Frequency of thromboembolic events associated with endovascular aneurysm treatment: retrospective case series

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Object. There is little evidence addressing whether procedures requiring adjunctive devices lead to an increased frequency of thromboembolic complications. The authors report their experience with 155 aneurysms treated with and without adjunctive devices.

Methods. The authors retrospectively reviewed their last 155 aneurysm coil placement procedures. The patients’ records were reviewed for the following phenomena: 1) evidence of procedure-related thrombus formation; 2) clinical evidence of stroke; and 3) the presence of acute ischemia in the treated vascular territory on diffusion-weighted (DW) imaging.

Results. Of the 155 aneurysms treated in 132 patients, 66 were treated with coils only, 45 had stent-assisted coil placement, 33 underwent balloon remodeling, and in 11 stents were placed after balloon remodeling. Small DW imaging abnormalities were present in the treated vascular territory in 24% of cases (37 lesions). Specifically, 21 (32%) of 66 lesions in the coil-treated group, 6 (13%) of 45 in the stent-assisted coil treatment group, 8 (24%) of 33 in the balloon remodeling group, and 2 (18%) of 11 in the balloon and stent group showed DW imaging positivity. Furthermore, 25 (68%) of the 37 cases that were positive on DW imaging occurred in patients presenting with subarachnoid hemorrhage (SAH). Clinically evident stroke or transient ischemic attack was present in 10 (27%) of 37 cases, with 70% occurring in patients presenting with SAH.

Conclusions. Use of adjunctive devices in treating aneurysms does not appear to increase the frequency of embolic or ischemic events. The presence of DW imaging abnormalities and clinically evident stroke was actually less frequent when adjunctive devices were used and in electively treated cases. This was probably related to perioperative antiplatelet medical management. (DOI: 10.3171/JNS/2008/108/6/1095)

Key Words • aneurysm • brain • endovascular procedure • stroke • thromboembolic complication

Endovascular coil embolization procedures have become an accepted method by which cerebral aneurysms can be repaired. The indications for treatment of aneurysms have expanded as new techniques and adjunctive devices are used. Guglielmi detachable coils were initially developed in 1991. The stent and coil technique was later described by Geremia et al. in 1994. The use of balloon remodeling was described by Moret et al. in 1997. These techniques have proven to be effective, at least in the short term, for aneurysm repair.

The safety and efficacy of coil insertion procedures has been studied fairly rigorously, albeit without the benefit of long-term follow-up, as compared with the “gold standard” of surgical clipping of aneurysms. The major complications of endovascular procedures are thromboembolic events. Thromboembolic complications can manifest as the following phenomena: 1) thrombus formation seen during the procedure; 2) clinically recognized ischemia on neurological evaluation, which can be a TIA or permanent ischemic infarction; or 3) “silent ischemia,” as represented by DW abnormalities on MR imaging (Fig. 1).

There is a fairly broad range of “silent ischemia” reported in the literature. Case series have demonstrated a frequency as high as 43–61%. Clinical evidence of stroke (TIAs and ischemic infarcts) can range from 3.8 to 40% of cases. However, none of these studies focused on the frequency of thromboembolic complications related to the use of adjunctive devices in aneurysm treatment.

This study was done to evaluate the frequency of thromboembolic events associated with coil insertion for treatment of aneurysms in the following situations: coil treatment only, stent placement and coil insertion, balloon remodeling, and balloon remodeling with stent placement. Our hypothesis was that the use of adjunctive devices increases the frequency of thromboembolic complications. This study represents a retrospective case series in which we evaluated all saccular aneurysms that had been treated endovascularly over the last 2 years at our institution.

Abbreviations used in this paper: DW = diffusion-weighted; MR = magnetic resonance; SAH = subarachnoid hemorrhage; TIA = transient ischemic attack.
Clinical Materials and Methods

Patient Population

After institutional review board approval, we retrospectively reviewed all aneurysm cases treated with coil insertion in the last 2 years. This consisted of 193 aneurysm coil treatment procedures in 158 patients. Thirty-eight of these procedures were not included due to the absence of a postprocedure MR image, leaving 155 cases in 132 patients. The patients’ demographic characteristics were documented and records reviewed for abnormalities on DW imaging seen on postprocedure MR images, intraoperative thrombus formation, clinical signs of stroke, and elective as opposed to SAH presentation. The aneurysm size was documented from the operative notes or preoperative computed tomography angiograms.

Of the 155 aneurysms in 132 patients, 66 (43%) were treated with coils, 45 (29%) had stent-assisted coil insertion, 33 (21%) underwent balloon remodeling, and in 11 (7%) stents were placed after balloon remodeling. There were 111 (72%) anterior circulation aneurysms and 44 (28%) of the lesions were located in the posterior circulation. There were 91 female and 41 male patients, and their mean age was 54 years (standard deviation 15 years, range 10–85 years of age). The mean aneurysm size was 7.5 mm (standard deviation 4.7 mm). Sixty-two (40%) of the aneurysms were found in patients with SAH, and 93 (60%) were treated electively.

All patients treated for aneurysms in our institution undergo MR imaging within 2 weeks of treatment, but the majority undergo imaging within 3 days of treatment for a baseline comparison. Postprocedure MR images were reviewed by an independent neuroradiologist for evidence of acute ischemia, which is seen as areas of restricted diffusion on DW imaging in the treated vascular territory. The DW imaging restriction was verified by assessing associated T2 changes. An example of positive DW imaging restriction changes occurring in a treated vascular territory includes a right middle cerebral artery aneurysm treatment with corresponding right frontal lobe DW imaging changes. The DW imaging abnormalities were considered to be incidental if they occurred outside the treated vascular territory.

We also reviewed the operative records for cases in which patients developed intra procedural thrombus requiring intra arterial thrombolysis administration. Patients who showed evidence of thrombus formation during the procedure received intra arterial thrombolysis with the intra arterial anti platelet agent abciximab (Reopro).

The records of patients found to have DW imaging changes or who required intra arterial thrombolysis were further reviewed for evidence of a clinically significant stroke; this is defined as any neurological change or loss of function corresponding to the territory in which DW imaging changes are seen. These can represent TIAs, if resolution occurred within 24 hours, or permanent infarction if the neurological deficit remained for longer than 24 hours. Two examples of this may include a dominant middle cerebral artery territory DW imaging change with evidence of transient aphasia, or right anterior cerebral artery territory DW imaging changes with permanent left lower extremity weakness.

All endovascular procedures were performed after endotracheally induced general anesthesia with sterile operating conditions. The anticoagulation protocol for treatment of aneurysms differs depending on the presentation; that is, whether lesions are ruptured or unruptured. In unruptured aneurysms, the patient is started on heparin therapy to an activated clotting time of at least twice baseline after arterial access is obtained in the femoral artery. Patients who are candidates for stent insertion are placed on a regimen of 75 mg clopidogrel and 325 mg aspirin at least 5 days prior to the surgery. Treatment with clopidogrel is then continued for 3 months and aspirin is continued indefinitely. For patients with a ruptured aneurysm, no heparin is given until blood flow is altered in the aneurysm after the placement of 1–2 coils. If the aneurysm requires balloon remodeling, the patient receives heparin prior to inflation of the balloon. In general, we do not administer anti platelet medications to patients with ruptured aneurysms, and therefore do not use stents unless necessary.

Statistical analyses assessing the relationship between baseline variables and outcomes were performed using logistic regression analysis with robust standard errors to account for multiple procedures within subjects. Statistical significance was defined as a probability value of $p < 0.05$.

Results

Overall, 24% of the cases (37 of 155) showed DW imaging abnormalities within the treated vascular territory. These were seen in 21 (32%) of 66 in the “coil-only” group,
6 (13%) of 45 in the stent-assisted coil insertion group, 8 (24%) of 33 in the balloon remodeling group, and 2 (18%) of 11 in the balloon remodeling and stent placement group (Fig. 2). The frequency of DW imaging change in the procedure groups was not significantly different (p = 0.17). Diffusion-weighted imaging abnormalities were seen incidentally in other vascular territories in 6% of procedures.

Restricted DW imaging changes were present in 25 (40%) of 62 cases presenting with SAH and only 12 (13%) of 93 electively treated aneurysms. Logistic regression analysis showed a significant difference in DW imaging frequency between groups based on presentation (p < 0.001). In cases presenting with SAH, DW imaging abnormalities were present in 19 (45%) of 42 coil-only procedures and 6 (43%) of 14 in the balloon remodeling group. No DW imaging abnormalities were present in the coil- and stent-treated group (4 procedures) or in the balloon remodeling and stent placement group (2 procedures). There was a statistically significant difference between patients with and without stent placement (p = 0.034). In cases presenting for elective aneurysm treatment, DW imaging abnormalities were present in 2 (8%) of 24 coil-only procedures, in 6 (15%) of 41 coil insertion and stent placement procedures, in 2 (11%) of 19 balloon remodeling procedures, and in 2 (22%) of 9 of the balloon remodeling and stent placement procedures (Fig. 3). There was no significant difference between procedure types among patients with elective presentation (p = 0.77).

There was clinical evidence of stroke or TIA in 10 (27%) of 37 patients with DW imaging abnormalities. Seven of these 10 patients presented with SAH. Five patients developed symptoms of TIA, and 5 had persistent deficits. Only 1 patient received intraarterial thrombolysis; this individual also developed a permanent neurological deficit related to an ischemic infarct. However, we were unable to assess 11 of these 37 patients adequately because of the underlying severity of their neurological compromise or inadequate documentation.

Intraprocedural thrombus requiring treatment occurred in 10 (6.5%) of 155 cases. This was seen in 6 (10%) of the 60 coil-only cases, in 2 (4.4%) of 45 coil- and stent-treated cases, in 1 (3%) of 33 balloon remodeling cases, and in 1 (9.1%) of 11 balloon remodeling and stent insertion cases. Seven (70%) of these 10 patients presented with SAH. Of these patients, only 4 of 10 developed DW imaging abnormalities, and 1 manifested as a clinically significant stroke.

**Discussion**

The evidence presented in our report does not support the hypothesis that embolization of aneurysms by using adjunctive devices is more likely to increase the frequency of thromboembolic complications within the treated vessel territory. Rather, the likelihood of DW imaging positivity was far greater in aneurysms treated acutely for SAH (40%) than those treated electively (13%). This has also been observed in a recent study by Cronqvist et al. We
found that positive changes within the treated vessel territory were present on DW imaging in 37 (24%) of the 155 aneurysm cases. Furthermore, the greatest numbers of positive results on DW imaging were in patients presenting with SAH and undergoing standard coil embolization without an adjunctive device (45%). Thrombus formation also followed a similar pattern: 70% of patients in whom thrombus developed presented with SAH. Although DW imaging changes were present in 24% of the aneurysms treated, only 8.4% resulted in a clinically evident stroke. None of the patients who required thrombolysis developed clinical evidence for stroke.

Other authors have published the following frequency rates of embolic complications with the use of adjunctive devices. Albayram et al. reported a 20% frequency of DW imaging changes, with balloon-assisted coil embolization performed in 20 cases. This study did not make a clear distinction between SAH and elective presentation, and all patients were treated with the same anticoagulation regimen. The frequency of DW imaging changes was thought to be related to the number of times that the catheter was repositioned. Cottier et al. performed angiographic demonstration of thromboembolic complications in 4% of 49 cases in which balloon-assisted coil embolization was used. Cronqvist et al. performed a prospective study in which they looked at the frequency of DW imaging changes in 40 patients (14 with SAH and 26 with elective procedures) and did find an association with the remodeling technique as well as aneurysm neck size. Soeda et al. reported a 61% frequency of DW imaging changes on 79 electively treated aneurysms. In 20% of treated patients, neurological deterioration developed. These authors also compared the use of balloon assistance to coil-only embolization, finding that there was a statistically significant association between balloon assistance and development of DW imaging changes. A recently completed study by van Rooij et al., evaluating 681 patients treated with ruptured aneurysms demonstrated a frequency of 4.6% of clinically significant thromboembolic events. Balloon assistance was found to be the only risk factor for development of complications. Nevertheless, the study did not compare this to any other procedure vari-

FIG. 3. Bar graph showing the percentage of patients with DW imaging abnormalities as a function of procedure type and presentation. Only patients with DW imaging abnormalities related to the procedure are represented in this graph.
Frequency of stroke related to endovascular aneurysm treatment

There are several limitations to this study. First, this is a retrospective study. Second, there are no preprocedure MR images for comparison. This could result in an artificially high rate of positivity on DW imaging. This is important because there is some evidence that aneurysms alone can cause thromboembolic phenomena. Additionally, patients with SAH may also have DW imaging changes, although these changes are often widespread in the cerebral cortex and tend to be associated with high-grade SAH (World Federation of Neurosurgical Societies Grade IV or V). The clinically evident strokes were determined by chart review. A much stronger method would have been formal pre- and postprocedure assessments performed using the National Institutes of Health Stroke Scale. Another limitation to this study is the fact that patients who have SAH, especially those in higher grades, are very difficult to evaluate for clinical signs of stroke. Also, we incorporated all of our treated patients into this study except for those in whom MR images were not available. The patients who did not undergo follow-up imaging were, for the most part, too unstable or had other considerations, such as hardware that precluded MR imaging. Nonetheless, this would have only strengthened the data supporting the hypothesis that urgently treated aneurysms were associated with higher positivity rates on DW imaging and that the use of adjunctive devices did not increase the rate of DW imaging positivity. Finally, the limited number of patients in the electively treated subgroup precludes meaningful statistical comparison of the cases by procedure, although there is a trend toward recognizing that procedures that include the use of stents have a higher frequency of DW imaging change. It would be important in the future to compile more of these cases and analyze this group.

Clinical evidence of infarction is relatively rare compared with DW imaging changes: 8.4% compared with 24%. Some authors have proposed using DW imaging data to help evaluate procedures and to improve safety. Our data support the contention that DW imaging changes do not translate into a clinically meaningful measure. Furthermore, endovascular treatment of aneurysms does not result in a high frequency of clinically relevant thromboembolic events; these were found to occur in only 8.4% of cases.

Conclusions

Use of adjunctive devices in treating aneurysms does not appear to increase the frequency of thromboembolic events. The presence of DW imaging abnormalities and clinically evident stroke was actually less in the following situations: 1) when adjunctive devices were used; and 2) in electively treated cases. This was probably related to perioperative antithrombotic medical management. Finally, the presence of DW imaging abnormalities does not necessarily translate into the presence of a clinically apparent stroke.

Disclosure

Dr. Turk receives research support from and is a consultant for Boston Scientific; Dr. Niemann is a consultant for ev3, Inc. (formerly MTI), Cordis, and Boston Scientific; Dr. Aagard-Kienitz is a consultant for Micrus Corp. (however, as of January 1, 2006, she has not accepted honoraria of any type), and she also owns Terumo Corp. stock, which is not traded in the US. Dr. Brooks, Mrs. Pulfer, and Dr. Cook have no financial disclosures to make.

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