

**World Neurosurgery: Original Article****The Natural History of Coiled Cerebral Aneurysms Stratified by Modified Raymond Roy Occlusion Classification**

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**ABSTRACT**

**OBJECTIVE** The natural history and long-term durability of Guglielmi detachable coil (GDC) embolization is still unknown. We hypothesize a stepwise decrease in durability of embolized cerebral aneurysms as stratified by the modified Raymond Roy Classification (MRRC).

**METHODS** First-time GDC embolized cerebral aneurysms were retrospectively reviewed from 2004 to 2015. Loss of durability (LOD) was defined by change in aneurysm size or patency seen on serial radiographic follow-up. Kaplan-Meier survival analysis was performed to evaluate embolization durability. Multivariate Cox Regression Modeling was used to assess baseline aneurysm and patient characteristics for their effect on LOD.

**RESULTS** There were 427 patients with 443 aneurysms who met inclusion criteria. Overall, 89 (21%) aneurysms met LOD criteria. Grade 1 aneurysms had statistically significantly greater durability than all other MRRC grades. Grade 3b aneurysms had significantly worse durability than all other aneurysm grades. There was no difference in durability between grade 2 and 3a aneurysms. Of aneurysms with LOD, 26 (29%) experienced worsening of MRRC grade. Interestingly, 35 (24%) initial MRRC grade 2, 72 (45%) initial MRRC grade 3a, and 6 (22%) initial MRRC grade 3b aneurysms progressed to MRRC grade 1 without retreatment. In our multivariate analysis, only initial MRRC grade was statistically significantly associated with treatment durability ( $p < 0.001$ ).

**CONCLUSIONS** MRRC grade is independently associated with first-time GDC embolized cerebral aneurysm durability. Achieving MRRC grade 1 occlusion outcome is significantly associated with greater long-term GDC durability. Although few aneurysms experience further growth and/or recanalization, a majority of incompletely obliterated aneurysms tend to remain stable over time or even progress to occlusion. Grading scales such as the MRRC are useful for characterizing aneurysm occlusion but may lack sensitivity and specificity for characterizing changes in aneurysm morphology over time.

**KEY WORDS:** Cerebral aneurysm; coil embolization; natural history; durability, Raymond Roy classification

## INTRODUCTION

The prevalence of unruptured intracranial aneurysms (IAs) is approximately 3.2% in the general population. Women are nearly twice as likely to have an aneurysm compared to men.<sup>1</sup> The approximate age- and sex-adjusted annual incidence of subarachnoid hemorrhage is 10 per 100,000.<sup>2</sup> IA rupture is a major source of neurologic morbidity and mortality.<sup>3,4,5</sup> Conventional treatment options for IAs include surgical clipping across the neck of the aneurysm and endovascular therapy, originally with the use of Guglielmi detachable coils (GDCs) and with subsequent innovations including balloon-assisted coil embolization, stent-assisted coil embolization, and stent-only treatment with flow diversion. While elective aneurysms are increasingly being treated with stent-assisted coiling and more recently with flow diversion, there nevertheless remains a large population of unruptured aneurysms treated with coil embolization only and the vast majority of ruptured aneurysms are treated with coil embolization.<sup>6</sup>

Since the invention of the GDC, endovascular treatment techniques and management guidelines for IAs have continually evolved.<sup>7,8</sup> The question of the preferred treatment strategy for unruptured IAs remains uncertain. There have been two major randomized controlled trials comparing endovascular coiling with surgical clipping of ruptured aneurysms, namely The International Subarachnoid Aneurysm Trial (ISAT)<sup>9</sup> and the Barrow Ruptured Aneurysm Trial (BRAT).<sup>10</sup> While there was no difference in the recurrent hemorrhage rate of aneurysms undergoing endovascular and surgical treatment in the BRAT trial, there was a statistically significant increase in retreatment of coiled patients at both the 3-year<sup>11</sup> and 6-year<sup>12</sup> follow-up time points.

Likewise, patients undergoing endovascular coiling in the ISAT trial were statistically significantly more likely to require retreatment and to experience a recurrent hemorrhage compared to patients treated with microsurgical clipping.<sup>13,14</sup> These studies, and others, have

brought the durability of endovascular coiling into question.<sup>14, 15, 16</sup> Additionally, aneurysm remnants are common after cerebral aneurysm coiling. A recent report utilizing ISAT data showed that 34% of coiled cerebral aneurysms had associated remnants.<sup>14</sup> Predicting which IAs will remain stable after initial endovascular coiling remains a challenge for neuroendovascular surgeons.

The Raymond Roy Occlusion Classification Scale is an angiographic classification scheme for grading occlusion of coiled cerebral aneurysms.<sup>17, 18</sup> Mascitelli et al.<sup>19</sup> expanded the classification to differentiate class 3 aneurysms into those that will completely occlude versus those that will not, thereby in the author's appraisal requiring further treatment. Their study focused on class 3 aneurysms only but showed the potential for the Modified Raymond Roy Classification (MRRC) to stratify patients with residual aneurysms into those at higher and lower risk for recurrence.<sup>19</sup>

The objective of our study is two-fold: 1) to characterize the natural history of first time coiled cerebral aneurysms, and 2) to identify risk factors associated with poor GDC durability. We hypothesize a stepwise decrease in durability of first time GDC-embolized cerebral aneurysms as stratified by the MRRC.

## **METHODS**

### *Patient Selection*

This retrospective study was approved by the Indiana University School of Medicine Institutional Review Board. Subject inclusion criteria included 1) first time GDC embolization (all coiling techniques) of saccular cerebral aneurysm, ruptured or unruptured; 2) age greater than 18 years old; 3) at least 6 months of radiographic follow-up; and 4) treatment performed between 2004 and 2015. Subjects were excluded if they had any of the following: 1) fusiform aneurysm architecture as well as traumatic or mycotic aneurysm etiology; 2) association with arteriovenous malformation; 3) association with a malignant brain tumor, and 4) previous endovascular or surgical treatment. Patient demographics, clinical presentation, treatment characteristics, and radiographic follow-up were assessed for each case.

### *Angiographic Review*

All initial and follow-up angiography was retrospectively reviewed. Initial arterial imaging was always performed with digital subtraction angiography (DSA). Follow-up angiography consisted of DSA and/or magnetic resonance angiography (MRA). Although the angiographic review was not blinded, the initial angiogram was always evaluated before the follow-up to reduce bias. All aneurysms were graded using the Modified Raymond Roy Classification.<sup>18,19</sup> Aneurysms were graded in at least two angiographic views. Aneurysms were classified as follows: Grade 1 - complete occlusion of aneurysm lumen and neck; Grade 2 - complete occlusion of aneurysm lumen with residual neck; Grade 3a - residual flow within the aneurysm but within the confines of the coil mass; Grade 3b - residual contrast opacification through a portion of the aneurysm neck with continuation along the aneurysm wall.

Aneurysm size classification was based on the International Study of Unruptured Intracranial Aneurysms definition.<sup>20</sup> The maximum aneurysm dome diameter was measured on initial preoperative angiogram and categorized as less than 7 mm, 7-12 mm, 13-24 mm, or greater than 25 mm.

#### *Defining Loss of Durability*

At our institution, all patients with endovascularly treated aneurysms receive serial DSA and/or MRA to evaluate treatment durability. For each patient, all follow-up imaging was assessed for dynamic changes in post-treatment aneurysm morphology as well as change in MRRC grade. Loss of durability (LOD) was defined by change in aneurysm size or patency discovered on serial radiographic follow-up and included 1) aneurysm re-rupture, 2) aneurysm recanalization, and 3) remnant aneurysm enlargement. The authors believe that these factors are signs of aneurysm instability.

#### *Statistical Analysis*

The MRRC was calculated for each aneurysm on pretreatment DSA as described previously. Kaplan Meier curves were created to graphically depict time to aneurysm LOD based on MRRC. The log-rank test was used to identify any statistical differences between the constructed Kaplan

Meier curves. Baseline patient, aneurysm, and treatment characteristic effects on coil durability were evaluated using multivariate Cox Regression analysis. Intraoperative complications and admission neurologic complications were assessed for differences between MRRC groups using the Pearson  $\chi^2$  test. All statistical analysis was performed using SPSS V.24.0 (IBM, Armonk, New York, USA).

## RESULTS

### *Baseline Patient, Aneurysm, and Treatment Characteristics*

From 2004 to 2015, 718 consecutive patients with 740 first time coil-embolized cerebral aneurysms were identified. Sixty-four patients (9%) died during their initial hospitalization from sequela of subarachnoid hemorrhage. Of the remaining 654 patients, 427 (65%) had radiographic follow-up greater than 6 months. Mean (SD) patient age at treatment was 56.0 (10.7) years. Most patients were female (75.5%). Mean (SD) follow-up was 36 (30) months.

The cohort was divided nearly in half for ruptured vs. unruptured aneurysm presentation (48.3% vs. 51.7%, respectively). Aneurysm size distribution was as follows: < 7 mm, 191 (43.2%); 7-12 mm, 215 (48.5%); 13-24 mm, 29 (6.5%); and > 25 mm, 8 (1.8%). There were 294 aneurysms (66.4%) in the anterior circulation. Most aneurysms were treated with coil embolization alone (76.8%). Stent assist and balloon assist was performed in 20.3% and 2.9%, respectively (Table 1).

### *Change in MRRC Over Time*

Immediate post-treatment MRRC grade 1 (n = 114) aneurysms at the time of last follow-up or time of retreatment were reclassified as follows: grade 1, n = 105 (92%); grade 2, n = 5 (4%); grade 3a, n = 1 (1%); grade 3b, n = 3 (3%). Immediate post-treatment MRRC grade 2 (n = 143) aneurysms at the time of last follow-up or time of retreatment were reclassified as follows: grade 1, n = 35 (24%); grade 2, n = 98 (69%); grade 3a, n = 2 (1%); grade 3b, n = 8 (6%).

Immediate post-treatment MRRC grade 3a (n = 159) aneurysms at the time of last follow-up or time of retreatment were reclassified as follows: grade 1, n = 72 (45%); grade 2, n = 67 (42%); grade 3a, n = 13 (8%); grade 3b, n = 7 (5%). Immediate post-treatment MRRC grade 3b (n = 27)

aneurysms at the time of last follow-up or time of retreatment were reclassified as follows: grade 1, n = 6 (22%); grade 2, n = 14 (52%); grade 3a, n = 1 (4%); grade 3b, n = 6 (22%) (Figure 1).

#### *Loss of Durability*

Overall, 89 (21%) aneurysms met LOD criteria. Two (2%) patients experienced post-treatment aneurysm rupture (both with hemorrhage at presentation), 15 (17%) experienced aneurysm enlargement, and 72 (81%) experienced recanalization. Nine MRRC grade 1 aneurysms experienced LOD at time of retreatment as follows: grade 1, n = 0 (0%); grade 2, n = 5 (56%); grade 3a, n = 1 (11%); grade 3b, n = 3 (33%). Thirty-two MRRC grade 2 aneurysms experienced LOD at time of retreatment as follows: grade 1, n = 0 (0%); grade 2, n = 22 (69%); grade 3a, n = 2 (6%); grade 3b, n = 8 (25%). Thirty-six MRRC grade 3a aneurysms experienced LOD at time of retreatment as follows: grade 1, n = 0 (0%); grade 2, n = 22 (62%); grade 3a, n = 7 (19%); grade 3b, n = 7 (19%). Twelve MRRC grade 3b aneurysms experienced LOD at time of retreatment as follows: grade 1, n = 0 (0%); grade 2, n = 6 (50%); grade 3a, n = 0 (%); grade 3b, n = 6 (50%) (**FIGURE 2**). Overall, 26 (29%) aneurysms experienced worsening of MRRC grade with associated LOD.

#### *Kaplan Meier Analysis*

Mean (SD) time to LOD for grade 1, 2, 3a, and 3b aneurysms was 99 (6), 106 (6), 104 (6), and 57 (10) months, respectively. Grade 1 aneurysms were found to have statistically significantly greater durability than grade 2 ( $p = 0.002$ ), 3a ( $p = 0.003$ ), and 3b ( $p < 0.001$ ) aneurysms. Grade 3b aneurysms had significantly worse durability than all other aneurysm grades ( $p < 0.015$ ). There was no difference in durability between grade 2 and 3a aneurysms ( $p = 0.845$ ). Estimated long-term cumulative durability (SD) at 10 years for grade 1, 2, 3a, and 3b aneurysms was 76.9 (1.0), 70.9 (4.6), 67.5 (5.7), and 47.2 (10.8) percent, respectively (FIGURE 3).

#### *Cox Regression Analysis*

Multivariate Cox Regression analysis revealed that only MRRC is statistically significantly associated with aneurysm durability ( $p = 0.001$ ). All MRRC grades when compared to MRRC grade 1 portend significantly worse durability (Table 2). Specifically, the following variables did

not significantly affect aneurysm treatment durability in our multivariate analysis: age ( $p = 0.500$ ), sex ( $p = 0.298$ ), smoker ( $p = 0.379$ ), hypertension ( $p = 0.106$ ), ruptured ( $p = 0.158$ ), anterior vs. posterior circulation ( $p = 0.847$ ), aneurysm size ( $0.074$ ), and aneurysm treatment type ( $p = 0.773$ ) (Table 2).

#### *Complications and Clinical Outcome*

There was no statistically significant difference in intraoperative complications between MRRC groups: rupture ( $p = 0.911$ ), coil migration ( $p = 0.408$ ), parent vessel compromise ( $p = 0.237$ ), dissection ( $p = 1.00$ ), thromboembolic event ( $p = 0.761$ ), and femoral artery injury ( $p = 1.000$ ). There was no statistically significant difference between MRRC groups for development of new hydrocephalus ( $p = 0.479$ ), need for external ventricular drain placement ( $p = 0.882$ ), need for ventriculoperitoneal shunt placement ( $p = 0.420$ ), development of vasospasm ( $p = 0.807$ ), new ischemic stroke ( $p = 0.896$ ), or new intracranial hemorrhage ( $p = 0.683$ ).

Across MRRC groups there was a statistically significant difference in new neurologic deficit ( $p = 0.008$ ). A significant difference in new neurologic deficits was found between MRRC grade 1 and 3b ( $p = 0.0024$ ). MRRC grade 1 aneurysm patients were statistically significantly less likely to have a new neurologic deficit post treatment. There was a trend toward greater neurologic deficits between MRRC grade 3b and grades 2 and 3a ( $p = 0.0523$  and  $p = 0.0587$ , respectively). MRRC grade 2 and 3a aneurysm patients were less likely to have a new neurologic deficit post treatment, although this did not reach statistical significance. There was a trend toward significantly different mortality rates across MRRC groups, but this did not reach statistical significance ( $p = 0.057$ ) (Table 3).

## **DISCUSSION**

The natural history of coiled cerebral aneurysms remains debated. There is a large body of literature describing rates of aneurysm recurrence, retreatment, and re-bleeding but there is a paucity of data on long-term coil stability. In our study, we defined loss of durability as dynamic change in aneurysm morphology (i.e., aneurysm growth or interval increase in aneurysm patency) because it identifies aneurysms that are thought to require, by a high-volume tertiary care academic practice, additional treatment. While this metric on the one hand is dependent on



radiographic interpretation, it may very well also represent the most objective endpoint for a treated aneurysm apart from (re)rupture.

This standard categorizes aneurysm coil durability into reproducible subsets; the aneurysm is either unchanged (or less patent) from the original coiling or it is more patent. This standard, however, reflects only coil durability and not aneurysm stability. There may very well be small post-coil aneurysm remnants which remain unchanged on follow-up imaging but which can (re)rupture. In the end, the most objective system for evaluating aneurysm treatment is one that dichotomizes between cure versus non-cure.<sup>21</sup>

Evaluating aneurysm coil durability by morphologic change versus MRRC eliminates estimations of whether aneurysm patency extends to the saccular wall and does not rely on a somewhat arbitrary distinction between aneurysm neck and dome. The MRRC is limited to categorizing variations in filling only if the aneurysm can be reclassified as a different grade, i.e., if the dome versus the neck becomes patent or if the patent portion of the aneurysm extends to the saccular wall.

In our study, aneurysms were stratified by the MRRC because it is a well-known grading system commonly used to evaluate treatment outcome after cerebral aneurysm coiling. The MRRC grading system proved to be far less sensitive to changes thought by our neurovascular treatment group to be clinically significant than examining more subtle differences in patency. For example, seven aneurysms initially graded MRRC 3a remained grade 3a at the time of retreatment. They were retreated for subtle coil compaction and increased filling within the coil mass, not because of a change in MRRC grade. In the era of flow diversion in which true cure is an achievable goal for all aneurysms, this more sensitive evaluation system may reflect a more appropriate standard in evaluating for retreatment.

Changes in post-treatment aneurysm morphology over time after coiling is not well-documented in the scientific literature. Hayakawa et al.<sup>22</sup> described the natural history of the neck remnant shortly after popularization of coiling. They concluded that small aneurysms with small necks were able to be definitively treated with GDCs however, large or giant aneurysms with wide

necks experienced a high rate of recanalization.<sup>18</sup> To the authors knowledge, this is the only study that has examined GDC coil durability over time. While this study provides a framework for understanding factors associated with recanalization of neck remnants, it fails to address recanalization of MRRC type 3a and 3b remnants. Additionally, this study was underpowered to statistically identify factors independently associated with aneurysm loss of durability.

Our study examines post-treatment changes based on both MRRC and our more sensitive patency estimation through serial radiographic imaging. Initial MRRC grade 1 aneurysms tend to be the most stable over time, though aneurysms in each baseline MRRC grade tended to stay the same or improve. The implication of this radiographic improvement in persistently patent aneurysms has however not been demonstrated; i.e. until an aneurysm is cured, there is some risk of rupture and that risk may or may not be affected by decreased post-treatment aneurysm patency. In our experience, 89 (21%) aneurysms experienced LOD on serial imaging. This is in line with published recanalization rates.<sup>23</sup> Interestingly, only 26 (6%) of these aneurysms had associated changes in MRRC highlighting the increased sensitivity of a standard that utilizes increased patency following coiling versus change in MRRC categories.

Twenty-two (69%) grade 2 aneurysms experiencing LOD, had further coil compaction and remnant recanalization at the neck but without changes in MRRC grading (**FIGURE 4**). Similarly, 22 (62%) grade 3a aneurysms experiencing LOD had decreased patency and reversion to grade 2, but subsequently demonstrated recanalization at the neck (**FIGURE 5**).

To our knowledge, no studies have directly compared durability across all four MRRC groups.<sup>18,22,24,25-29</sup> In our study, grade 1, 2, and 3a aneurysms had similar mean time to LOD – approximately 100 months (8.3 years). Class 3b aneurysms had a significantly shorter time to LOD - 57 months (4.75 years). Kaplan Meier analysis demonstrated a step-wise decrease in aneurysm durability across MRRC grades (**FIGURE 1**). As hypothesized, we demonstrated a statistically significant stepwise decrease in LOD across MRRC grades - LOD grade 3b > grade 3a = grade 2 > grade 1.

Risk factors for aneurysm recurrence have been studied extensively. Incomplete aneurysm occlusion/recurrence leads to further interventional procedures and carries risk for aneurysm re-rupture. Prior studies have identified aneurysm size,<sup>23,27,30,31-33</sup> neck diameter,<sup>27,32,34</sup> packing density,<sup>23,30,35,36</sup> rupture status,<sup>2,23,32,33</sup> aneurysm location,<sup>23,37</sup> patient age,<sup>30,36,37</sup> and incomplete initial occlusion<sup>27,32</sup> as factors associated with aneurysm recurrence. Our study, although limited by its retrospective nature, is representative of a typical large volume academic aneurysm treatment center.

In our multivariate survival analysis, only MRRC grade was statistically significantly associated with aneurysm retreatment. Age, sex, smoking status, hypertension, rupture status, location, aneurysm size, and aneurysm treatment had no effect on coil durability. Our results indicate that immediate post coiling MRRC grade is the single most important factor in predicting coil occlusion longevity.

An interesting observation in our study was that incompletely treated aneurysms can progress to complete occlusion over time. In fact, in our study this occurrence was more common than LOD. Overall, 113 (34%) of all aneurysms that were not initially MRRC grade 1 progressed to complete occlusion over time without retreatment. MRRC grade 3a aneurysms were most likely to progress to complete occlusion. This finding demonstrates the need for close aneurysm follow-up. Treatment is warranted for changes in aneurysm morphology, not for persistent filling without changes in flow dynamics.

The most common complications following endovascular coiling of cerebral aneurysms are thromboembolic with a frequency of 2.4 to 10% in the literature.<sup>38-41</sup> In our series this occurred in 16 (3.7%) of patients. Of these patients, 11 (69%) suffered from an infarct on follow-up MRI. One patient developed ischemic stroke due to parent vessel compromise. Intraoperative rupture is another frequently cited complication occurring in 0 to 8% of studies.<sup>15,42-45</sup> In our series, this occurred in 4 (1%) of the patients. No patient died or suffered permanent neurologic deficit as a direct result of intraoperative rupture. Mortality from coiling procedures ranges from 0 to 2% in the literature.<sup>41,42,46</sup> In our cohort, 6 (1.4%) patients died, but no deaths were recorded in the immediate perioperative period. There was no statistically significant difference in intraoperative

complications across different MRRC groups. MRRC 3b aneurysms had statistically greater chance of new neurologic deficits than the MRRC group 1. Two grade 1 patients experienced new neurologic deficits – both due to vasospasm after coiling and consequences of subarachnoid hemorrhage. Four grade 3b patients experienced new neurologic deficits – two patients experienced vasospasm after coiling, one patient developed hemiparesis and ischemic stroke symptoms, and one patient developed double vision after coiling. All new neurologic deficits in both groups resolved by the time of last follow-up.

This study has a number of limitations. It is a retrospective study which inherently introduces bias. The study spanned a 12-year period during which significant innovation in the endovascular technologies occurred. The number of patients lacking long-term follow-up that were unable to be included in our study is also a potential source of selection bias that cannot be ignored. The subjective nature of the angiographic grading system is an additional shortcoming. Although the Raymond Roy Classification system is widely accepted, it has not been prospectively validated for intra- and inter-observer reliability. Lastly, this is a single center study and therefore our results may not be generalizable.

## **CONCLUSIONS**

MRRC grade is independently associated with durability of coil occlusion among the first time GDC-embolized cerebral aneurysms. Achieving MRRC grade 1 occlusion outcome is significantly associated with greater long-term coil durability, particularly as compared with grade 3b occlusion. Although few aneurysms experience further growth and/or recanalization, it appears that a majority of incompletely obliterated aneurysms tend to remain stable and/or occlude over time. Grading scales such as the MRRC are useful for characterizing aneurysm occlusion but appear to lack sensitivity and specificity for characterizing more sensitive changes in aneurysm morphology over time.

## **REFERENCES**

1. Vlak MH, Algra A, Brandenburg R, Rinkel GJ: Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. *Lancet Neurol* 10:626-636, 2011
2. van Gijn J, Rinkel GJ: Subarachnoid haemorrhage: diagnosis, causes and management. *Brain* 124:249-278, 2001
3. Kassell NF, Sasaki T, Colohan AR, Nazar G: Cerebral vasospasm following aneurysmal subarachnoid hemorrhage. *Stroke* 16:562-572, 1985
4. Sarti C, Tuomilehto J, Salomaa V, Sivenius J, Kaarsalo E, Narva EV, et al: Epidemiology of subarachnoid hemorrhage in Finland from 1983 to 1985. *Stroke* 22:848-853, 1991
5. Solenski NJ, Haley EC, Jr., Kassell NF, Kongable G, Germanson T, Truskowski L, et al: Medical complications of aneurysmal subarachnoid hemorrhage: a report of the multicenter, cooperative aneurysm study. Participants of the Multicenter Cooperative Aneurysm Study. *Crit Care Med* 23:1007-1017, 1995
6. Jalbert JJ, Isaacs AJ, Kamel H, Sedrakyan A: Clipping and Coiling of Unruptured Intracranial Aneurysms Among Medicare Beneficiaries, 2000 to 2010. *Stroke* 46:2452-2457, 2015
7. Guglielmi G, Vinuela F, Sepetka I, Macellari V: Electrothrombosis of saccular aneurysms via endovascular approach. Part 1: Electrochemical basis, technique, and experimental results. *J Neurosurg* 75:1-7, 1991
8. Guglielmi G, Vinuela F, Dion J, Duckwiler G: Electrothrombosis of saccular aneurysms via endovascular approach. Part 2: Preliminary clinical experience. *J Neurosurg* 75:8-14, 1991
9. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, et al: International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet* 360:1267-1274, 2002
10. McDougall CG, Spetzler RF, Zabramski JM, Partovi S, Hills NK, Nakaji P, et al: The Barrow Ruptured Aneurysm Trial. *J Neurosurg* 116:135-144, 2012

11. Spetzler RF, McDougall CG, Albuquerque FC, Zabramski JM, Hills NK, Partovi S, et al: The Barrow Ruptured Aneurysm Trial: 3-year results. *J Neurosurg* 119:146-157, 2013
12. Spetzler RF, McDougall CG, Zabramski JM, Albuquerque FC, Hills NK, Russin JJ, et al: The Barrow Ruptured Aneurysm Trial: 6-year results. *J Neurosurg* 123:609-617, 2015
13. Campi A, Ramzi N, Molyneux AJ, Summers PE, Kerr RS, Sneade M, et al: Retreatment of ruptured cerebral aneurysms in patients randomized by coiling or clipping in the International Subarachnoid Aneurysm Trial (ISAT). *Stroke* 38:1538-1544, 2007
14. Molyneux AJ, Kerr RS, Birks J, Ramzi N, Yarnold J, Sneade M, et al: Risk of recurrent subarachnoid haemorrhage, death, or dependence and standardised mortality ratios after clipping or coiling of an intracranial aneurysm in the International Subarachnoid Aneurysm Trial (ISAT): long-term follow-up. *Lancet Neurol* 8:427-433, 2009
15. Gallas S, Pasco A, Cottier JP, Gabrillargues J, Drouineau J, Cognard C, et al: A multicenter study of 705 ruptured intracranial aneurysms treated with Guglielmi detachable coils. *AJNR Am J Neuroradiol* 26:1723-1731, 2005
16. Koivisto T, Vanninen R, Hurskainen H, Saari T, Hernesniemi J, Vapalahti M: Outcomes of early endovascular versus surgical treatment of ruptured cerebral aneurysms. A prospective randomized study. *Stroke* 31:2369-2377, 2000
17. Stapleton CJ, Torok CM, Rabinov JD, Walcott BP, Mascitelli JR, Leslie-Mazwi TM, et al.: Validation of the Modified Raymond-Roy classification for intracranial aneurysms treated with coil embolization. *J Neurointerv Surg* 8:927-933, 2016
18. Roy D, Milot G, Raymond J: Endovascular treatment of unruptured aneurysms. *Stroke* 32:1998-2004, 2001
19. Mascitelli JR, Moyle H, Oermann EK, Polykarpou MF, Patel AA, Doshi AH, et al: An update to the Raymond-Roy Occlusion Classification of intracranial aneurysms treated with coil embolization. *J Neurointerv Surg* 7:496-502, 2015

20. Wiebers DO, Whisnant JP, Huston J, 3rd, Meissner I, Brown RD, Jr., Piepgras DG, et al: Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet* 362:103-110, 2003
21. Becske T, Kallmes DF, Saatci I, McDougall CG, Szikora I, Lanzino G, et al: Pipeline for uncoilable or failed aneurysms: results from a multicenter clinical trial. *Radiology* 267:858-868, 2013
22. Hayakawa M, Murayama Y, Duckwiler GR, Gobin YP, Guglielmi G, Vinuela F: Natural history of the neck remnant of a cerebral aneurysm treated with the Guglielmi detachable coil system. *J Neurosurg* 93:561-568, 2000
23. Ferns SP, Sprengers ME, van Rooij WJ, Rinkel GJ, van Rijn JC, Bipat S, et al: Coiling of intracranial aneurysms: a systematic review on initial occlusion and reopening and retreatment rates. *Stroke* 40:e523-529, 2009
24. Gallas S, Januel AC, Pasco A, Drouineau J, Gabrillargues J, Gaston A, et al: Long-term follow-up of 1036 cerebral aneurysms treated by bare coils: a multicentric cohort treated between 1998 and 2003. *AJNR Am J Neuroradiol* 30:1986-1992, 2009
25. Mascitelli JR, Oermann EK, De Leacy RA, Moyle H, Patel AB: Angiographic outcome of intracranial aneurysms with neck remnant following coil embolization. *J Neurointerv Surg* 7:484-489, 2015
26. Ng P, Khangure MS, Phatouros CC, Bynevelt M, ApSimon H, McAuliffe W: Endovascular treatment of intracranial aneurysms with Guglielmi detachable coils: analysis of midterm angiographic and clinical outcomes. *Stroke* 33:210-217, 2002
27. Ries T, Siemonsen S, Thomalla G, Grzyska U, Zeumer H, Fiehler J: Long-term follow-up of cerebral aneurysms after endovascular therapy prediction and outcome of retreatment. *AJNR Am J Neuroradiol* 28:1755-1761, 2007
28. Willinsky RA, Peltz J, da Costa L, Agid R, Farb RI, terBrugge KG: Clinical and angiographic follow-up of ruptured intracranial aneurysms treated with endovascular embolization. *AJNR Am J Neuroradiol* 30:1035-1040, 2009

28. Yamazaki T, Sonobe M, Nakai Y, Sugita K, Matsumaru Y, Yanaka K, et al: Predictors of angiographic changes in neck remnants of ruptured cerebral aneurysms treated with Guglielmi detachable coils. *Neurol Med Chir (Tokyo)* 46:1-9; discussion 9-10, 2006
29. Leng B, Zheng Y, Ren J, Xu Q, Tian Y, Xu F: Endovascular treatment of intracranial aneurysms with detachable coils: correlation between aneurysm volume, packing, and angiographic recurrence. *J Neurointerv Surg* 6:595-599, 2014
30. Murias Quintana E, Gil Garcia A, Vega Valdes P, Cuellar H, Meilan Martinez A, Saiz Ayala A, et al: Anatomical results, rebleeding and factors that affect the degree of occlusion in ruptured cerebral aneurysms after endovascular therapy. *J Neurointerv Surg* 7:892-897, 2015
31. Raymond J, Guilbert F, Weill A, Georganos SA, Juravsky L, Lambert A, et al: Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. *Stroke* 34:1398-1403, 2003
32. Tan IY, Agid RF, Willinsky RA: Recanalization rates after endovascular coil embolization in a cohort of matched ruptured and unruptured cerebral aneurysms. *Interv Neuroradiol* 17:27-35, 2011
33. Vanzin JR, Mounayer C, Abud DG, D'Agostini Annes R, Moret J: Angiographic results in intracranial aneurysms treated with inert platinum coils. *Interv Neuroradiol* 18:391-400, 2012
34. Chalouhi N, Dumont AS, Hasan D, Tjoumakaris S, Gonzalez LF, Starke RM, et al: Is packing density important in stent-assisted coiling? *Neurosurgery* 71:381-386; discussion 386-387, 2012
35. Grunwald IQ, Balami JS, Weber D, Mutter J, Kuhn AL, Krick C, et al: Different factors influence recanalisation rate after coiling in ruptured and unruptured intracranial aneurysms. *CNS Neurol Disord Drug Targets* 12:228-232, 2013



36. Corns R, Zebian B, Tait MJ, Walsh D, Hampton T, Deasy N, et al: Prevalence of recurrence and retreatment of ruptured intracranial aneurysms treated with endovascular coil occlusion. *Br J Neurosurg* 27:30-33, 2013
37. Cronqvist M, Wirestam R, Ramgren B, Brandt L, Nilsson O, Saveland H, et al: Diffusion and perfusion MRI in patients with ruptured and unruptured intracranial aneurysms treated by endovascular coiling: complications, procedural results, MR findings and clinical outcome. *Neuroradiology* 47:855-873, 2005
38. Derdeyn CP, Cross DT, 3rd, Moran CJ, Brown GW, Pilgram TK, Diringner MN, et al: Postprocedure ischemic events after treatment of intracranial aneurysms with Guglielmi detachable coils. *J Neurosurg* 96:837-843, 2002
39. Murayama Y, Nien YL, Duckwiler G, Gobin YP, Jahan R, Frazee J, et al: Guglielmi detachable coil embolization of cerebral aneurysms: 11 years' experience. *J Neurosurg* 98:959-966, 2003
40. Park HK, Horowitz M, Jungreis C, Genevro J, Koebbe C, Levy E, et al: Periprocedural morbidity and mortality associated with endovascular treatment of intracranial aneurysms. *AJNR Am J Neuroradiol* 26:506-514, 2005
41. Batista LL, Mahadevan J, Sachet M, Alvarez H, Rodesch G, Lasjaunias P: 5-year Angiographic and Clinical Follow-up of Coil-embolised Intradural Saccular Aneurysms. A Single Center Experience. *Interv Neuroradiol* 8:349-366, 2002
42. Groden C, Eckert B, Ries T, Probst EN, Kucinski T, Zeumer H: Angiographic follow-up of vertebrobasilar artery aneurysms treated with detachable coils. *Neuroradiology* 45:435-440, 2003

43. Kole MK, Pelz DM, Kalapos P, Lee DH, Gulka IB, Lownie SP: Endovascular coil embolization of intracranial aneurysms: important factors related to rates and outcomes of incomplete occlusion. *J Neurosurg* 102:607-615, 2005
44. Levy E, Koebe CJ, Horowitz MB, Jungreis CA, Pride GL, Dutton K, et al: Rupture of intracranial aneurysms during endovascular coiling: management and outcomes. *Neurosurgery* 49:807-811; discussion 811-803, 2001
45. Henkes H, Fischer S, Mariushi W, Weber W, Liebig T, Miloslavski E, et al: Angiographic and clinical results in 316 coil-treated basilar artery bifurcation aneurysms. *J Neurosurg* 103:990-999, 2005

## FIGURE LEGENDS

**FIGURE 1** – Immediate post-treatment modified Raymond Roy Classification (MRRC) grade (Black) versus last follow-up MRRC Grade or MRRC Grade at loss of durability (Grey).

**FIGURE 2** – Immediate post-treatment modified Raymond Roy Classification (MRRC) grade (Black) for aneurysms experiencing LOD versus Grade at loss of durability (Grey).

**FIGURE 3.** Kaplan Meier Time to Loss of Durability Curve stratified by Modified Raymond Roy Classification Grading.

**FIGURE 4.** **A:** Initial angiogram demonstrating a 12-mm anterior communicating artery aneurysm on right internal carotid artery injection. **B:** Post-coiling angiogram demonstrating modified Raymond Roy Classification (MRRC) Grade 2 remnant. **C:** 6-month post-treatment MRA demonstrating enlargement of base remnant. **D:** Follow-up angiogram after MRA evidence of base recanalization demonstrating clear evidence of coil compaction with base enlargement but grade remains MRRC 2. **E:** Retreatment of base recurrence. **F:** Final outcome after retreatment demonstrating MRRC Grade 3a.

**FIGURE 5.** **A:** Initial angiogram demonstrating a 17mm basilar apex aneurysm. **B:** Post-coiling angiogram demonstrating MRRC Grade 3 remnant (note filling within the coil mass), **C:** 1-month post-treatment angiogram demonstrating MRRC Grade 2 with significant coil-compaction at the base of the aneurysm: **D:** Post-retreatment angiogram demonstrating MRRC Grade 1 result. **E:** 6-month post-retreatment MRA demonstrating coil compaction at the base resulting in MRRC Grade 2. **F:** 12-month Post-retreatment MRA demonstrating stability of MRRC Grade 2 aneurysm.

**TABLE 1** - Baseline Patient, Aneurysm, and Treatment Characteristics.

<b>Patient Demographics</b>	
Patients, n	427
Aneurysms, n	443
Age, mean(SD), y	56.0 (10.7)
Female, n (%)	330 (75.5)
Smoker, n (%)	287 (64.7)
Hypertension, n (%)	237 (53.4)
Aneurysm Retreatment	89 (20.1)
<b>Modified Raymond Roy Treatment Grade</b>	
1, n (%)	114 (25.7)
2, n (%)	143 (32.3)
3a, n (%)	159 (35.9)
3b, n (%)	27 (6.1)
<b>Rupture Status</b>	
Ruptured, n (%)	214 (48.3)
Unruptured, n (%)	229 (51.7)
▶ Symptomatic, n (%)	48 (21.0)
<b>Aneurysm Size (mm)</b>	
< 7, n (%)	191 (43.2)
7-12, n (%)	215 (48.5)
13-24, n (%)	29 (6.5)
>25, n (%)	8 (1.8)
<b>Aneurysm Location</b>	
<i>Anterior Circulation, n (%)</i>	294 (66.4)
▶ Anterior communicating, n (%)	97 (21.9)
▶ Posterior communicating, n (%)	59 (13.3)
▶ Ophthalmic, n (%)	49 (11.1)
▶ ICA bifurcation, n (%)	16 (3.6)
▶ Pericallosal, n (%)	14 (3.2)
▶ MCA, n (%)	14 (3.2)
▶ Cavernous ICA, n (%)	12 (2.7)
▶ ICA paraclinoid, n (%)	12 (2.7)
▶ Superior hypophyseal, n (%)	11 (2.5)
▶ Anterior choroidal, n (%)	5 (1.1)
▶ ACA other, n (%)	3 (0.7)
▶ ICA other, n (%)	2 (0.5)
<i>Posterior Circulation, n (%)</i>	149 (33.6)
▶ Basilar tip, n (%)	102 (23.0)
▶ Basilar trunk, n (%)	16 (3.6)
▶ SCA, n (%)	11 (2.5)
▶ PCA, n (%)	9 (2.0)

▶ PICA, n (%)	7 (1.6)
▶ Vertebral, n (%)	2 (0.5)
▶ AICA, n (%)	1 (0.2)
▶ Basilar Fenestration, n (%)	1 (0.2)
<b>Procedure Assistance</b>	
Stand-alone, n (%)	340 (76.8)
Stent assist, n (%)	90 (20.3)
Balloon assist, n (%)	13 (2.9)

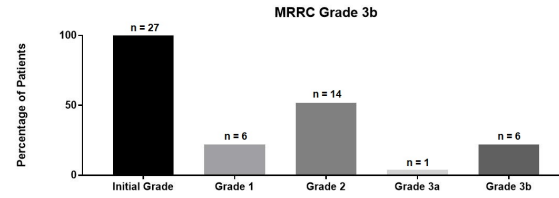
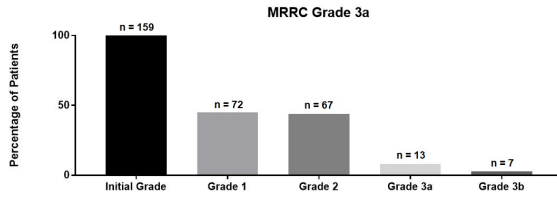
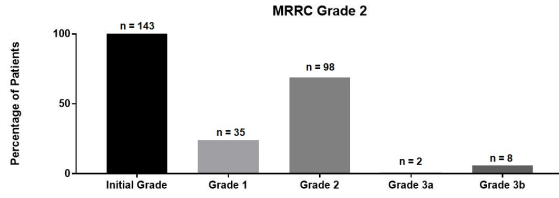
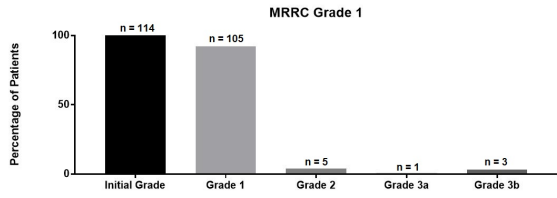
ICA = Internal Carotid Artery; MCA= Middle Cerebral Artery; ACA = Anterior Cerebral Artery; SCA = Superior Cerebellar Artery; PCA = Posterior Cerebral Artery; PICA= Posterior Inferior Cerebellar Artery; AICA = Anterior Inferior Cerebellar Artery

**Table 2.** Multivariate Cox Regression Analysis of Variables associated with Aneurysm Treatment Durability

	Sig.	Exp(B)	95.0% CI for Exp(B)	
			Lower	Upper
Age	.500	.992	.970	1.015
Sex	.298	.779	.487	1.247
Smoker	.379	.808	.502	1.300
Hypertension	.106	.690	.440	1.081
Ruptured	.158	.713	.445	1.141
Anterior vs. Posterior Circulation	.847	1.045	.667	1.639
<b>Aneurysm Size</b>				
< 7 mm (Reference)	.074			
7–12 mm	.161	.410	.118	1.427
13–24 mm	.592	.718	.213	2.415
> 25 mm	.977	.980	.259	3.713
<b>Aneurysm Treatment</b>				
Coil only (Reference)	.773			
Stent assist	.910	.940	.323	2.737
Balloon assist	.631	.752	.234	2.411
<b>Raymond Roy Classification</b>				
Grade 1 (Reference)	.001			
Grade 2	.000	.166	.069	.399
Grade 3a	.050	.505	.255	.999
Grade 3b	.026	.466	.238	.912

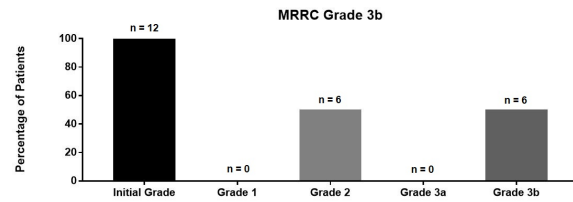
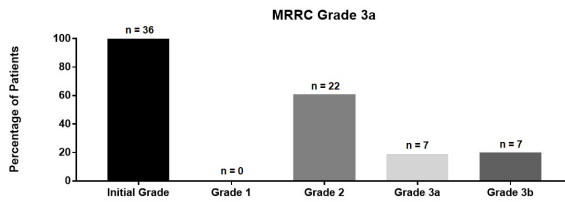
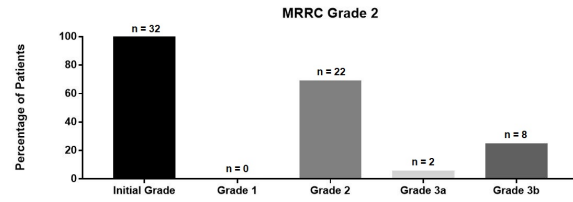
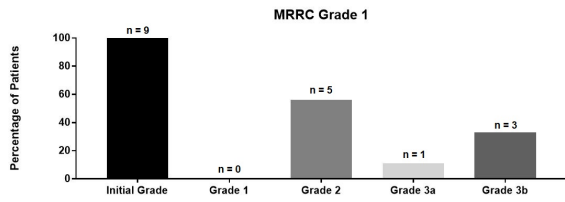
Table 3. Complications Stratified by Modified Raymond Roy Classification Grade. Across Group Comparisons Evaluated by Chi-Squared Statistical Method

	Modified Raymond Roy Classification Grade				p value
	1	2	3a	3b	
<b>Intraoperative Complications</b>					
Rupture, n (%)	1 (0.8)	1 (0.7)	2 (1.3)	0 (0)	0.911
Coil Migration, n (%)	1 (0.8)	0 (0)	0 (0)	0 (0)	0.408
Parent Vessel Compromise, n (%)	5 (4.4)	4 (2.8)	1 (0.6)	1 (3.7)	0.237
Dissection, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	1.000
Thromboembolic Event, n (%)	4 (3.5)	6 (4.2)	6 (3.8)	0 (0)	0.761
Femoral Artery Injury, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	1.000
<b>Admission Neurologic Complications</b>					
Hydrocephalus, n (%)	14 (12.3)	14 (10.0)	25 (15.7)	3 (11.1)	0.479
External Ventricular Drain Placement, n (%)	22 (19.3)	25 (17.5)	7 (4.4)	6 (22.2)	0.882
Ventriculoperitoneal Shunt Placement, n (%)	11 (9.6)	13 (9.1)	13 (8.2)	0 (0)	0.420
Vasospasm, n (%)	18 (15.8)	19 (13.3)	19 (11.9)	3 (11.1)	0.807
Ischemic Stroke, n (%)	4 (3.5)	3 (2.1)	4 (2.5)	1 (3.7)	0.896
Hemorrhage, n (%)	1 (0.8)	1 (0.7)	0 (0)	0 (0)	0.683
New Neurologic Deficit, n (%)	2 (1.8)	5 (3.5)	6 (3.8)	4 (14.8)	0.008
Death, n (%)	1 (0.8)	5 (3.5)	0 (0)	0 (0)	0.057
<b>Aneurysm Loss of Durability, n (%)</b>	<b>9 (7.9)</b>	<b>32 (22.4)</b>	<b>36 (22.6)</b>	<b>12 (44.4)</b>	<b>&lt;0.001</b>

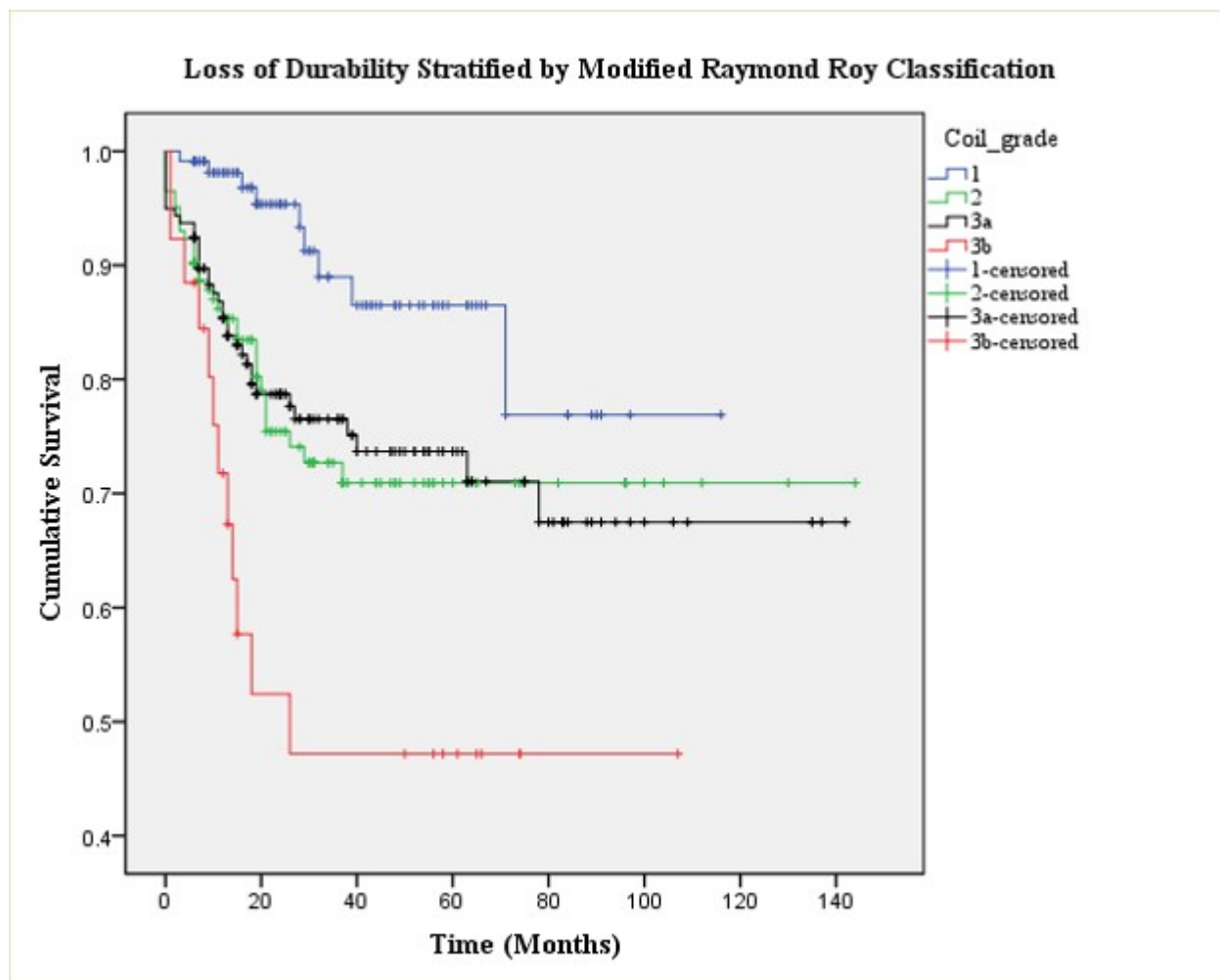


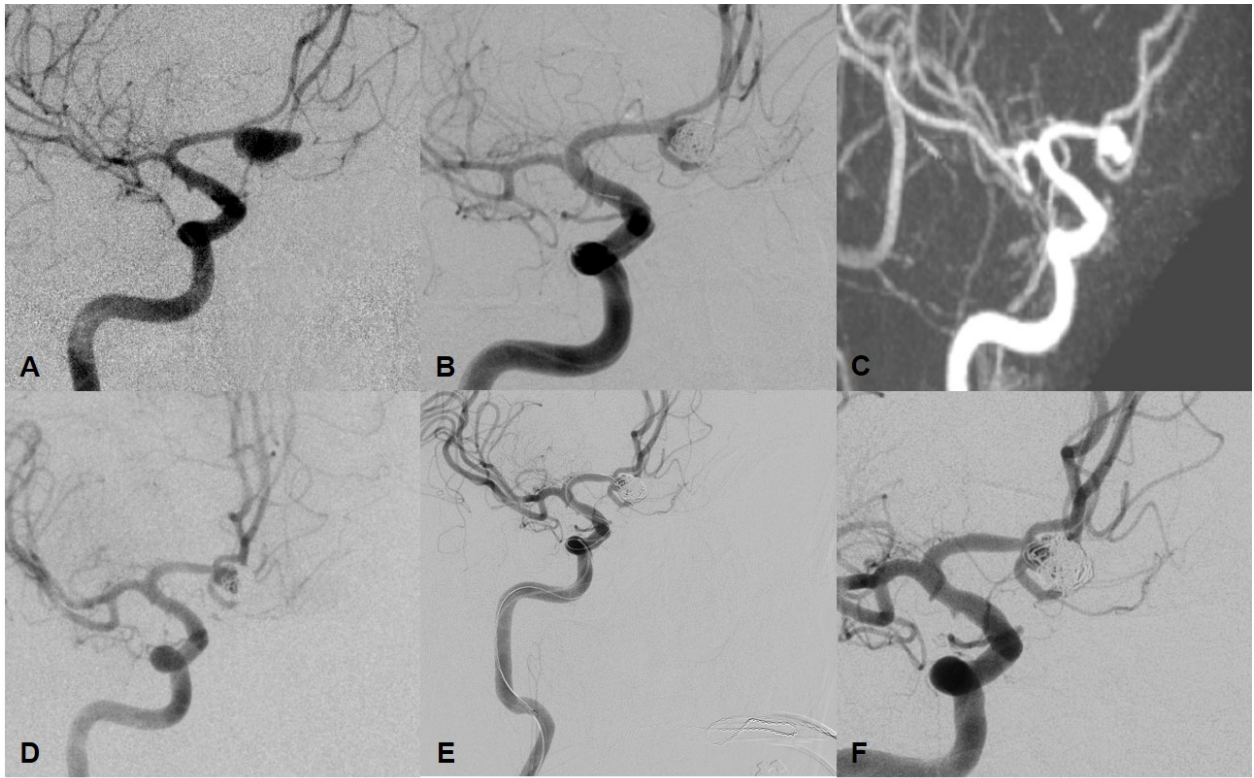
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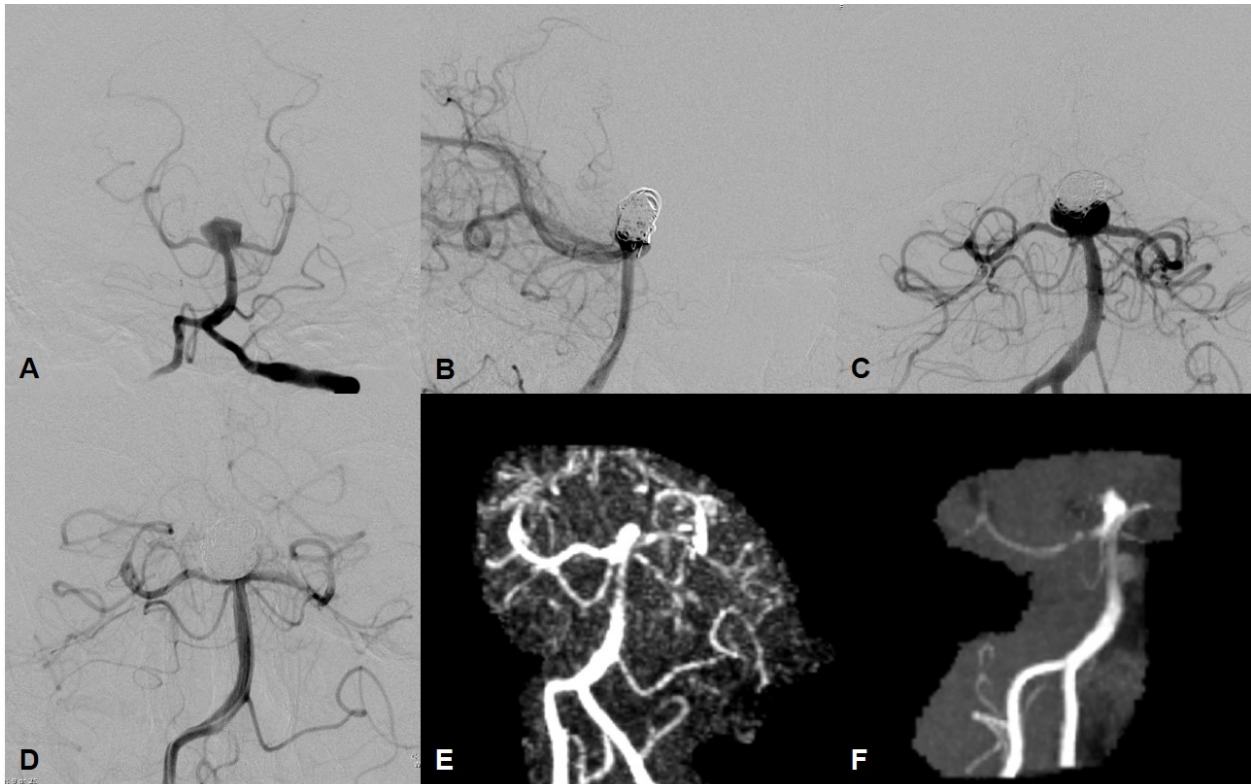




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**Abbreviations**

Guglielmi detachable coil = GDC

Loss of durability = LOD

modified Raymond Roy Classification = MRRC

intracranial aneurysms = IA

International Subarachnoid Aneurysm Trial = ISAT

Barrow Ruptured Aneurysm Trial = BRAT

digital subtraction angiography = DSA