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K.F. Layton, H.J. Cloft, L.A. Gray, D.A. Lewis and D.F. Kallmes

This information is current as of April 24, 2024.

AJNR Am J Neuroradiol 2007, 28 (6) 1172-1175
doi: https://doi.org/10.3174/ajnr.A0490
http://www.ajnr.org/content/28/6/1172

ORIGINAL RESEARCH

Balloon-Assisted Coiling of Intracranial Aneurysms: Evaluation of Local Thrombus Formation and Symptomatic Thromboembolic Complications

K.F. Layton
H.J. Cloft
L.A. Gray
D.A. Lewis
D.F. Kallmes

BACKGROUND AND PURPOSE: Remodeling balloons are used to assist in endovascular coiling of aneurysms. We evaluated our experience with balloon-assisted coiling (BAC) in an attempt to determine whether this technique increased the rate of thrombus formation or symptomatic thromboembolic complications.

MATERIALS AND METHODS: In 3 years, we treated 221 patients with intracranial aneurysms. Statistical analysis was performed to assess whether BAC increased the rate of thrombus formation or symptomatic thromboembolic complications. Patient demographics, aneurysm size, location, neck width, antiplatelet therapy, and rupture status were evaluated.

RESULTS: We detected no statistically significant difference in rates of thrombus formation (14% versus 9% with and without BAC, respectively, $P = 0.35$) or symptomatic thromboembolic events (7% versus 5% with and without BAC, respectively, $P = 0.76$), though our power to detect small differences was limited. There was also no correlation with age, sex, rupture status, aneurysm size, or location. There was a significant increase in the rates of thrombus formation (6% versus 16%, $P = 0.02$) and symptomatic thromboembolic complications (3% versus 10%, $P = 0.04$) in aneurysms that were classified as narrow- or wide-necked, respectively. The use of clopidogrel was associated with a decrease in the rate of complications ($P = 0.01$).

CONCLUSION: In this series, we detected no significant increase in the rates of either intraprocedural thrombus formation or symptomatic thromboembolic events in patients treated with BAC. Larger studies are required to confirm our observations. Wide-necked aneurysms were independently associated with increased rates of thrombus formation and symptomatic thromboembolic complications, whereas the use of clopidogrel was protective ($P = 0.01$).

Intracranial aneurysm treatment with minimally invasive endovascular techniques has progressed rapidly in the last decade.[1-6] In many centers, endovascular coiling is now the treatment of choice for most aneurysms. Interventional neuroradiologists have developed several important adjuncts to assist in their treatment of intracranial aneurysms, such as balloon- and stent-assisted coiling of wide-necked aneurysms.[7,8] These techniques have made it possible to treat many aneurysms that would have previously required more invasive open neurosurgical clipping. It remains theoretically possible that the introduction of a remodeling balloon might lead to increases in the rate of thrombus formation and thromboembolic events, though prior studies have not shown such an association.[9] This theoretic risk is due to 2 factors: First, the presence of a balloon in the parent vessel promotes stasis and can lead to thrombus formation or platelet aggregation. Second, the presence of any foreign object in the vascular system can be a nidus for thrombus formation.

In this article, we report our experience treating intracranial aneurysms with balloon-assisted coiling (BAC). The incidence of thrombus formation localized to the region of the aneurysm (local thrombus formation) and of symptomatic thromboembolic complications encountered in patients treated with BAC is compared with that in those patients who were treated without balloon assistance.

Received June 26, 2006; accepted September 19.

From the Department of Radiology (K.F.L., H.J.C., L.A.G., D.A.L., D.F.K.), Mayo Clinic, Rochester, Minn. and Department of Radiology (K.F.L.), Baylor University Medical Center, Dallas, Tex.

Please address correspondence to Kennith F. Layton, MD, Baylor University Medical Center, Department of Radiology, 3500 Gaston Ave, Dallas, TX 75246; e-mail: klayton@americanrad.com

DOI 10.3174/ajnr.A0490

Materials and Methods

Institutional review board approval was granted for this retrospective single-center study. From our interventional neuroradiology data base, we identified all patients who underwent endovascular coiling of intracranial aneurysms between March 2003 and February 2006. Patients who were treated with stent-assisted coiling were excluded from the analysis, as were patients whose aneurysms were treated with parent-vessel sacrifice.

Patient Population. Two-hundred twenty-one patients were included in the study. BAC was used in 73/221 (33%) patients, whereas 148/221 (67%) were treated without the use of remodeling balloons. A review of the patients' electronic medical records, procedure notes, and angiograms was performed. Patient demographics, incidence of local thrombus formation, thromboembolic complications, and preprocedural antiplatelet regimen were recorded. The overall size of the aneurysms was recorded as the largest diameter, and aneurysms were divided into those with wide necks versus those with narrow necks. An aneurysm was arbitrarily assigned to the wide-necked group if the neck was 4 mm or greater.[10] In those patients in whom the original angiogram report recorded the aneurysm and neck size, this size was used as the measurement. In patients in whom no measurement was given in the original report, the aneurysm and its neck size were measured from the 2D digital subtraction angiography (DSA) images. Preprocedural antiplatelet regimen was classified as none, aspirin

alone, clopidogrel alone, or aspirin combined with clopidogrel. Aneurysm locations were classified as basilar tip, other posterior fossa locations, anterior cerebral artery (ACA), middle cerebral artery (MCA), or internal carotid artery (ICA).

In those patients in whom we anticipated the need for BAC before the procedure, premedication with aspirin and/or clopidogrel was instituted. Furthermore, preprocedural antiplatelet therapy was often administered to those patients with wide-necked aneurysms even if BAC was not anticipated. Typical doses for antiplatelet medications included 325-mg aspirin per day and 75-mg clopidogrel per day by mouth. If the procedure was scheduled sooner than 5 days from the initiation of clopidogrel, an initial loading dose of 300–450 mg was given.

Statistical Analysis. Statistical calculations were performed by using JMP software version 6.0.0 (SAS, Cary, NC). The relationship between local thrombus formation or symptomatic thromboembolic complications and other variables was determined by using logistic regression. Specific variables that were analyzed included age, sex, aneurysm location, rupture status, neck width, overall aneurysm size, use of BAC, and preprocedural antiplatelet regimen. In the analysis of symptomatic thromboembolic complications, the significance of intraprocedural local thrombus formation was also investigated.

Procedural Description. Using a standard technique, all procedures were performed by using transfemoral or transradial arterial access in a dedicated biplane neuroangiography suite.[11] All procedures were performed with the patient under general anesthesia after obtaining informed consent from the patient and/or family members. After obtaining arterial access, we routinely administered an initial intravenous bolus of 3000-U heparin for both ruptured and unruptured aneurysms. After determining that an aneurysm was to be treated, heparinization was adjusted to keep the activated clotting time (ACT) between 250 and 300 seconds. We routinely used 5F or 6F guiding catheters (Envoy, Cordis Neurovascular, Miami Lakes, Fla) or sheaths (Shuttle; Cook, Indianapolis, Ind) and placed both the microcatheter and balloon catheter coaxially through the guiding sheath. HyperForm and HyperGlide remodeling balloons (ev3, Plymouth, Minn) were used in those patients who required BAC. If the use of BAC was anticipated before placement of the microcatheter on the basis of neck size and aneurysm location, we would generally place the deflated balloon catheter across the neck of the aneurysm. If prolapse of the coil was demonstrated during the procedure, the remodeling balloon was inflated to provide secure placement of the coil in the aneurysm without compromise of the parent-vessel lumen. For those coils that were placed with the balloon inflated, we would deflate the balloon under fluoroscopic guidance to ensure that there was no migration of the coil before detachment.

We defined "local thrombus formation" as filling defects noted on DSA in the region of the aneurysm, either adherent to the coil mass or the parent artery adjacent to the aneurysm neck. To evaluate for local thrombus formation, we performed working projection DSA runs periodically during the placement of coils and at the end of the procedure, especially in prolonged procedures that required the use of many coils. If local thrombus formation was noted, an immediate ACT evaluation was performed and additional heparin was given to achieve an ACT greater than 300. If the aneurysm had been at least partially coiled, a normotensive or slightly hypertensive state was ensured. If the degree of parent vessel compromise was minor, serial angiograms were obtained to assess the stability of the thrombus after removing the microcatheter and remodeling balloon to improve flow. If the thrombus was stable for 20–30 minutes of observation and no significant flow compromise was present, the procedure was terminated without further medical management. In those patients in whom the degree of thrombus formation was enough to cause flow compromise or if there was progression of thrombus volume despite the measures described previously, an intravenous and/or intra-arterial platelet glycoprotein (GP IIb/IIIa) agent was administered. In most cases, an initial intravenous or intra-arterial loading dose of abciximab (0.25 mg/kg) was administered. If there was no angiographic response after 20–30 minutes, a continuous intravenous infusion of the agent (0.125 μg/kg per minute) was begun in the angiography suite and continued in the neurologic intensive care unit for 12 hours.

Results

The mean age of patients in our study was 58 years (range, 19–90 years). Seventy-eight percent (172/221) of patients were female. Of the 221 patients treated, 139/221 (63%) of the aneurysms were unruptured. The mean maximum aneurysm dimension was 6.7 mm (SD, 3.5) with a median size of 6 mm (range, 2–25 mm). Of the aneurysms treated, 51 involved the ACA (including the anterior communicating artery); 34, the basilar tip; 100, the ICA (including posterior communicating artery aneurysms); 17, the MCA; and 19, other posterior fossa sites. No correlation between age, sex, rupture status, aneurysm location, or overall aneurysm size and the formation of local thrombus or symptomatic thromboembolic complication was seen.

In the 73 patients who underwent BAC, local thrombus formation was documented in 10 (14%). Thirteen of the 148 (9%) patients treated without balloon assistance were complicated by local thrombus formation; however, the increased rate seen in patients treated with BAC was not significant ($P = 0.35$). Although the increased rates of local thrombus formation were not found to be statistically significant between those treated with and without BAC, we only had a 20% power to detect a 5% difference. For this reason, we cannot exclude the possibility that there is a small increase in the rate of local thrombus formation in aneurysms treated with BAC. Five of 13 (38%) patients with symptomatic thromboembolic complications were treated with BAC, whereas 8/13 (62%) were treated without balloon assistance ($P = 0.76$).

Only 1/23 patients (4%) who demonstrated local thrombus formation became clinically symptomatic. Furthermore, only 1 of 13 (8%) patients complicated by a symptomatic thromboembolic event was associated with intraprocedural local thrombus formation. Therefore, there was no correlation between the development of symptomatic thromboembolic complications and the presence of local thrombus formation ($P = 1.0$).

Symptomatic thromboembolic complications were demonstrated in 13/221 patients (6%). The relationship between preprocedural antiplatelet regimen and symptomatic thromboembolic complications is shown in the Table. There were no symptomatic thromboembolic complications or cases of local thrombus formation in those patients who were on clopidogrel alone or aspirin combined with clopidogrel. Preprocedural antiplatelet therapy was used in 34% (25/73) of patients with BAC compared with 27% (40/148) of patients with aneurysms coiled without balloon assistance. Thirty-four percent of patients (31/91) with wide-necked aneurysms were

Number of thromboembolic complications and the associated preprocedural antiplatelet regimen

	Complications	
Antiplatelet Regimen	No	Yes
None	144	12
Aspirin and clopidogrel	25	0
Clopidogrel alone	7	0
Aspirin alone	32	1

pretreated with antiplatelets compared with 26% of patients (34/130) with aneurysms with a narrow neck. The use of clopidogrel (either alone or combined with aspirin) was the only preprocedural antiplatelet factor that showed a significant difference in local thrombus formation ($P = 0.01$) or symptomatic thromboembolic complication ($P = 0.04$).

Of the 221 aneurysms, 91 (41%) were classified as having a wide neck. The presence of a wide neck did correlate with an increased rate of both local thrombus formation and symptomatic thromboembolic complications. Local thrombus formation was seen in 15/91 (16%) of wide-necked aneurysms compared with 8/130 (6%) of those with a narrow neck ($P = 0.02$). Nine of 91 (10%) wide-necked aneurysms had symptomatic thromboembolic complications compared with 4/130 (3%) aneurysms with a narrow neck ($P = 0.04$).

Discussion

In this study, we detected no statistically significant difference in rates of local thrombus formation or of symptomatic thromboembolic events between aneurysms treated with and without BAC. We noted a 5% difference between rates of local thrombus formation with and without BAC, but our study population of 221 patients offers only a 20% power to detect such a small difference. A study population of approximately 610 patients would be needed to have adequate power to show an increase of 5%; thus, we cannot exclude a type 2 error for this outcome measure. Similarly, we noted no difference in rates of symptomatic thromboembolic events between patients treated with and without BAC. Again, our power to detect such a small difference was limited. We consider these findings important in that they suggest relatively similar safety profiles for patients treated with and without BAC, but we also acknowledge that these findings point to a need for studies of larger aneurysm populations to better understand the relative risks. Our results are in agreement with previous reports that documented no increase in complications related to the use of BAC.[9,12]

Among multiple independent variables, including age, sex, rupture status, neck width, aneurysm location, overall aneurysm size, and use of BAC, the only predictor of increased rate of thrombus formation in our study was the presence of a wide neck, even when accounting for the use of BAC. A previous article by Derdeyn et al[13] found no specific factor associated with intraprocedural thrombus formation. However, their study did demonstrate a significant correlation between the development of postprocedural ischemic events and larger aneurysms or protruding coils. We noted a poor correlation between the presence of local thrombus formation and symptomatic thromboembolic events. This is likely related to our aggressive management with GP IIb/IIIa agents in those patients with intraprocedural local thrombus formation. The use of these agents may afford some protection against subsequent symptomatic thromboembolic events.[14-16] It seems intuitive that the use of antiplatelet agents before coiling would decrease the risk of thrombus formation and associated complications. On the basis of our results, the use of clopidogrel was associated with a decreased rate of symptomatic thromboembolic complications and local thrombus formation. In fact, none of the patients in our study who were premedicated with clopidogrel developed these complications. A large multicenter randomized trial is needed to evaluate the optimum antiplatelet regimens before coiling. Such a trial should account for patients who are resistant to aspirin or clopidogrel because this resistance could potentially affect the dosage of medications used.

Our study has several limitations. First, it is a single-center retrospective study and is limited in this regard as are all single-center nonrandomized studies that assess endovascular coiling techniques. Although it was possible to identify those patients who were on scheduled aspirin and clopidogrel therapy before the procedure, it was not possible in many cases to determine the precise daily dose of aspirin. It is possible that high-dose aspirin regimens may be more effective than low-dose therapy. Furthermore, we did not evaluate the efficacy of platelet inhibition produced by aspirin and clopidogrel. It is possible that many patients may be relatively resistant to these antiplatelet drugs when given in standard doses.[17-20] Further investigation is warranted to determine how the lack of response to antiplatelet medications can affect the incidence of thrombus formation.

Conclusions

The use of BAC coiling does not seem to significantly increase the rate of local thrombus formation or symptomatic thromboembolic complications during aneurysm coiling. Aneurysms with necks 4 mm and larger are at a greater risk for local thrombus formation and symptomatic thromboembolic complications. Given the fact that we did not have any thromboembolic complications in patients who were pretreated with clopidogrel or a combination of aspirin and clopidogrel, practitioners should consider pretreating patients with these medications before intervention in wide-necked aneurysms. Further studies are needed to clarify which antiplatelet dosing schemes and platelet-function monitoring parameters are optimal.

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