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Detection of Microemboli Distal to Cerebral Aneurysms before and after Therapeutic Embolization

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PURPOSE: **Recently developed interventional radiologic techniques, such as embolization with platinum coils, may induce thrombus formation within an aneurysm. The aim of the present study was to investigate the frequency of microemboli distal to untreated and treated cerebral aneurysms.**

***METHODS*: Among a total of 110 patients treated with platinum coil embolization, 35 patients (27 women and eight men, aged 50 ± 10 years) who were at high risk of ischemic complications underwent emboli detection with a transcranial Doppler sonographic monitoring system. All patients were studied before and after coil embolization. The aneurysms were located at the internal carotid artery (n = 14), the basilar artery (n = 10), the middle cerebral artery (n = 7), or the vertebral artery (n = 4). Twenty-nine (85%) of 35 patients were monitored within 6 hours of the completion of treatment.**

***RESULTS*: Microemboli distal to the aneurysm were not detected in any of the patients before treatment. Microemboli were detected in 11 patients (31%) after embolization (mean, 16 ± 21 per hour; range, 1–74 per hour). Microemboli were detected in five (71%) of seven patients in whom ischemic complications occurred after treatment, but in only six (21%) of 28 asymptomatic patients. This difference was statistically significant. The rate of occurrence of emboli in patients with ischemic complications (23 ± 30 emboli per hour) was higher than in asymptomatic patients (10 ± 7 emboli per hour), but this difference was not statistically significant.**

***CONCLUSION*: Microemboli were detected significantly more often in patients who suffered from cerebral ischemia after coil embolization of an intracranial aneurysm. This observation supports the definition of a high-risk group of patients with incomplete embolization or with a large-diameter, broad-neck aneurysm. The early detection of microemboli after treatment may be an indicator for excessive intraaneurysmal thrombus formation and could influence the decision for prophylactic treatment with heparin or aspirin.**

In recent years, the improvement of interventional neuroradiologic techniques has made possible the selective treatment of cerebral aneurysms (1–7). At present, the most frequently used method is embolization of the aneurysmal lumen with platinum coils (3). This material induces the formation of thrombus, which consequently achieves a stable occlusion of the aneurysm (8). During or immediately after treatment, a subset of patients suffer from transient ischemic attacks or cerebral infarctions. The occurrence of ischemic attacks during treatment could be caused by thrombotic material at the tip of the catheter or by air embolism (9). Cerebral ischemia occurring after treatment might be a consequence of thrombus formation within the aneurysm, with subsequent aneurysm-to-distal artery embolism (2–4, 6).

The aims of the present study were to observe the frequency of microemboli distal to treated aneurysms using transcranial Doppler sonography and to investigate the correlation of such emboli with cerebral ischemic events (10). In addition, the effect of heparin on the number of emboli and the occurrence of ischemic complications were evaluated.

Methods

Patients

The study involved 35 patients selected nonconsecutively between April 1995 and March 1996 from a total of 110 pa-

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tients treated with platinum coil embolization. Twenty-seven patients were women and eight were men, with a mean age of 50 ± 10 years (±SD). All patients had at least one angiographically proved intracranial aneurysm, which was not accessible for surgical clipping. Patients were admitted for platinum coil embolization after subarachnoid hemorrhage (n = 23) or because of a cranial nerve palsy (n = 12). Electrolytically detachable platinum coils (Target Therapeutics, Fremont, CA) were used exclusively (2, 3). Most aneurysms were located at the distal segment of the internal carotid artery (n = 14) or at the top of the basilar artery (n = 10). In the remaining cases, the patients had an aneurysm of the middle cerebral artery (n = 7) or the vertebral artery (n = 4).

Risk factors for the development of ischemic complications were based on our experience with 139 patients who were treated with coil embolization during a period of 30 months (11). Transient ischemic complications related to coil embolization occurred in 34 patients, whereas two patients experienced permanent deficits. These complications were strongly related to the presence of a large- or giant-diameter, broad-necked aneurysm or to incomplete occlusion of the aneurysm or prolapse of a coil into the parent vessel.

On the basis of these empirical data, all 35 patients in the current study were at high risk for ischemic complications after treatment. Twenty-six patients harbored large aneurysms (diameter, 15–25 mm), and nine patients harbored giant aneurysms (diameter, >25 mm). Further risk factors included having a broad- necked aneurysm (n = 8) or suffering incomplete embolization (n = 8) or pending coils within the neck of the aneurysm (n = 6). Patients with such embolic sources as atrial fibrillation or stenosis proximal to the aneurysm and patients with severe vasospasm after subarachnoid hemorrhage were excluded from the present study.

Twenty patients (16 women and four men; mean age, 46 ± 12 years) with small aneurysms (diameter, <15 mm) and without additional risk factors as described above served as a control group. The aneurysms were located in the internal carotid artery (n = 7), the basilar artery (n = 8), the middle cerebral artery (n = 2), the anterior cerebral artery (n = 2), and the vertebral artery (n = 1). The mean diameter of the aneurysms was 9.5 ± 3 mm (±SD).

Emboli Detection

Emboli detection was performed distal to the aneurysm before and after coil embolization using a bilateral transcranial Doppler sonographic monitoring system (MultidopX, DWL, Sipplingen, Germany) combined with an automatic emboli recognition system using a neural network (STAC, Erkrath, Germany) (12). The vessels of interest were insonated through the temporal bone window with a monitoring device that fixed the two probes. In patients with aneurysms of the vertebral or basilar arteries, the sample volumes were located on the precommunicating segments of both posterior cerebral arteries. In patients with cavernosal internal carotid artery aneurysms, the most distal segment of the internal carotid artery (C1 segment) was monitored. Aneurysms of the proximal middle cerebral artery were investigated by focusing the sample volume on a distal middle cerebral artery at a depth of 35 to 40 mm. After identifying the vessel distal to the aneurysm and adjusting the probe, the gain was reduced to produce a homogeneous background signal. All embolic signals were stored on a digital audiotape and were additionally analyzed audiovisually by two independent, experienced interpreters. To rule out possible biases, both investigators were blinded to ischemic complications, and the two neurologists who performed the neurologic examinations were blinded to the results of emboli detection. Standard criteria were used to differentiate emboli from artifactual signals; that is, emboli were distinguished from artifacts both by their acoustic qualities and the increase in intensity detected on-line and by their characteristic spectral distribution in off-line analysis (13, 14). The mean duration of monitoring was 28 ± 8 minutes. The mean interval between treatment and detection of emboli was 14 ± 25 hours, but 29 (83%) of 35 patients were monitored within 6 hours of the completion of coil embolization. Most patients received 3 to 10,000 U of heparin intravenously during embolization, the dosage being dependent on the duration of treatment. At completion of embolization, the partial thromboplastin time was elevated to twice the normal value. Five patients received 3 × 5000 U of heparin subcutaneously, because they had an additional untreated cerebral aneurysm. Patients in whom embolic signals were detected distal to the aneurysms were followed up by daily monitoring until these signals disappeared.

Statistical analysis of differences between subgroups was performed using Fisher's exact test and the Wilcoxon rank sum test.

Results

No embolic signals were observed during emboli detection performed before coil embolization. After treatment, emboli detection was positive in 11 (31%) of 35 patients, with from one to 74 microemboli detected per hour distally to the aneurysm (see Table). The mean rate of occurrence of emboli was 16 ± 21 emboli per hour. Twenty percent of patients experienced cerebral ischemic events after coil embolization; that is, six patients had transient ischemic attacks, and one patient suffered an ischemic infarction. Microemboli were detected in five (71%) of seven patients with ischemic complications (see Table), but in only six (21%) of the remaining 28 asymptomatic patients. This difference was statistically significant (Fisher's exact test, $P < .03$). The rate of occurrence of emboli in patients with ischemic complications (23 ± 30 emboli per hour) was higher than in asymptomatic patients (10 ± 7 emboli per hour), but this difference was not statistically significant (Wilcoxon rank sum test, $P = .84$). In four (57%) of seven symptomatic patients, the detection of emboli (within 0.5 to 5 hours after treatment) revealed the presence of microemboli before the ischemic complications occurred. No significant differences were observed for microemboli detection or for the onset of cerebral ischemic events in terms of the different locations of the investigated aneurysms (see Table). The sample was too small to perform a detailed evaluation of single risk factors, such as having a broad-necked aneurysm or incomplete occlusion of the aneurysm.

The results of emboli detection in 30 patients who received high-dose heparin after treatment (partial thromboplastin time, 2 × normal value) did not differ from those of the five patients who received heparin subcutaneously (3 × 5000 U) (see Table). Follow-up monitoring of patients with embolic signals showed these signals to disappear in 10 patients within 1 to 7 days (mean, 3 ± 2.4 days [SD]). An increasing rate of occurrence of emboli (up to 122 embolic signals) was found in one patient during the 18 days after therapeutic embolization (patient 4; see Table). In this patient, the peak value decreased to 14 emboli per hour after a switch from heparin to aspirin (300 mg/day).

Embolic signals were not detected in the 20 patients in the control group who were monitored within 7 ± 4 hours (±SD) after coil embolization for

Emboli detection in 35 patients after coil embolization of intracranial aneurysms

Patient*	Site of Aneurysm	Heparin (IV)	Time Interval	Emboli/hour	Cerebral Ischemia	Risk Factor for Ischemic Complications
1	ICA	+	5	1	TIA	Prolapsing coil
2	BAS	+	1.5	3	TIA	Incomplete embolization
3	MCA	+	0.5	15	TIA	Giant aneurysm
4	ICA	+	92	74	TIA	Incomplete embolization, giant aneurysm
5	ICA	+	1	24	TIA	Large aneurysm
6	BAS	+	3.5		TIA	Large aneurysm
7	BAS	+	90		Stroke	Giant aneurysm
8	ICA	−	71	3		Incomplete embolization
9	MCA	+	7	5		Broad aneurysmal neck
10	BAS	+	70	8		Giant aneurysm
11	VA	+	0.5	12		Incomplete embolization
12	BAS	+	1.5	12		Antiphospholipid syndrome
13	ICA	+	5	23		Incomplete embolization, giant aneurysm

* Patients 14–35: ICA (n = 9), BAS (n = 5), MCA (n = 5), VA (n = 3); heparin + (n = 18), heparin − (n = 4); time interval: 6 ± 5 hours (± SD); emboli/hour (n = o); − cerebral ischemia (n = 0); risk factors for ischemic complication (n = 0).

Note.—ICA, internal carotid artery; MCA, middle cerebral artery; BAS, basilar artery; VA, vertebral artery; PTT, partial thromboplastin time; TIA, transient ischemic attack.

30 ± 11 minutes (±SD). No patient in this group suffered cerebral ischemia during or after coil embolization.

Discussion

Coil Embolization

Significant advances have been made during the past decade with the use of endovascular techniques in the treatment of patients with intracranial aneurysms (1–7). In the case of aneurysms of the posterior circulation and cavernosal internal carotid artery aneurysms, the effectiveness of these techniques rivals those of open surgical treatment (6). Morbidity associated with this treatment is caused mostly by distal aneurysm-to-artery embolism and has been reported with rates from 2.5% to 14% (2–4, 6, 15, 16). Using empirical data, we studied 35 patients from a total of 110 patients treated with platinum coil embolization who belonged to a high-risk group for the development of ischemic complications. All patients harbored large- or giant-diameter, broad-necked aneurysms or had incomplete embolization or pending coils within the lumen of the parent vessel.

Emboli Detection

Results of a histologic study have shown undifferentiated thrombus formation within the aneurysm as a potential embolic source (8). The usefulness of transcranial emboli detection during surgical procedures, such as heart surgery (17) and carotid endarterectomy (18, 19), has been described previously. To our knowledge, this is the first study of emboli detection after endovascular treatment of cerebral aneurysms in which the rate of occurrence of emboli has been compared with possible ischemic complications in high-risk patients. The findings of the present study show that the occurrence of embolic signals distal to the aneurysm is significantly more frequent in patients with ischemic complications after coil embolization than in asymptomatic patients. The rate of occurrence of emboli itself was not a marker for the development of ischemic complications, because the difference in the number of emboli found in symptomatic patients as compared with the number found in asymptomatic patients was not statistically significant. Although no significant differences were observed for microemboli detection in terms of the different locations of the investigated aneurysms, this could be a result of the small number of patients investigated. The detection of microemboli may reflect excessive thrombus formation within the aneurysm, with subsequent aneurysm-to-distal artery embolism. The presence of emboli immediately after coil embolization might signal that the patient is at high-risk for ischemic complications, because embolic signals were detected in 57% of symptomatic patients before cerebral ischemia occurred.

Prevention of Complications

High-dose intravenous heparin applied after coil embolization did not prevent cerebral ischemic complications and did not significantly influence the rate of occurrence of emboli (6). The slight influence of anticoagulants on the rate at which emboli were detected by transcranial Doppler sonography has been described previously for mechanical heart valves (20) and atrial fibrillation (21). Possibly, early intravenous treatment with aspirin is more effective in preventing cerebral ischemic events after platinum coil embolization.

Conclusion

The present study supports the hypothesis that detection of emboli may be able to identify patients who are at high risk of ischemic complications after coil embolization. A second study has been initiated at our hospital to evaluate the effect of early intravenous administration of aspirin in preventing cerebral ischemia after coil embolization.

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