanalization was correlated with clinical presentation (Hunt and Hess grade) prior to endovascular treatment. In the male cohort, 5 patients underwent treatment of unruptured aneurysms and 2 (40%) of these patients experienced recurrence. Three of the 4 men who presented with Grade I or II had evidence of coil compaction during follow-up. Nine (75%) of the 12 men who presented with Grade III or IV had evidence of coil compaction during follow-up.

In the female cohort, 10 (24.4%) of the 41 patients treated for unruptured aneurysms had recurrences during follow-up. Thirteen (36%) of the 36 women who presented with Grade I or II had evidence of coil compaction. Nine (53%) of the 17 women who presented with Grade III or IV had evidence of coil compaction. These rates of aneurysm recanalization were ranked in relation to the patient’s Hunt and Hess grades at original presentation using the Mann–Whitney U-test. A t-test was performed to determine if a correlation existed between a high Hunt and Hess grade (that is, IV) and aneurysm recanalization. The two-tailed probability value was found to be 0.001, which represents a statistically significant difference based on the established alpha value of 0.05. Hence, a positive correlation was found between Hunt and Hess grade and rate of aneurysm recanalization. The comparison of the recurrence rate in patients who were cigarette smokers and recurrence by Hunt and Hess grade demonstrated a significant trend toward a higher incidence of recanalization in smokers who suffered SAH and had low Hunt and Hess grades at original presentation (Fig 1).

We reviewed the correlation between the location of the treated aneurysm, the aneurysm size, the incidence of coil compaction and recanalization, and the history of smoking. There was no significant correlation between aneurysm location or size and incidence of recanalization. The type of coils, packing density, and use of balloons and stents to assist in the coil embolization procedures were similar in the patients with evidence of coil compaction and in those without.

Discussion

The ISAT concluded that “in patients with a ruptured intracranial aneurysm, for which endovascular coiling and neurosurgical clipping are therapeutic options, the outcome in terms of survival free of disability at 1 year is significantly better with endovascular coiling.” Since the results of the ISAT were reported, the percentage of aneurysms treated by endovascular means has increased significantly, but the durability of the endoscopic coiling procedures has been questioned during the past decade. Remnant regrowth has been observed at the level of the neck of the aneurysm on angiograms obtained during long-term follow-up in cases in which total occlusion was initially achieved with the detachable coils. Not every patient with remnant regrowth and recanalization will require retreatment. In many cases it is possible to retreat the aneurysm with detachable coils with or without placement of a stent for vessel remodeling. In some cases of aneurysm recanalization the patient will require craniotomy and clip ligation or wrapping with or without coil mass extraction. Previous neurosurgical reports of this patient population have shown
good results, although technical challenges were frequently encountered.28

In our group of patients we defined coil compaction as change in the shape of the coil mass. Aneurysm recanalization or regrowth was defined as an increase in inflow to the aneurysm in comparison with baseline. The majority of these patients did not require retreatment because the remnant regrowth was small (< 10%) and stable (no change in follow-up studies). Only 3 (13%) of the 23 men required retreatment. One of these 3 men underwent a craniotomy with clip ligation while the other 2 underwent retreatment with detachable coils. Two of the 3 men requiring retreatment were smokers. Twelve (14%) of the 87 women required retreatment for aneurysm recurrence described as unstable based on > 10% regrowth. Two women required craniotomy and clip ligation and 10 women underwent retreatment with detachable coils. Seven (58%) of the 12 women requiring retreatment were smokers. Two of the women with a history of cigarette smoking had fatal SAH due to aneurysm rupture after treatment by endovascular obliteration.

The increased incidence of aneurysm recanalization after endovascular occlusion of high-grade SAH has been documented in the literature. This increase may be due to the fact that many patients with poor-grade SAH are treated with endovascular techniques based on the severity of their condition as demonstrated by neurological examination and the possibility of medical complications after a prolonged craniotomy regardless of the anatomical characteristics of the aneurysm. Our study showed an increased risk of recanalization especially in low-grade SAH patients with a history of cigarette smoking.

Our sample of patients represents a fraction of the patients treated with endovascular occlusion of cerebral aneurysms during the period reviewed. Many of the patients were excluded from the review due to absence of follow-up, while others were excluded because their aneurysm was fusiform and/or treated with balloon occlusion. A retrospective chart review is not the ideal way to study this patient population because information about smoking history was not included in every chart and we had to exclude patients for whom this information was unavailable. Another limitation of our study is the fact that we did not correlate the aneurysm neck-to-dome ratio in our analysis.

Cigarette smoking has been directly correlated with an increased risk of intracranial aneurysm formation and growth.11,20 Despite this evidence, more than one third of prior smokers continue to use nicotine after suffering an SAH, especially the patients who started smoking at a young age and those with a history of depression or alcohol abuse.2 In our group of patients we did not find a significant trend between smoking cessation after aneurysm treatment and the incidence of aneurysm recurrence, but the sample size was not large enough to demonstrate statistical significance. The pathophysiology of the risk of aneurysm growth and rupture with cigarette smoking has been linked to a deficiency in α1-antitrypsin, which represents the most relevant inhibitor of elastase.6,7,24–26 The increased incidence of recanalization in our cohort may be related to a deficiency in α1-antitrypsin, but pathological studies are required to confirm this.

Despite the extensive evidence of the correlation between aneurysm growth and rupture and cigarette smoking there has been until now no literature evidence documenting a link between cigarette smoking and coil compaction after endovascular aneurysm obliteration. Patients with known cerebral aneurysms should be aggressively coun-

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**TABLE 1**

<table>
<thead>
<tr>
<th>Sex</th>
<th>No. of Pts</th>
<th>No. of Aneurysms</th>
<th>History of Smoking</th>
<th>H &amp; H Grade†</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>M</td>
<td>23</td>
<td>23</td>
<td>16 (69.6)</td>
<td>7 (30.4)</td>
</tr>
<tr>
<td>F</td>
<td>87</td>
<td>91</td>
<td>45 (51.7)</td>
<td>42 (48.3)</td>
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<tr>
<td>total</td>
<td>110</td>
<td>114</td>
<td>61 (55.5)</td>
<td>49 (44.5)</td>
</tr>
</tbody>
</table>

* Unless otherwise specified, values represent numbers of patients (%). Abbreviations: H & H = Hunt and Hess; pts = patients.
† The low H & H grade group includes patients assessed at Grades I–III as well as patients with unruptured aneurysms; the high-grade group includes only patients assessed at Grade IV.

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**TABLE 2**

<table>
<thead>
<tr>
<th>Group &amp; Variable</th>
<th>No. of Pts</th>
<th>History of Smoking</th>
<th>OR (95% CI)</th>
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<tr>
<td></td>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>male cohort</td>
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<tr>
<td>coil compaction</td>
<td>14</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
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<td>9</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>total</td>
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<td>16</td>
<td>7</td>
</tr>
<tr>
<td>female cohort</td>
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<td></td>
<td></td>
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<tr>
<td>coil compaction</td>
<td>32</td>
<td>23</td>
<td>9</td>
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<tr>
<td>no coil compaction</td>
<td>55</td>
<td>22</td>
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</tr>
<tr>
<td>combined cohort</td>
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<tr>
<td>coil compaction</td>
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<td>11</td>
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<tr>
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<td>64</td>
<td>26</td>
<td>38</td>
</tr>
<tr>
<td>total</td>
<td>110</td>
<td>61</td>
<td>49</td>
</tr>
</tbody>
</table>

* Unless otherwise indicated, values represent numbers of patients.
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seled about the risks associated with cigarette smoking. Although coil embolization is a durable and safe procedure, cigarette smoking is an isolated risk factor that significantly increases the risk of recanalization. Attempts are being made to decrease the recanalization rate after endovascular occlusion of aneurysms by vessel remodeling using stents, liquid embolic agents, and endothelial denudation before coil embolization. A prospective trial using the different treatment alternatives in the subgroup of patients who are cigarette smokers is necessary to confirm or refute the evidence demonstrated in our study. Until the results of such a trial are available, patients should be counseled about smoking cessation by primary care physicians, neurosurgeons, neurologists, endovascular surgeons, and anyone involved in their care. This type of study may help in our decision-making ability to determine which type of treatment is better suited for a specific type of aneurysm in a specific type of patient, especially now in an era of new developments in coil embolization technology.

Conclusions

Our patient population revealed an increased risk of recanalization especially in SAH patients who had low Hunt and Hess grades at presentation and had a history of cigarette smoking. Patients with known cerebral aneurysms should be aggressively counseled about the risk of cigarette smoking. Studies evaluating the outcome of cigarette smokers with aneurysms treated by clip ligation and endovascular obliteration are needed.

References


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