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Aneurysm Characteristics, Coil Packing, and Post-Coiling Hemodynamics Affect Long-Term Treatment Outcome

Robert J. Damiano, MS[1,2], **Vincent M. Tutino, PhD**[2,3,4,5], **Nikhil Paliwal, PhD**[1,2], **Tatsat R. Patel, MS**[1,2], **Muhammad Waqas, MBBS**[3], **Elad I. Levy, MD**[3], **Jason M. Davies, MD-PhD**[3], **Adnan H. Siddiqui, MD-PhD**[2,3], **Hui Meng, PhD**[1,2,3,4,*]

[1]Department of Mechanical and Aerospace Engineering, University at Buffalo, State University of New York, Buffalo NY, USA, 14260

[2]Canon Stroke & Vascular Research Center, University at Buffalo, State University of New York, Buffalo NY, USA, 14260

[3]Department of Neurosurgery, University at Buffalo, State University of New York, Buffalo NY, USA, 14260

[4]Department of Biomedical Engineering, University at Buffalo, State University of New York, Buffalo NY, USA, 14260

[5]Department of Pathology and Anatomical Sciences, University at Buffalo, State University of New York, Buffalo NY, USA, 14260

[*]Correspondence: Hui Meng, PhD, Department of Mechanical and Aerospace Engineering, University at Buffalo, State University of New York, Buffalo, NY 14260, USA, huimeng@buffalo.edu, Phone: (716) 645-1458 / Fax: (716) 645-2883.

CONTRIBUTORSHIP STATEMENT

Study conception and design: RJD, VMT, NP, MW, JMD, AHS, HM. Acquisition of data: all authors. Analysis and interpretation of data: RJD, VMT, NP, MW, HM. Drafting of manuscript: RJD, VMT, NP, HM. Critical revision: all authors. All authors read and approved the final manuscript.

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DATA SHARING

All data relevant to the study are included in the article or uploaded as supplementary information.

Abstract

Background: Recurrence of intracranial aneurysms after endovascular coiling is a serious clinical concern.

Objective: We hypothesized that recurrence is associated with aneurysm morphology and flow, as well as the coil intervention and the induced flow modifications.

Methods: We collected 52 primary-coiling aneurysm cases that were either occluded (n=34) or recurrent (n=18) at >1 year follow-up. We created aneurysm models from pre-coiling digital subtraction angiographic images, calculated aneurysm morphology, simulated pre-coiling hemodynamics, modeled coil deployment, and obtained post-coiling hemodynamics for each case. We performed univariable analysis on 26 morphologic, treatment-specific, and hemodynamic parameters to distinguish between recurrent and occluded groups, and multivariable analysis to identify independently significant parameters associated with recurrence. Univariable analysis was also performed on ruptured and unruptured aneurysm subcohorts separately to investigate if they shared specific significant parameters.

Results: Recurrence was associated with pre-coiling aneurysm morphologic and flow parameters including larger size (maximum dimension and volume), larger neck (diameter, area, and neck-to-parent-artery ratio), and higher flow momentum and kinetic energy. Recurrence was also associated with lower coil packing (packing density and uncoiled volume), higher post-treatment flow (velocity, momentum, and kinetic energy), lower post-treatment washout time, and higher post-treatment impingement force at the neck. Multivariable analysis identified two aneurysmal characteristics (neck diameter and pre-coiling flow kinetic energy), one coil packing parameter (uncoiled volume), and one post-treatment hemodynamic parameter (flow momentum) that were independently associated with recurrence. In ruptured aneurysms, recurrence was associated with larger neck (diameter and area), whereas in unruptured aneurysms, recurrence was associated with larger size (maximum dimension and volume). In both subcohorts, recurrence was associated with higher post-coiling flow momentum and kinetic energy.

Conclusion: Recurrence at >1 year after coil treatment is associated with intrinsic aneurysm characteristics, coiling itself, and flow changes induced by coiling. Larger aneurysm size and neck, less coil packing, and higher intra-aneurysmal flow before and after coiling predict recurrence.

INTRODUCTION

Endovascular treatment with embolic coils is the primary intervention strategy for unruptured and ruptured intracranial aneurysms (IAs). Coiling excludes an IA from the cerebral circulation by creating flow stasis, thereby inducing thrombosis and occluding the sac. Despite widespread use, the major drawback of coiling is its efficacy at permanently occluding the IA. A systematic review of clinical literature on coiled IAs demonstrated that 16.6% recur and 20.8% recanalize based on follow-up imaging at an average of 14.1 months after treatment.[1] This is a serious clinical concern, as incomplete occlusion exposes the IA to further risk of rupture, while retreatment options are limited and can be risky.[2]

In the literature, recurrence following coil embolization has been associated with aneurysm characteristics including morphology and hemodynamics. In a study of 501 IAs, Raymond et al. found that IAs with size >10 mm and neck size >4 mm were at significantly higher risk of recurrence after coiling.[3] Additionally, using computational fluid dynamics (CFD) to study 57 basilar tip IAs, Sugiyama et al. demonstrated that the ratio of aneurysmal inflow rate to the basilar artery flow rate was significantly higher in IAs that recurred after coiling.[4] Thus, these evidence suggest that some IAs may be at higher risk of recurrence due to their intrinsic morphologic and flow characteristics. On the other hand, since the deployed coils cause flow stasis, the extent to which the sac is packed and how much flow modification the coils induce could also influence the occlusion outcome. Leng et al. found that recurrence was significantly higher in IAs that had <20% of their sac volume filled with coils.[5] Some CFD studies also found that recurrence was associated with higher flow at the IA neck post-coiling.[6, 7] Based on all these observations, we hypothesized that recurrence may be associated with both the intrinsic characteristics of the aneurysm (i.e. morphology and flow before coiling) and the coil intervention along with its induced flow modifications.

To test this hypothesis, we retrospectively collected 52 unruptured and ruptured IAs that were treated by primary-coiling, created patient-specific computer models from their pre-coiling digital subtraction angiography (DSA) images, calculated aneurysm morphology, and simulated pre-coiling hemodynamics using CFD. We then used our previously established finite element method (FEM) coiling technique to virtually recapitulate coil treatments in these aneurysm and performed post-coiling CFD.[8, 9] Univariable analysis was performed on 26 morphologic, treatment-specific, and hemodynamic parameters to find significant metrics that could discriminate treatment outcome (occluded vs. recurrent) at >1 year follow-up. Statistically significant parameters were further subjected to a multivariable analysis to identify independently significant parameters associated with recurrence. Additionally, because ruptured IAs require emergent care and thus are approached differentially in their treatment, we investigated ruptured and unruptured IAs separately to identify parameters associated with treatment outcome in each subcohort using univariable analysis.

METHODS

Patient selection

Under institutional review board approval, we collected de-identified images and medical record data for patients with unruptured or ruptured IAs treated by primary-coiling from 2006 to 2016 at Gates Vascular Institute (Buffalo, NY). We included IAs that: (1) had no prior treatment, (2) had pre-coiling 3D DSA images with sufficient quality for computational modeling, (3) were treated only with bare platinum coils, (4) were not retreated <1 year after treatment, and (5) had follow-ups >1 year after treatment. We excluded IAs that were treated with bioactive coils, hydrogel coils, or adjunctive stents.

For all included cases, we collected pre-coiling angiographic images, follow-up images, and medical record data including patient age, gender, smoking history, hypertension, IA location and rupture status, initial occlusion status, and brand, type, and size of the coils used for treatment. Aneurysms were classified as “occluded” or “recurrent” based on their most recent follow-up >1 year.

IA model creation

We created 3D computer models of each IA from pre-coiling DSA images using The Vascular Modeling Toolkit (VMTK, http://www.vmtk.org/). Images were segmented using the level set and marching cube algorithms in VMTK to create STL (stereolithography) models of the IAs. Segmented STL models were imported into ICEM CFD (ANSYS Inc., Canonsburg, PA) where the IA domain was cleaned of artifacts and isolated.

Computational fluid dynamics methods

We simulated pre- and post-coiling hemodynamics using CFD in Star-CCM+ (ver. 12.06, Siemens PLM Software, Plano, TX). Blood flow was assumed to be pulsatile, incompressible, and laminar. We modeled blood as a non-Newtonian fluid with a density of 1056 kg/m^3 and a viscosity determined by the Carreau-Yasuda model. Coefficients for the model were provided in supplemental material and were taken from a previous study.[10]

At the vessel inlets in all cases, we imposed a pulsatile velocity waveform obtained from a healthy subject due to lack of patient-specific waveforms.[11] For each specific case, we scaled the waveform using published flow rates for given vessel locations,[12] assuming that flow rate scales with the cube of the inlet vessel diameter.[13] At each vessel outlet, we specified the fraction of total mass flow assuming that the fraction was proportional to the cube of the outlet diameter.[14] Aneurysms, vessels, and coils were assumed non-compliant to avoid prohibitively costly fluid-structure interaction simulations, and their surfaces were assigned as no-slip boundaries for the viscous blood flow.

We generated computational grids for each IA model using polyhedral cells in Star-CCM+. A mesh independence study is described in supplemental material. For each simulation, 3 cardiac cycles were run to ensure solution convergence, and the third cycle was output to calculate the investigated hemodynamic parameters. The time for one cardiac cycle was 0.928 s with a solver time-step of 0.001 s.

FEM modeling of coil interventions

To recapitulate the specific coil intervention in each case virtually, we used our previously established FEM coiling technique to model coil deployments.[8, 9] For each case, we created beam element models of the specific coils used in the intervention based on their physical properties, which included their length, diameter, pre-shape diameter, and material properties of their primary wire. We consulted with the post-coiling angiographic images to see how the coils were deployed in the actual treatment. Then, we recreated the treatment in the aneurysm model using our FEM technique in Abaqus (ver.2016, SIMULIA, Providence, RI). The full technical details of this technique are published elsewhere.[8, 9]

Parameter definitions

Table 1 shows a summary of all the parameters investigated, divided into three categories:

Aneurysm characteristics—Also referred to as intrinsic aneurysmal characteristics, these are 3D morphologic and hemodynamic parameters of the patient's IA before treatment. For IA morphology, we calculated parameters that in various ways describe the aneurysm's "*size*", "*neck*", and "*shape*", as shown in Table 1. Here, italicized words refer to a group of parameters. All morphology parameters were previously defined,[15] except for 3D neck ratio (NR_{3D}), which we introduce in this study as the ratio of average neck dimension to average parent vessel diameter, both measured in 3D. It is a 3D version of our previously introduced 2D neck ratio, NR_{2D}, which was found to be significantly associated with outcomes of flow diverter (FD)-treated IAs.[16]

From CFD, we calculated pre-coiling hemodynamic parameters that characterize flow entering the IA at its neck, i.e. "*trans-neck flow*", and parameters that describe flow inside the IA sac volume, i.e. "*intra-aneurysmal flow*", as shown in Table 1. The reason for investigating these characteristics was that histopathologic findings on coiled human IAs suggested roles of thrombus formation in the IA sac and neointima formation at the IA neck in healing after coiling.[17] In total, we investigated seven hemodynamic parameters, including three that we defined previously in studies of FD-treated IAs: aneurysm-averaged velocity (Vel.), aneurysm-averaged shear rate ($\dot{\gamma}$), and inflow rate at the IA neck (Q_{in}).[18, 19] We also defined four new hemodynamic parameters for coiling: aneurysmal flow momentum (M – energy content of flow in the IA sac), aneurysmal flow kinetic energy (KE – another measure of flow energy in the sac), washout time (t_w–quantified flow stasis in the sac), and impingement force (F_i – amount of flow force at the IA neck plane). Details of their definitions can be found in supplemental material. For visualization of flow in occluded and recurrent IAs, we also calculated time-averaged blood streamlines and volume-rendered velocity magnitudes in representative cases.

Coil packing—To characterize the degree of coil packing inside the aneurysm, we calculated two parameters: coil packing density (PD) and uncoiled volume (V_o). Packing density is a well-established clinical parameter and is defined as the percentage of IA volume taken up by coils. Uncoiled volume (V_o) was defined previously as the aneurysm volume (before coiling) minus the total volume of deployed coils and was found to be associated with recurrence.[20]

Post-treatment hemodynamics—To characterize post-coiling flow, we used the hemodynamic quantities as defined above in terms of *trans-neck* and *intra-aneurysmal flow* (Table 1), but calculated after virtual deployment of coils into the IAs and post-coiling CFD.

Statistical analysis

Univariable analysis was performed on the 26 investigated parameters to determine which were significantly different between the occluded and recurrent groups. Sharpiro-Wilk tests were performed to test parameters for normality. To test parameters for significance, we performed a Student's t-test (for normally distributed parameters) or a Mann-Whitney U test (for non-normally distributed parameters). A parameter was determined significant if $p<0.05$. We also performed the univariable analysis on the ruptured and unruptured IA subcohorts separately.

Additionally, parameters found in univariable analysis to be statistically significant in the entire IA dataset were subjected to multivariable logistic regression to remove co-dependence and identify independently significant parameters associated with recurrence.

The regression used a stepwise, backwards conditional method with a removal criteria of p>0.1. A parameter was determined to be significant and independently associated with recurrence if the p-value for its regression coefficient was <0.05. Before multivariable analysis, parameters were scaled and standardized to have a median of 0 and an interquartile range of 1. All statistical analyses were performed in SPSS (ver.25, IBM, Armonk, NY).

RESULTS

Study population

A total of 52 IAs (30 unruptured, 22 ruptured) from 50 patients met the inclusion criteria for this study. Of the 52 IAs, 34 were occluded at a mean follow-up time of 4.16 years while 18 were recurrent at a mean follow-up time of 3.96 years. Table 2 summarizes the recorded clinical parameters for all IAs in the study. The unruptured IA subcohort consisted of 19 occluded and 11 recurrent cases and the ruptured IA subcohort consisted of 15 occluded and 7 recurrent cases.

Examples of Analyses Results on Coiled IAs

Figure 1 demonstrates the analyses we conducted in this study to calculate the 26 parameters in the retrospectively collected coil treatment IA cases and correlate them with long-term (>1 year) treatment outcome. Here we use two representative IAs from our cohort as examples, with their pre-treatment DSA images shown in the left panel, and their DSA images at >1 year after treatment shown in the rightmost panel.

In both of these examples, the coiling procedures were successful, but their outcomes were different at >1 year after treatment. The internal carotid artery IA (top, Figure 1) was completely occluded, whereas the basilar tip IA (bottom) had residual filling at its neck. Although the goal of this study was to identify parameters that were *statistically* associated with poor outcome, namely recurrence at >1 year, a study of these two cases can provide some insight as well. As shown in the pre-treatment DSA images (left panel), the recurrent IA (bottom) was larger and had a larger neck than the occluded IA (top). The placement of coils disrupted flow patterns in both IAs and decreased flow speed, as shown by changes in the time-averaged blood streamlines and volume-rendered velocity magnitude in the post-treatment CFD images in the middle panel. Unlike the occluded IA, however, the recurrent IA had regions of higher flow velocity in its dome and at its neck after coil treatment. At >1 year, the recurrent IA had persistent filling of the neck (right panel).

We have also given the values of several significant aneurysm characteristics and coil packing parameters (from statistical analysis of the entire cohort, to be presented below) for these two example cases.

Aneurysm morphology and hemodynamic characteristics are associated with long-term outcome

Figure 2 shows aneurysm morphology characteristics of the occluded and recurrent groups (normalized by the values in the occluded group) for all, unruptured, and ruptured IAs. For all IAs (Figure 2A), the recurrent group had significantly larger *size* (D_{max}, p=0.026; V, p=0.021) and *neck* (ND, p=0.004; NA, p=0.003; NR_{3D}, p=0.03) compared to the occluded group. For unruptured IAs (Figure 2B), the recurrent group had significantly larger *size* (D_{max}, p=0.033; V, p=0.047). For ruptured IAs (Figure 2C), the recurrent group had significantly larger *neck* (ND, p=0.02; NA, p=0.039). Aneurysm *shape* was not significantly different between the occluded and recurrent groups in either the combined or the separate cohorts.

Figure 3 shows pre-coiling hemodynamics of the occluded and recurrent groups for all, unruptured, and ruptured IAs. For all IAs, the recurrent group had significantly higher *intra-aneurysmal flow* (M, p=0.015; KE, p=0.015) (Figure 3A) than the occluded group, but *trans-neck flow* was insignificant between the groups. Pre-coiling *intra-aneurysmal flow* and *trans-neck flow* were insignificant in either unruptured or ruptured subcohorts alone (Figure 3B and 3C).

Coil packing and post-treatment hemodynamics are also associated with long-term outcome

Figure 4 shows coil packing and post-coiling hemodynamics of the occluded and recurrent groups for all, unruptured, and ruptured IAs. For all IAs (Figure 4A), the occluded and recurrent groups had significantly different coil packing: the recurrent group had significantly lower PD (p=0.004) and significantly higher V_o (p=0.011) compared to the occluded group. For unruptured IAs (Figure 4B), the recurrent group had significantly higher V_o (p=0.03) whereas for the ruptured IAs (Figure 4C), it had significantly lower PD (p=0.001). Post-coiling *trans-neck flow* was significantly different between the occluded and recurrent groups for all IAs (Figure 4A): the recurrent group had significantly higher F_i (p=0.033) than the occluded group. *Trans-neck flow* was insignificant in the unruptured and ruptured subcohorts.

Post-coiling *intra-aneurysmal flow* was also significantly different between the occluded and recurrent group for all IAs (Figure 4A). The recurrent group had significantly higher Vel. (p=0.02), M (p=0.001) and KE (p=0.002), and significantly lower t_w (p=0.028) than the occluded group. *Intra-aneurysmal flow* was also significantly different between the occluded and recurrent groups for the unruputred and ruptured subcohorts. For the unruptured IAs (Figure 4B), the recurrent group had significantly higher M (p=0.005) and KE (p=0.026). For the ruptured IAs (Figure 4C), the recurrent group had significantly higher Vel. (p=0.032), M (p=0.026), and KE (p=0.026), and significantly lower t_w (p=0.004). For convenience, all data presented in Figures 2-4 were also presented as tables in supplemental material, with parameters expressed as mean ± SE.

Aneurysm characteristics, coil packing, and post-treatment hemodynamics are independently associated with long-term outcome

Multivariable logistic regression analysis of the significant parameters in the entire IA dataset retained 4 independent parameters (2 aneurysm characteristics, 1 coil packing parameter, and 1 post-coiling hemodynamic parameter) that were significantly associated with recurrence (Table 3): ND (p=0.023), pre-coiling flow KE (p=0.039), V_o (p=0.047), and post-coiling flow M (p=0.014).

Parameters associated with recurrence in unruptured and ruptured IA subcohorts

Table 4 summarizes the aneurysm characteristics, coil packing parameters, and post-treatment hemodynamic parameters that were significantly different between the occluded and recurrent groups for all, unruptured, and ruptured IAs. For all IAs combined, recurrence was significantly associated with aneurysm characteristics, coil packing parameters, and post-coiling hemodynamic parameters. Unruptured and ruptured IA subcohorts had different significant aneurysm characteristics associated with recurrence: for the unruptured IAs, *size* (D_{max} and V) was significantly associated with recurrence, whereas for the ruptured IAs, it was *neck* (ND and NA). In addition, the two subcohorts also had different significant coiling packing parameters: PD was significantly associated with recurrence in the unruptured subcohort, whereas for the ruptured subcohort, it was V_o. However, both IA subcohorts shared significant post-coiling hemodynamic parameters, specifically flow momentum (M) and flow kinetic energy (KE).

DISCUSSION

We hypothesized that aneurysm recurrence >1 year after coil embolization is associated with both the intrinsic characteristics of the aneurysm, the coil intervention, and how it affects flow. To test this, we calculated 26 morphologic, treatment-specific, and hemodynamic parameters from 52 retrospectively collected coiled IA cases using image-based computational modeling. We tested which of them were significantly different between recurrent and occluded IAs at >1 year follow-up. Overall, outcome was associated with both the intrinsic aneurysm characteristics and the coil intervention. Even after controlling for co-dependencies between parameters in multivariable analysis, two aneurysm characteristics (ND and pre-coiling flow KE), one coil packing parameter (V_o), and one post-treatment hemodynamic parameter (flow M) were independently associated with recurrence.

Aneurysm characteristics and recurrence

Many studies have demonstrated an association between IA morphology and recurrence.[1, 3, 21-23] For example, in a retrospective study of 501 coiled IAs, Raymond et al. found that IA size >10 mm and ND >4 mm were significant predictors of recurrence.[3] In a systematic review of over 8,000 coiled IAs, Ferns et al. also demonstrated recurrence was greater in IAs >10 mm.[1] A more recent study of 609 coiled IAs by Neki et al. found that recurrent IAs had significantly larger V (in addition to larger D_{max} and ND) than occluded IAs.[23] Our results confirmed all of these findings, showing recurrent cases have significantly larger *size* (D_{max} and V) and *neck* (ND, NA, and NR_{3D}) than occluded IAs (Figure 2A). We also showed in multivariable analysis that ND is independently associated with recurrence. The consistent findings of larger IA size and neck being associated with recurrence can be understood from higher burden for coiling to create flow stasis and thrombosis to fill the IA volume, and larger coverage of the IA neck for neointima formation to achieve complete occlusion.[17]

Besides IA *size* and *neck*, we also examined aneurysm *shape* (e.g. UI, NSI, EI) in occluded and recurrent IAs. Although these parameters can classify rupture status,[24] they were not associated with coiling outcome in our data (Figure 2).

Since coils work by modifying *intra-aneurysmal flow*, we also conjectured that some types of pre-treatment aneurysmal flow could lend the IA to less effective coiling and predispose it to recurrence after coiling. In the literature, few groups have investigated the relationship between aneurysmal flow and treatment outcome. In one publication, Sugiyama et al., found that in coil-treated basilar tip IAs, the ratio between pre-treatment inflow rate and the basilar artery flow rate was significantly higher in recurrent cases compared to occluded cases.[4] In our study, however, we did not find inflow rate (Q_{in}) (either pre- or post-coiling) to be significantly associated with outcome (Figures 3 and 4). This difference may be attributed to the fact that our cohort only contained ~10% bifurcation-type IAs, while Sugiyama et al. studied exclusively basilar tip aneurysms. On the other hand, our data did show that recurrent cases have significantly higher pre-coiling aneurysmal flow momentum (M) and kinetic energy (KE) (Figure 3A), and in multivariable analysis, we found pre-coiling KE to be independently associated with recurrence. Therefore, in addition to large IA *size* and *neck*, more energetic aneurysmal flow also puts greater burden on the coils to create a static flow environment in the sac that can propagate thrombotic occlusion.[17]

Coil packing and recurrence

It is widely known that treatment outcomes are affected by the degree of coil packing.[21] Our results show that recurrent cases have significantly lower coil packing density (PD), which is consistent with previous studies that showed an association of recurrence with low aneurysm packing with coils.[5, 25, 26] We also found that recurrent cases have significantly higher uncoiled volume (i.e. V_o, Figure 4), and that this coil packing parameter is independently associated with recurrence (Table 3), which is consistent with a study by Sadato et al.[20] Our observation that recurrence was associated with both larger IA *size* and lower PD, may reflect the relationship described in a mathematical analysis by Taussky et al.; the larger the size of the IA, the harder it is to sufficiently pack it with coils.[27] Lower PD in the IA likely reduces the coils' ability to disrupt incoming pulsatile flow and the amount of scaffold for thrombus, both of which may contribute to incomplete occlusion.[17]

Post-treatment hemodynamics and recurrence

In addition to inherent aneurysm characteristics and the degree of coil packing, long-term outcome is also influenced by the flow modifications by coils. To characterize how the coils alter the flow in each IA case, we used our recently-validated FEM coiling technique, which is among the most realistic modeling techniques as it explicitly models physical coil properties and coil deployment mechanics.[8, 9] Because it models coils explicitly, our technique enabled the investigation of *intra-aneurysmal flow* around the coils in each case. Previous computational studies could not examine flow around the coils because they used angiographic images of coil masses or represented coils implicitly as homogenous porous media.[6, 7, 22, 28]

Using our FEM coiling technique combined with post-coiling CFD, we showed that recurrence is associated with post-coiling hemodynamic parameters. Specifically, *intra-aneurysmal flow* in recurrent cases is faster (higher Vel.), more energetic (higher M and KE), and spends less time in the IA sac (lower t_w). These results are consistent with what is observed on angiography in recurrent cases, which shows persistent contrast filling of the aneurysm. Persistent energetic flow in the IA after coiling likely inhibits stable thrombus formation. The less static flow we found in recurrent IAs could be related to them having low coil packing, since there may not be enough coils to sufficiently disrupt the flow and provide a stable scaffold for thrombus in these cases.

In addition to energetic *intra-aneurysmal flow*, we found that recurrent cases have more forceful *trans-neck flow* after coiling (higher post-coiling F_i,) (Figure 4A). Forceful post-treatment flow impingement at the IA neck and on the coil mass could inhibit neointima formation across the IA neck or potentially cause adverse events like coil compaction.[17, 25]

Ruptured and unruptured IA subcohorts have distinct and shared parameters associated with recurrence

Since ruptured IAs require emergency repair, coiling ruptured IAs may be approached differently than unruptured IAs. For example, they might not receive framing coils and may be treated with softer, undersized coils to limit the radial force on the IA wall and prevent dislocation of a fibrous cap. Furthermore, an immediate goal of coiling a ruptured IA is to shutdown aneurysm flow and to stop the hemorrhage.[29] We found ruptured and unruptured IAs indeed present different characteristics predicting recurrence (Table 4). In ruptured IAs, large *neck* was significantly associated with recurrence, whereas in unruptured IAs, large *size* predicted recurrence. This may be related to the fact that ruptured IAs that have wide necks cannot be treated by FDs or adjunctive stents, since these patients cannot be placed on anti-platelet therapy.[29] Therefore, IAs with wide necks are likely more prevalent in the ruptured subcohort. On the hand, unruptured IAs with wide necks are typically treated with adjunctive stents or FDs, but these treatment cases were excluded in our study.[30] Consequently, IAs in our unruptured subcohort may not have as wide of necks, but still might have large sizes. We do note that, in a larger cohort consisting of both unruptured and ruptured IAs (n=501), Raymond et al. found that both IA size and neck size were significantly associated with recurrence, as we found in our entire IA dataset.[3]

In addition to morphology, the significant coil packing parameter predicting recurrence was also different between the ruptured and unruptured subcohorts: low packing density (PD) for ruptured cases, and high uncoiled volume (V_o) for unruptured cases. Both suggest that insufficient coil packing of the aneurysm is associated with recurrence, regardless of rupture status.

Our analysis revealed that the ruptured and unruptured subcohorts shared significant post-coiling hemodynamic parameters associated with recurrence — higher post-treatment flow momentum (M) and kinetic energy (KE) (Table 4). These results suggest that, regardless of rupture status, long-term occlusion of coiled IAs is associated with less energetic flow after coiling. This could indicate that coils primarily promote IA healing through the slowing of blood flow. Thus, analyzing the flow modification induced by coils may be an effective means at predicting long-term outcome.

Future directions: simulation-based predictive models of treatment outcome

In the future, the parameters we found in this study to be associated with recurrence could be used to build predictive models of coil treatment outcome. The ability to predict recurrence prior to actual coil interventions could enable evaluation of candidate treatment strategies and thus optimize treatment for individual patients. While geometric parameters like neck diameter (ND) are easily calculated before treatment, other significant parameters such as post-coiling aneurysmal flow momentum (M) and kinetic energy (KE) require CFD calculations. With future advancements in modeling techniques and computing power, simulation-based treatment planning and optimization may become possible.

Limitations

This study has several limitations. First, we used non-patient-specific flow boundary conditions in our CFD simulations. While this assumption is commonly used in practice because patient-specific *in vivo* data is not routinely measured, flow simulations should ideally use accurate patient-specific flow boundary conditions. Second, we assumed both IAs and virtually deployed coils to be rigid in the CFD simulations to avoid prohibitively expensive fluid-structure interaction simulations. However *in vivo*, coils may migrate or compact due to the pulsatile blood forces. Third, it was impossible to recapitulate the exact *in vivo* coiling procedure done on each patient and thus the deployed coil configurations in our models may differ from in the patients, but we believe our high-fidelity FEM modeling technique captured the essential features. Finally, our sample size is small and limited to a single center. Future studies are needed to confirm the findings of this study in a larger dataset.

CONCLUSION

This study found that aneurysm recurrence at >1 year after coiling is associated with both intrinsic aneurysmal characteristics and changes induced by coils, including larger IA size and neck, less coil packing, and higher intra-aneurysmal flow before and after coiling. Furthermore, we found that ruptured and unruptured IAs have both distinct and shared significant parameters associated with recurrence. These results provide compelling evidence for future studies aimed at developing simulation-based predictors of treatment outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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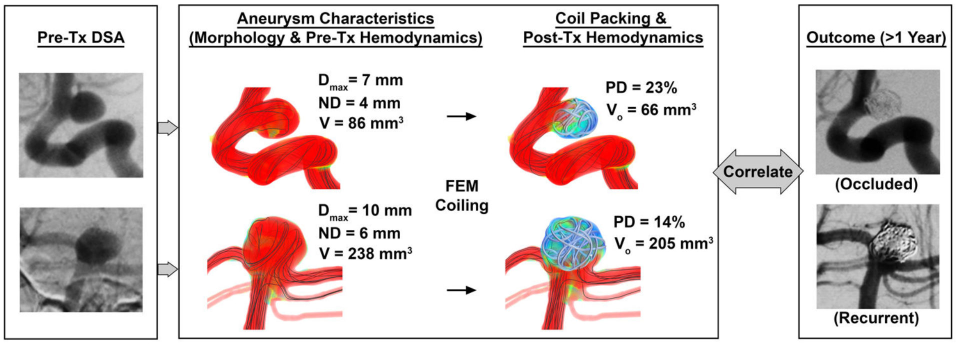

Figure 1.

Two examples showing the analyses we conducted on the 52 primary-coiling IA cases to calculate 26 aneurysmal characteristics, coil packing parameters, and post-treatment hemodynamic parameters, and correlate them with treatment outcome at >1 year. The left panel shows the pre-treatment (Tx) DSA images of 2 representative IAs from the study population: an internal carotid artery IA (top) and a basilar tip IA (bottom). The rightmost panel shows the treatment outcome of these IAs at >1 year: the internal carotid artery IA was completely occluded, whereas the basilar tip IA had residual filling at its neck. The middle panel shows our study analyses. The values we calculated from these analyses for several significant aneurysm characteristics (including D_{max}, ND, and V) and coil packing parameters (PD and V_o) are also shown for each as examples.

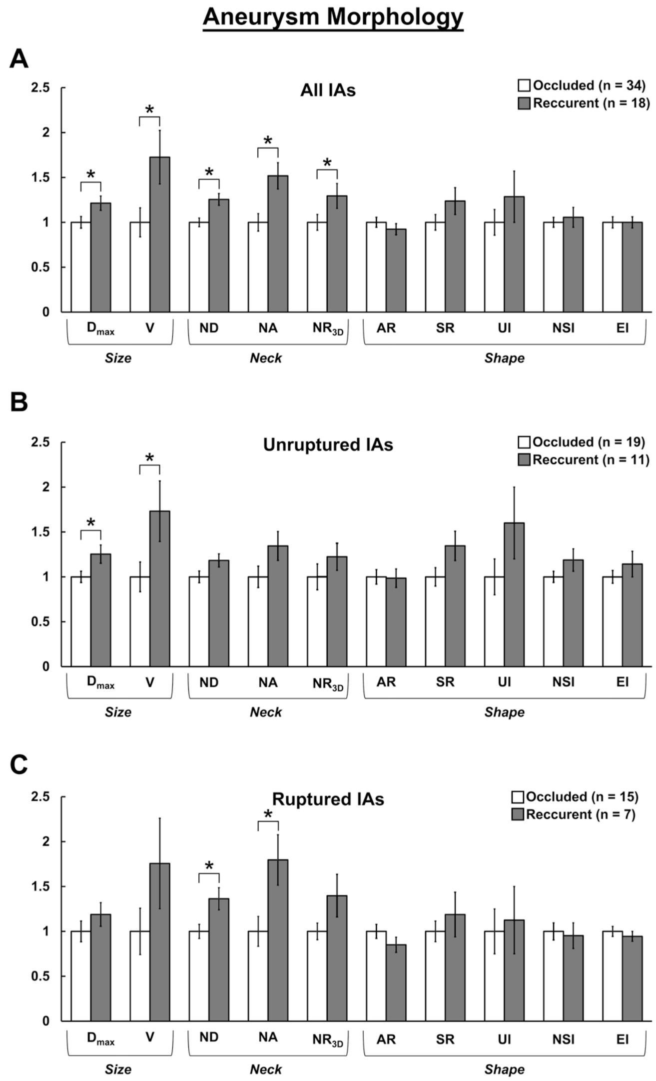

Figure 2.
Comparison of aneurysm morphology characteristics between occluded and recurrent groups in all (A), unruptured (B), and ruptured (C) IAs. Asterisk indicate significant parameters ($p<0.05$) and error bars represent standard error.

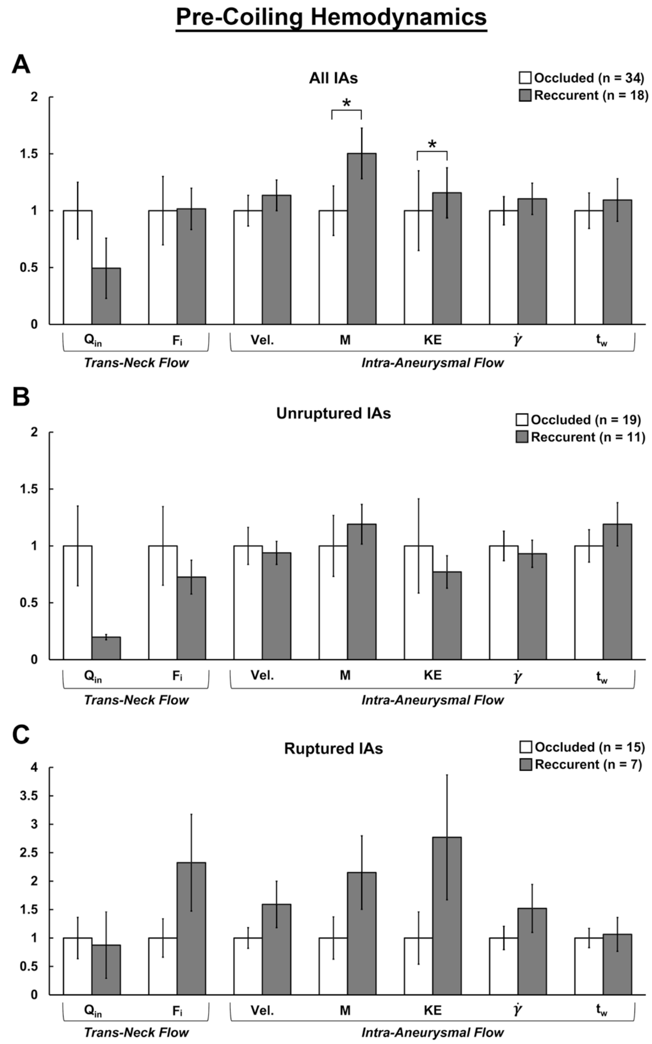

Figure 3.

Comparison of pre-coiling hemodynamics between occluded and recurrent groups in all (A), unruptured (B), and ruptured (C) IAs. Asterisk indicate significant parameters ($p<0.05$) and error bars represent standard error.

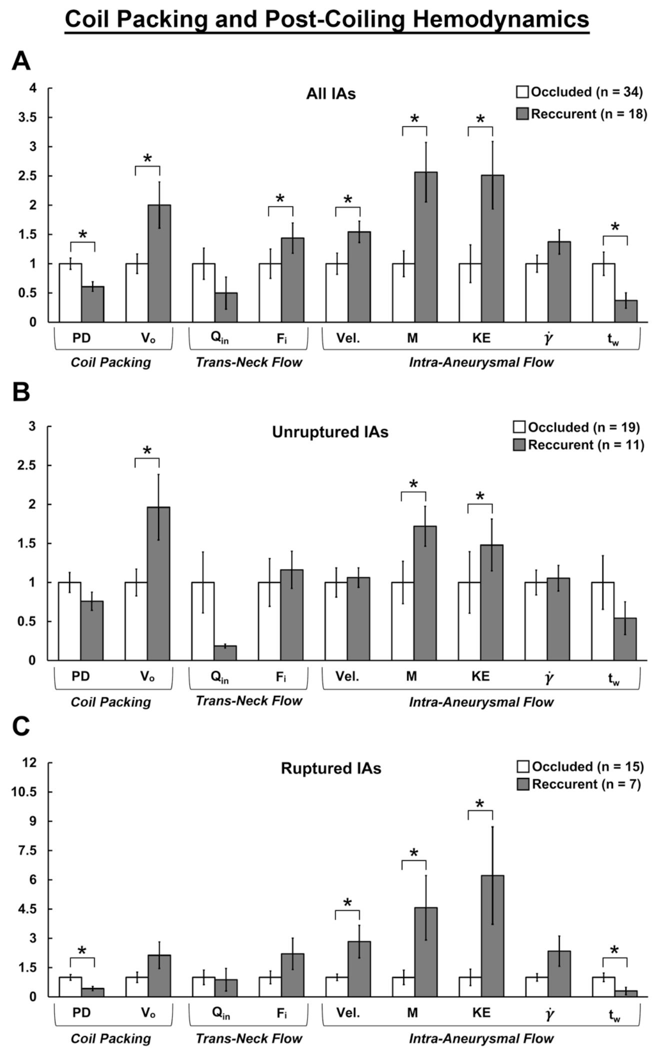

Figure 4.

Comparison of coil packing and post-treatment hemodynamics between occluded and recurrent groups in all (A), unruptured (B), and ruptured (C) IAs. Asterisk indicate significant parameters ($p<0.05$) and error bars represent standard error.

Table 1.

Summary of the investigated parameters for coiling.

Aneurysm Characteristics	Morphology	*Size*	Maximum Dimension (D_{max}) Volume (V)
		Neck	Neck Diameter (ND) Neck Area (NA) 3D Neck Ratio (NR_{3D})
		Shape	Aspect Ratio (AR) Size Ratio (SR) Undulation Index (UI) Non-Sphericity Index (NSI) Ellipticity Index (EI)
	Pre-Coiling Hemodynamics	*Trans- Neck Flow*	Inflow Rate (Q_{in}) Impingement Force (F_i)
		Intra-Aneurysmal Flow	Velocity (Vel.) Momentum (M) Kinetic Energy (KE) Shear Rate ($\dot{\gamma}$) Washout Time (t_w)
Coil Packing		—	Packing Density (PD) Uncoiled Volume (V_o)
Post-Coiling Hemodynamics		*Trans- Neck Flow*	Inflow Rate (Q_{in}) Impingement Force (F_i)
		Intra-Aneurysmal Flow	Velocity (Vel.) Momentum (M) Kinetic Energy (KE) Shear Rate ($\dot{\gamma}$) Washout Time (t_w)

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Table 2.

Comparison of clinical parameters for occluded and recurrent groups in the study population. Parameters are expressed as mean ± standard error (SE) or total number and percentage in each group.

Parameter	Occluded (n=34)	Recurrent (n=18)
	Mean ± SE or Total Number (%)	Mean ± SE or Total Number (%)
Age (Years)	60.09 ± 2.47	55.28 ± 2.00
Follow-Up Time (Years)	4.16 ± 0.41	3.96 ± 0.62
Female Sex	24 (71%)	14 (78%)
Smoking History	13 (38%)	11 (61%)
Hypertension	22 (65%)	8 (44%)
Ruptured	15 (44%)	7 (39%)
Posterior Location	5 (15%)	1 (6%)
Initially Occluded	27 (79%)	12 (67%)

Table 3.

Results of multivariable logistic regression analysis for all IAs.

Parameter Categories		**Independently Significant Parameters Predicting Recurrence**
Aneurysm Characteristics	Morphology	*Neck Diameter, ND (p=0.023)*
	Pre-Coiling Hemodynamics	*Flow Kinetic Energy, KE (p=0.039)*
Coil Packing		*Uncoiled Volume,* V_o *(p=0.047)*
Post-Coiling Hemodynamics		*Flow Momentum, M (p=0.014)*

Table 4.

Summary of aneurysm characteristics, coil packing parameters, and post-coiling hemodynamics that were significantly different between the occluded and recurrent groups for all, unruptured, and ruptured IAs.

	Aneurysm Characteristics					**Coil Packing**	**Post-Coiling Hemodynamics**	
	Morphology			**Pre-Coiling Hemodynamics**				
	Size	***Neck***	***Shape***	***Trans-Neck Flow***	***Infra-Aneurysmal Flow***	**—**	***Trans-Neck Flow***	***Infra-Aneurysmal Flow***
All IAs	D_{max}, V	ND, NA, NR_{3D}	—	—	M, KE	PD, V_o	F_i	Vel., M, KE, t_w
Unruptured IAs	D_{max}, V	–	—	—	—	V_o	—	M, KE
Ruptured IAs	—	ND, NA	—	—	—	PD	—	Vel., M, KE, t_w