Long-term Angiographic and Clinical Outcomes in Completely Versus Incompletely Coiled Ruptured Intracranial Aneurysms

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Subarachnoid hemorrhage secondary to ruptured intracranial aneurysms is a devastating disease with an incidence of 6 to 7 per 100 000 person-years in most populations.[1] Direct treatment of the aneurysm has involved either open microsurgical clipping or endovascular coiling. The International Subarachnoid Aneurysm Trial (ISAT) was a randomized trial that demonstrated a statistically significant advantage of endovascular coiling over microsurgical clipping in the rates of death or dependency at 1 year for ruptured aneurysm patients (23.5% vs 30.9%; $P = .001$).[2,3] Since the publication of ISAT in 2002, ruptured cerebral aneurysms are increasingly treated by endovascular coiling. Although complete aneurysm occlusion is desired, it may not be feasible in every case owing to anatomic or procedural issues. There is a balance between the need to pack the ruptured aneurysm optimally to prevent rebleeding and the risk of aneurysm perforation and coil herniation. Often, a residual aneurysm neck or fundus is left behind on the immediate postcoiling angiogram. Is this safe? The purpose of this study is to retrospectively evaluate the long-term clinical and angiographic outcomes of coiled ruptured intracranial aneurysms stratified by the immediate postcoiling occlusion status.

METHODS

Patient Population

This study was approved by the Conjoint Health Research Ethics Board. Consecutive patients with ruptured intracranial aneurysms initially treated with endovascular coiling within a 5-year period between January 2002 and December 2006 were identified. This information was obtained from a prospective neurointerventional procedure log at the Foothills Medical Centre in Calgary, Alberta, Canada, which is a tertiary care centre with a catchment population of approximately 1.5 million people in southern Alberta and adjacent provinces. The time period chosen allowed an opportunity for at least 3 years of clinical and angiographic follow-up. A patient was excluded if the aneurysm of interest was a mycotic or traumatic aneurysm, if the ruptured aneurysm had a prior clipping procedure, or if there was a failure to deploy at least a single coil during endovascular treatment. If multiple aneurysms were present, the ruptured aneurysm was determined from the distribution of subarachnoid and/or intraventricular blood and the overall aneurysm size.

Acute Management Paradigm

During the time period of this study, the overall management strategy was endovascular coiling as the first treatment option if feasible. Each case was discussed and consensus reached by members of both open cerebrovascular surgery and neurointerventional radiology. Patients with a large intracerebral hemorrhage associated with a ruptured aneurysm generally undergo urgent evacuation of the hematoma with microsurgical clipping of the aneurysm. Patients with very poor clinical status, eg, absent brainstem reflexes and decerebrate posturing despite external ventricular drain insertion and in the absence of a surgical mass lesion, typically have not proceeded to early intervention. Ruptured intracranial aneurysms are generally treated within 24 to 72 hours from admission. The majority of endovascular-treated aneurysms used detachable coils (Guglielmi, GDC, Target Therapeutics, Fremont, California) with the goal of occluding as much of the aneurysm as possible in a safe manner.

Clinical Parameters and Long-term Follow-up

Baseline clinical information was retrospectively abstracted from hospital charts and stratified on the basis of initial coiling occlusion status. This information included age, sex, Hunt and Hess grade[4] before external ventricular drain, aneurysm location, and the presence or absence of an external ventricular drain.

Computed tomography head scans were analyzed to determine the modified Fisher grade.[5] Cerebral angiogram

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runs before the first coil was deployed were analyzed for aneurysm diameter, aneurysm neck size, and the aspect ratio (ratio of dome to neck).[6] The use of an endovascular assist device (balloon or stent) and the presence of any procedural complications were noted.

Patients are followed up in a multidisciplinary neurovascular clinic with members of both open cerebrovascular surgery and neurointerventional radiology available. Patients are generally seen 3 months after the initial coiling procedure and then annually. The overall duration of follow-up and timing between clinic visits are based on the clinical and angiographic status. The long-term clinical outcomes are determined from the neurovascular clinic notes and use the modified Rankin Scale (mRS), a validated measure of global disability in cerebrovascular patients.[7] The scale is graded from 0 to 6 (asymptomatic status to death). A good outcome is an mRS of $\leq$ 2, which represents patient functional independence.

Angiographic Analysis and Long-term Follow-up

Patients are followed up angiographically with a magnetic resonance angiogram (MRA) at 3 to 6 months after coiling and a digital subtraction angiogram (DSA) and MRA scans at the 1-year mark. Patients have annual MRA scans, with additional DSA scans performed if there is coil compaction or recanalization. The overall duration of follow-up scans and timing between scans are based on the clinical and angiographic status. It has been shown in the literature that MRA scans for follow-up of coiled intracranial aneurysms correlate well with DSA in their ability to detect aneurysm remnants.[8,9]

Three sets of angiograms were analyzed: the immediate postcoiling angiogram just after the last coil was deployed, the DSA or MRA at the time of aneurysm recurrence if applicable, and the most recent follow-up DSA or MRA scan if available. All imaging were graded on the basis of the Raymond-Roy occlusion classification[10] (see Figure 1): complete obliteration (class 1), residual neck (class 2), and residual aneurysm or fundus filling (class 3). The angiograms were evaluated by 2 reviewers independently in a blinded fashion. Any discrepancies were resolved by consensus. Worsening angiographic progression or recanalization was defined as progression to a higher occlusion class or further fundus enlargement in a class 3 coiled aneurysm.

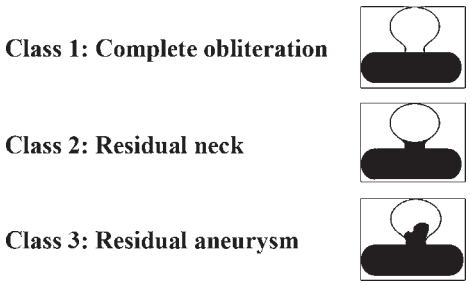

FIGURE 1. Raymond-Roy occlusion classification.

Statistical Analysis

Associations between initial occlusion status and continuous quantitative variables (age, aneurysm diameter, aneurysm neck size, and aspect ratio) were analyzed with the nonparametric Kruskal-Wallis test. Associations between initial occlusion status and categorical variables (sex, aneurysm size category, Hunt and Hess grade, modified Fisher grade, location, endovascular assist, presence of an external ventricular drain, long-term mRS, mortality, reintervention, and recanalization) were analyzed with the χ^2 test. Values of $P < .05$ were regarded as significant.

RESULTS

Eighty-six patients with ruptured intracranial aneurysms were identified. After the primary coiling treatment, 12 aneurysms (14.0%) were completely occluded, 66 aneurysms (76.7%) had a residual neck, and 8 aneurysms (9.3%) had residual fundus filling. Nearly half (47.0%) of the patients with initial residual neck had a neck size of 1 mm or less.

Baseline Clinical Characteristics

The baseline characteristics of all the patients are presented in the Table, stratified by the initial Raymond-Roy occlusion status. Overall, there were no significant differences among the 3 groups with regard to age, sex, Hunt and Hess grade, aneurysm location, aneurysm diameter (actual size and size category), neck size, aspect ratio, modified Fisher grade, presence of an external ventricular drain, or assisted coiling.

In terms of aneurysm size categories, 21 aneurysms were $\leq$ 5 mm (24.4%), 47 aneurysms were 6 to 10 mm (54.7%), and 18 aneurysms were $\geq$ 11 mm (20.9%). There was no significant difference in the distribution of the Raymond-Roy occlusion status among the 3 aneurysm size categories ($P = .74$).

Sixty-three aneurysms (73.3%) were found in the anterior circulation, whereas 23 aneurysms (26.7%) were found in the posterior circulation. The most common aneurysm location was at the anterior communicating artery (36%), followed by the posterior communicating artery (22%) and basilar tip (15%). Of note, only 3% of the coiled aneurysms in this series were found at the middle cerebral artery bifurcation.

Intraprocedural Complications

Coil prolapse or herniation into the parent vessel resulting in a thromboembolic event was observed in 3 patients (3.5%). Overall, thromboembolic events were

TABLE. Patient Baseline Characteristics[a]

	Complete	Residual Neck	Residual Fundus	*P*
Patients, n	12	66	8	
Age, y	58.9 (13.9)	57.8 (14.0)	60.4 (11.6)	.87
Sex, M/F	3/9	14/52	1/7	.79
Hunt and Hess grade, n				
Average	2.7	2.5	3.5	.55
1	3	20	1	
2	3	15	0	
3	3	12	3	
4	1	13	2	
5	2	6	2	
Location, n				
Anterior	10	48	5	.58
Posterior	2	18	3	
Aneurysm size, mm	7.5 (4.0)	8.3 (3.9)	7.8 (4.4)	.68
Aneurysm neck, mm	2.7 (0.7)	3.3 (1.1)	3.6 (1.8)	.22
Body/neck ratio	2.8 (1.3)	2.7 (1.2)	2.4 (1.2)	.76
Modified Fisher grade	3.0	2.7	3.1	.81
External ventricular drain, %	58.3	45.5	50.0	.71
Endovascular assist (balloon and/or stent), %	8.3	27.3	50.0	.12

[a]Values in parentheses are standard deviations.

observed in 23 patients, of which 15 patients (17.4%) developed immediate postprocedural neurologic deficit or deterioration. Intraoperative perforation of the aneurysm or parent vessel was observed in 14 patients, of which 3 patients (3.5%) developed immediate postprocedural neurologic deficit or deterioration. Seven patients (8.1%) had more than 1 complication. Two patients (2.3%) died as a result of intraprocedural complications.

There was no association between Raymond-Roy occlusion status and the presence of intraprocedural complications ($P = .24$). Intraprocedural complications were associated with in-hospital mortality ($P < .001$), but there was no significant association between complications and long-term mRS in surviving patients ($P = .11$).

Long-term Clinical Outcome

Fifteen patients died before hospital discharge and 4 patients died after hospital discharge of unrelated causes. Fifty-one patients (76.1% of patients available for clinical follow-up) had available clinical follow-up at a mean of 33.3 months (SD, 21.3 months; range, 3.7-90.6 months). There were no significant differences in long-term clinical outcomes among the 3 groups in surviving patients (mean mRS, 1.1-1.2; $P = .58$). When patients who died before hospital discharge were accounted for, there still was no significant difference in long-term clinical outcome among the 3 groups (mean mRS, 2.2-2.6; $P = .77$). The majority of surviving patients (90.2%) had a good clinical outcome, defined as mRS ≤ 2. For the 26 patients with at least 3-year follow-up at a mean of 50.5 months (SD, 14.8 months; range, 35.1-90.6 months), the mean mRS was 1.0 to 1.3 with no significant difference based on initial occlusion status ($P = .77$).

Long-term Angiographic Outcome

Fifty-six patients (83.6% of patients available for clinical follow-up) had angiographic follow-up. Twenty-nine patients (51.8%) had worsening angiographic progression before any reintervention. The mean time to angiographic progression was 13.0 months (SD, 12.1 months; range, 2.6-59.6 months). Eighteen of 43 patients (41.9%) who initially had a residual neck were found to have recanalization on follow-up imaging. Patients who had initial complete obliteration or initial fundus filling had a recanalization rate of 87.5% (7 of 8 patients) and 80% (4 of 5 patients), respectively. There is an association between initial occlusion status and recanalization ($P = .03$). However, recanalization had no significant effect on long-term mRS ($P = .90$).

The most recent angiographic follow-up in 56 patients, regardless of interval reintervention, was obtained at a mean of 37.2 months (SD, 22.4 months; range, 5.9-98.3 months). Seven of 43 patients (16.3%) who initially had a residual neck were found to have worsening angiographic progression. Patients who had initial complete obliteration or initial fundus filling had worsening progression of 87.5% (7 of 8 patients) and 60% (3 of 5 patients), respectively. Again, there was an association between initial occlusion status and worsening angiographic progression regardless of intervening reintervention ($P \leq .001$).

Reintervention

Of the 29 patients who had interval recanalization after coiling, 18 patients had angiographic progression deemed concerning enough for attempted reintervention (62.1% of recanalized patients and 32.1% of all patients with angiographic follow-up). Further interventions were performed in 16 patients (18.6% of all patients) at a mean of 12.0 months (SD, 11.0 months; range, 0.4-40.5 months) after the initial coiling: 11 were coiled twice, 1 was coiled 3 times, 1 was coiled 4 times, 2 underwent subsequent surgical clipping, and 1 underwent coiling 3 times and an extracranial-to-intracranial bypass. Two patients had aborted reintervention attempts. Initial occlusion status was not associated with the need for further intervention ($P = .58$). In addition, reintervention had no significant effect on long-term clinical outcomes (mRS, 1.5-1.6; $P = .55$).

Rebleeding

Recurrent rupture occurred in 1 patient (1.2%) 33.1 months after the initial coiling procedure. This patient had a ruptured basilar tip aneurysm that had residual fundus filling after initial coiling. This aneurysm experienced a sizeable enlargement of the residual fundus on follow-up cerebral angiograms (see Figure 2).

DISCUSSION

In the setting of a ruptured intracranial aneurysm, the primary goal of an endovascular coiling procedure is to prevent rebleeding.

Of the 86 ruptured intracranial aneurysm patients identified, only 12 (14.0%) were completely occluded after the primary coiling treatment. The majority of ruptured aneurysms had initial incomplete occlusion, with 76.7% and 9.3% of aneurysms having residual neck and residual fundus filling, respectively. The percentage of complete occlusion appears to be substantially less than those reported in the literature. The ISAT revealed a complete occlusion rate of 66% (584 of 988) in the coiled patients,[2] whereas other case series of ruptured coiled aneurysms revealed complete occlusion rates ranging from 33% to 81%.[11-18] For this retrospective review, all the angiograms were analyzed by 2 reviewers in a blinded fashion. It is our impression that if one were to carefully scrutinize the immediate postcoiling angiograms, there would be a significant number of patients with small residual necks that would look completely occluded on first glance. Not uncommonly, the official angiographic report would indicate that an aneurysm was well occluded, but a residual neck would be present. Not surprisingly, nearly half of the patients with residual neck had a neck size of 1 mm or less.

In our case series, there was no significant difference in the baseline characteristics of the patients stratified by initial occlusion status. Intuitively, it would appear that patients with larger aneurysm diameter or larger relative neck size would have a higher frequency of incomplete occlusion on immediate postcoiling angiogram. However, this was not seen in this study and may be due to the relatively small number of patients.

Ruptured aneurysms have a tendency for higher procedural morbidity and mortality compared with unruptured aneurysms.[19] Other case series of coiled ruptured aneurysms reported intraprocedural complications at a rate ranging from 8.2% to 22.6%.[11-13,16,18] Our procedural mortality was 2.3% which is similar to other reported series.[11-18] In a situation in which thrombus formation is formed near the parent vessel and coil interface, we typically use abciximab (ReoPro; Eli Lilly, Indianapolis, Indiana). With an intraoperative rupture, our treatment objective changes to packing the aneurysm fundus with coils and terminating the procedure as quickly as safely possible. There is also a strong possibility of inserting an external ventricular drain if not already performed. Intraoperative perforation, however, was not associated with incomplete occlusion status ($P = .48$). Not surprisingly, there was an association between intraprocedural complication and in-hospital mortality ($P \leq .001$). There was no association between intraprocedural complication and long-term mRS in survivors ($P = .11$). In fact, 17 of 18 patients (94.4%) who had a complication and had available clinical follow-up were functionally independent (mRS ≤ 2).

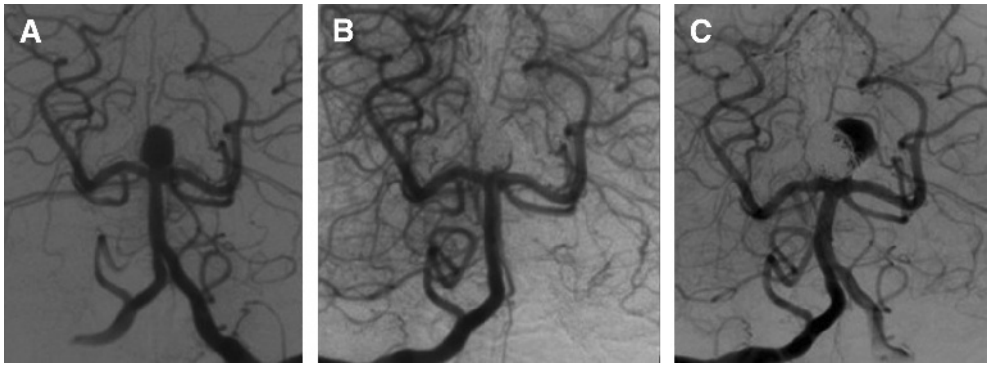

FIGURE 2. A 58-year-old woman with Hunt & Hess grade 3 subarachnoid hemorrhage secondary to a ruptured 10 × 7-mm basilar tip aneurysm (A). Residual fundus filling was seen on immediate postcoiling angiogram (B). Further recanalization 2 years after initial coiling procedure was seen (C). This patient would later suffer from a recurrent subarachnoid hemorrhage despite repeated interventions.

Despite a significant proportion of patients having either residual neck or residual fundus filling on immediate postcoiling angiogram, incomplete occlusion status was not associated with mortality ($P = .92$). For the 51 patients (76.1% of patients available for clinical follow-up) who survived past hospital discharge and had follow-up at the Foothills Medical Centre neurovascular clinic, the clinical outcomes were remarkably good and were not associated with initial occlusion status ($P = .58$). The average mRS was 1.1 to 1.2 at a mean follow-up of 33.3 months. In fact, 46 of 51 patients (90.2%) had a good clinical outcome (mRS $\leq$ 2). The high proportion of good clinical outcome (88.5%) also applies to the 26 patients with at least 3 years of follow-up. Other case series have also reported relatively good clinical outcomes in surviving coiled ruptured aneurysm patients.[11-18] The results of this study indicate that patients with incomplete aneurysm occlusion on initial coiling despite best efforts can still do well clinically. Even among a subset of patients with high-grade aneurysmal subarachnoid hemorrhage (Hunt and Hess grade 4 or 5) who underwent endovascular coiling, 53% were documented to have a good clinical outcome at our institution.[20]

Recanalization was defined as progression from one occlusion class to a higher occlusion class or further residual fundus enlargement. In the 56 patients with angiographic follow-up (83.6% of all patients available for angiographic follow-up), there was a 51.8% recanalization rate at a mean of 13.0 months. This rate of worsening angiographic progression is relatively higher than the recanalization rates (14.7%-39.8%) reported in the literature.[11-18] In a series that included both ruptured and unruptured aneurysms, Raymond et al[21] demonstrated increasing recanalization rates depending on the duration of angiographic follow-up, with 22.1%, 39.3%, and 39.8% recanalization rates after 1 to 16, 17 to 37, and $>$ 37 months of angiographic follow-up, respectively. As expected, there was an association between initial occlusion status and recanalization in our series ($P = .03$). Interestingly, 7 of 8 patients with initial complete aneurysm occlusion progressed to form residual necks on follow-up imaging, likely because of mild coil compaction. None of these patients required retreatment. Recanalization is quite common and occurred as long as 59.6 months after the initial coiling procedure. This justifies long-term surveillance of recanalization of ruptured coiled aneurysms with MRA scans for many years. The duration of follow-up imaging required is still debatable. In our institution, we generally image patients for at least 5 years, or longer if recanalization is noted on follow-up imaging.

Only 18 of 29 patients had angiographic progression that was concerning enough to warrant further reintervention. This constitutes 32.1% of all patients with angiographic follow-up. Sixteen patients had retreatment, whereas 2 patients had to abort reintervention. Although initial occlusion status was associated with recanalization, there was no such association with retreatment in our series ($P = .58$). There were no intraprocedural complications during retreatment. A low rate of complications for repeat interventions was also seen by Slob et al,[22] who noted 35 procedural complications (7.1%) occurring in 488 initial coiling procedures but no complications occurring in 53 additional procedures. Other case series have demonstrated the same observation.[23-25] In addition, reintervention had no significant effect on long-term clinical outcomes ($P = .55$). This suggests that reintervention has a low procedural complication rate and is generally safe, especially when performed under an elective basis.

Despite angiographic recanalization in a significant proportion of patients, recurrent rupture was rare after coiling, occurring in 1 patient 33.1 months after the initial coiling (1.2% of all patients and 1.8% with available angiographic follow-up). This is equivalent to 1 case of rerupture after 174 person-years of angiographic follow-up or an annual rerupture rate of 0.57%. This compares favorably to the results from the Cerebral Aneurysm Rerupture After Treatment study, which revealed 10 cases of rebleeding after 904 person-years of follow-up, which is equivalent to a 1.1% annual rerupture rate.[26] However, only 1 patient had a rebleed beyond 1 year of follow-up in that study. With aggressive follow-up, surveillance of aneurysm remnants, and appropriate selection of patients for retreatment, overall rebleeding rates from previously coiled ruptured intracranial aneurysms are fairly low.

There are some limitations to this study. Clinical and angiographic follow-up was not available for all patients. Of the 67 patients who had the potential for follow-up, only 51 (76.1%) and 56 (83.6%) had clinical and angiographic follow-up respectively. Many of these patients who were lost to follow-up lived outside the province. The study was also limited by the retrospective nature of the analysis and the relatively small number of patients involved.

CONCLUSIONS

The majority of the ruptured aneurysms in this study were initially incompletely coiled. However, patients overall had good clinical outcomes in long-term follow-up regardless of initial occlusion status. Recurrent rupture was rare. Recanalization remains a significant long-term issue, but reintervention appears safe. Many years of angiographic follow-up are required for these patients. During the initial endovascular coiling, the decision to leave a neck or fundus remnant behind may not adversely affect the ultimate clinical outcome.

Disclosure

This study was awarded the Synthes Cerebrovascular Award at the 2010 Annual Meeting of the Congress of Neurological Surgeons. The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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