Angular Remodeling in Single Stent-Assisted Coiling Displaces and Attenuates the Flow Impingement Zone at the Neck of Intracranial Bifurcation Aneurysms

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BACKGROUND: Self-expanding intracranial stent-assisted coiling of bifurcation aneurysms has recently been shown to straighten target cerebral vessels, a phenomenon with unknown hemodynamic effect.

OBJECTIVE: To investigate the impact of angular remodeling in aneurysms treated with single stent-assisted coiling with the use of computational fluid dynamic techniques.

METHODS: Fourteen patients (7 women, mean age 55) who underwent stent coiling of 14 wide-necked bifurcation aneurysms were included based on the availability of high-resolution 3-dimensional rotational angiography. Pretreatment data sets underwent virtual aneurysm removal to isolate the effect of stenting. Wall shear stress and pressure profiles obtained from constant flow input computational fluid dynamic analysis were analyzed for apical hemodynamic changes.

RESULTS: Stenting increased the bifurcation angle with significant straightening immediately after treatment and at follow-up (107.3° vs 144.9°, $P < .001$). The increased stented angle at follow-up led to decreased pressure drop at the bifurcation apex (12.2 vs 9.9 Pa, $P < .003$) and migration of the flow impingement zone (FIZ) toward the contralateral nonstented daughter branch by a mean of 1.48 ± 0.2 mm. Stent-induced angular remodeling decreased FIZ width separating peak apical wall shear stress (3.4 vs 2.5 mm, $P < .004$). Analysis of FIZ distance measured from the parent vessel centerline showed it to be linearly ($r = .58$, $P < .002$) and FIZ width inversely correlated ($r = .46$, $P < .02$) to vessel bifurcation angle.

CONCLUSION: Stent-induced angular remodeling significantly altered bifurcation apex hemodynamics in a favorable direction by blunting apical pressure and inducing the narrowing and migration of the FIZ, a novel response to intracranial stenting that should be added to intimal hyperplasia and flow diversion.

KEY WORDS: Angular modification, Computational fluid dynamics Intracranial aneurysm, Stent-assisted coiling, Wall shear stress

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Endovascular treatment of wide-necked cerebral aneurysms at vascular bifurcations has increasingly relied on a stent-assisted coiling technique (Figure 1). In addition to the mechanical buttressing effect of intracranial stents to enable coil embolization, the reaction of the parent vessel to deployment of self-expanding microstents has important sequelae. In-stent stenosis is a known response of the vessel wall that may contribute to decreased recanalization in stent-coiled aneurysms compared with coiling alone.[1-5] More recently, a number of reports have identified another phenomenon of stent-induced immediate and delayed angular remodeling following self-expanding intracranial stent

ABBREVIATIONS: CFD, computational fluid dynamic; **D_{FIZ},** flow impingement zone distance; **FIZ,** flow impingement zone; **W_{FIZ},** width of the flow impingement zone; **WSS,** wall shear stress

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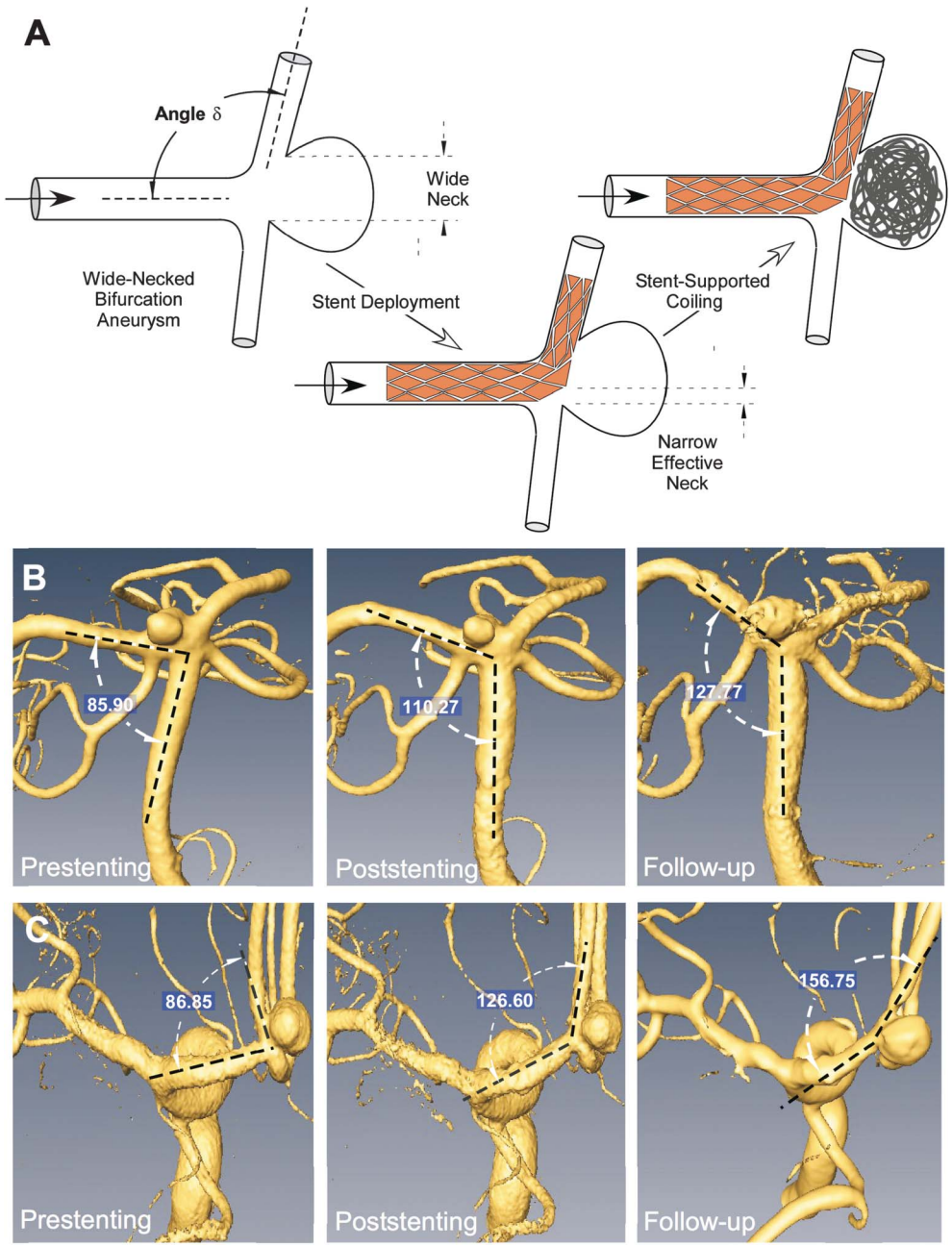


FIGURE 1. **A**, *schematic of sequential stent-mediated coiling of a wide-necked bifurcation aneurysm, with angle δ between mother vessel and stented daughter branch.* **B**, *stenting caused angular alteration in a wide-necked 3-mm basilar apex aneurysm in a 62-year-old woman. Angle is 85.9° before stenting, 110.3° immediately after stenting, and 127.8° at the latest follow-up (9 months) following stent-coiling.* **C**, *stenting-altered bifurcation angle in a wide-necked 5-mm anterior communicating artery aneurysm in a 60-year-old woman. Angle is 86.9° before stenting, 126.6° immediately after stenting, and 156.8° at the latest follow-up (13 months) after stent coiling. In* **B** *and* **C**, *the native mode rather than the digital subtraction 3-D angiography was used when collecting the original rotational data, and the aneurysm and associated coil mass are still visible.*

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deployment.[6-8] This response following Neuroform or Enterprise stent deployment results in effective straightening of the stented vessel segment (Figure 1).

Given the important role that bifurcation apex hemodynamics play in the development and progression and recurrence of cerebral aneurysms,[9,10] we hypothesized that such stent-induced angular alterations could lead to important hemodynamic changes with possible effects on the pathogenesis and risk of recurrence of stent-coiled bifurcation aneurysms.[11,12] In the current study, we sought to investigate the hemodynamic effects induced by stenting-related bifurcation angular alterations on aneurysm neck hemodynamics, namely, at the bifurcation apex wall. We present a technique that aims to isolate the effect of the stent-induced bifurcation angular change by using an aneurysm-capping method coupled with patient-specific computational fluid dynamic (CFD) analysis (Figure 2). This approach uncovered an important effect of the vessel angle-bending properties of self-expanding microstents on hemodynamics of the flow impingement zone (FIZ) at the bifurcation apex.

MATERIALS AND METHODS

Patient Population and Vascular Angular Remodeling After Stenting

Between March 2004 and January 2011, patients with wide-necked bifurcation aneurysms underwent stent-assisted coiling at our center with the use of intracranial Nitinol stents of either the open-cell design Neuroform (Stryker Neurovascular, Fremont, California) or the closed-cell design Enterprise (Codman Neurovascular, Raynham, Massachusetts) and were evaluated for inclusion in the study based on image quality sufficient to enable CFD analysis (Figure 1). The stented angle δ at the vascular bifurcation was measured pre- and poststenting and at latest follow-up.

Computational Fluid Dynamics and Postprocessing

Three-dimensional rotational angiography was performed on the identical Siemens Axiom-Artis VB22N unit before and after stenting, and at angiographic follow-up in a retrospective fashion approved by the institutional review board. Analysis was performed by using the patients' 3-dimensional rotational angiography volumetric data sets right before stent coiling and at the latest follow-up. Data were reconstructed and transferred for surface rendering by using Amira software (v. 4.1.2, Visage Imaging, San Diego, California), and the surface model used for CFD analysis was made with the same length of the daughter vessels beyond the bifurcation in each case. Surface smoothing was performed by using Meshlab software (v. 1.2.2, Visual Computing Lab, Institute of Information Science and Technologies "Alessandro Faedo," National Research Council of Italy), followed by virtual removal of the aneurysm. After the surface of the aneurysm dome was removed, the resulting wall defect was closed, repaired, and further smoothed to simulate coiling in the absence of stenting. Smoothing with Meshlab software enabled consistent reconstruction of the aneurysm neck defect following dome removal. High-resolution polyhedral meshes were generated with Star-CCM+ Version 4.02 (CD-Adapco, Melville, New York), with the mesh size ranging from 53 000 to 212 000 polyhedral cells (with 369 000-1 466 000 faces). Mesh size independence was evaluated and confirmed for the utilized meshes. Finite-volume solution used Fluent Version 6.3.26 (Ansys, Lebanon, New Hampshire) in laminar double-precision unsteady regime, assuming rigid nonslip wall conditions, constant flow input, blood viscosity of 3.5 cP, and density of 1070 kg/m^3 as previously described.[13] The flow rate for the inflow was set at 0.1 m/s and zero pressure for the outlet. After preliminary analysis was performed at peak systole by the use of time-dependent runs for 3 cases showing similar results to steady-state analysis, the analysis was performed using steady-state mode to minimize variability. Postprocessing was performed using the Ensight software (Version 9; CEI, Apex, North Carolina).[13] A line on the distal wall of the bifurcation apex including the aneurysm neck was sampled for comparison of hemodynamic parameters (Figure 2B). The distribution of pressure and wall shear stress (WSS) on the line was measured and plotted before treatment, with the aneurysm virtually removed, and at angiographic follow-up. Pressure sampling was performed by measuring the difference between 10 points at the impingement zone on the bifurcation apex and 10 points at the distal end of the parent artery (Figure 2C). The location of the FIZ on the bifurcation apex wall was obtained by measuring the distance from its center to the centerline of the distal portion of the parent artery on the bifurcation apex wall (Figure 3) as D_{FIZ}, which is a signed quantity taken as positive when the parent vessel centerline intersects the stented daughter branch.

Statistics

Statistical analysis was by use of matched paired t tests with the use of JMP software (Version 8.02, SAS Institute, Cary, North Carolina). Statistical significance was assumed for a value of $P < .05$.

RESULTS

Stent-Induced Immediate and Delayed Angular Remodeling

Three-dimensional volumetric data from 14 patients (7 women and 7 men, age range of 26-70 years, mean 55) underwent CFD analysis, including 6 basilar bifurcation apex aneurysms, 5 anterior communicating artery aneurysms, 2 middle cerebral artery bifurcation aneurysms, and 1 internal carotid bifurcation aneurysm. Stent coiling of the bifurcation aneurysms resulted in a highly statistically significant increase in the stented angle δ from a median/mean pretreatment value of 102.0°/107.3° (85.9°-139.2°) to 128.8°/129.8° (99.6°-146°) immediately posttreatment ($P < .001$), further increasing to 144°/144.9° at the latest follow-up ($P < .001$ vs both pre- and posttreatment) for a total mean difference of 37.6°, similar to previous reports.[7,8]

Stent-Induced Flow Direction Change

Stent-induced angular change in the bifurcation altered the direction of the flow toward the stented daughter branch (Figure 4A) and lower contribution to the nonstented counterpart. This led to a decrease in the zone of flow stasis characterized by low velocities at the bifurcation apex (arrowhead, Figure 4B) with a subtle shift in the apical pressure distribution (Figure 4C). Magnified analysis of the velocity vectors at the apex suggested a change in the hemodynamic pattern at the FIZ (Figure 4D).

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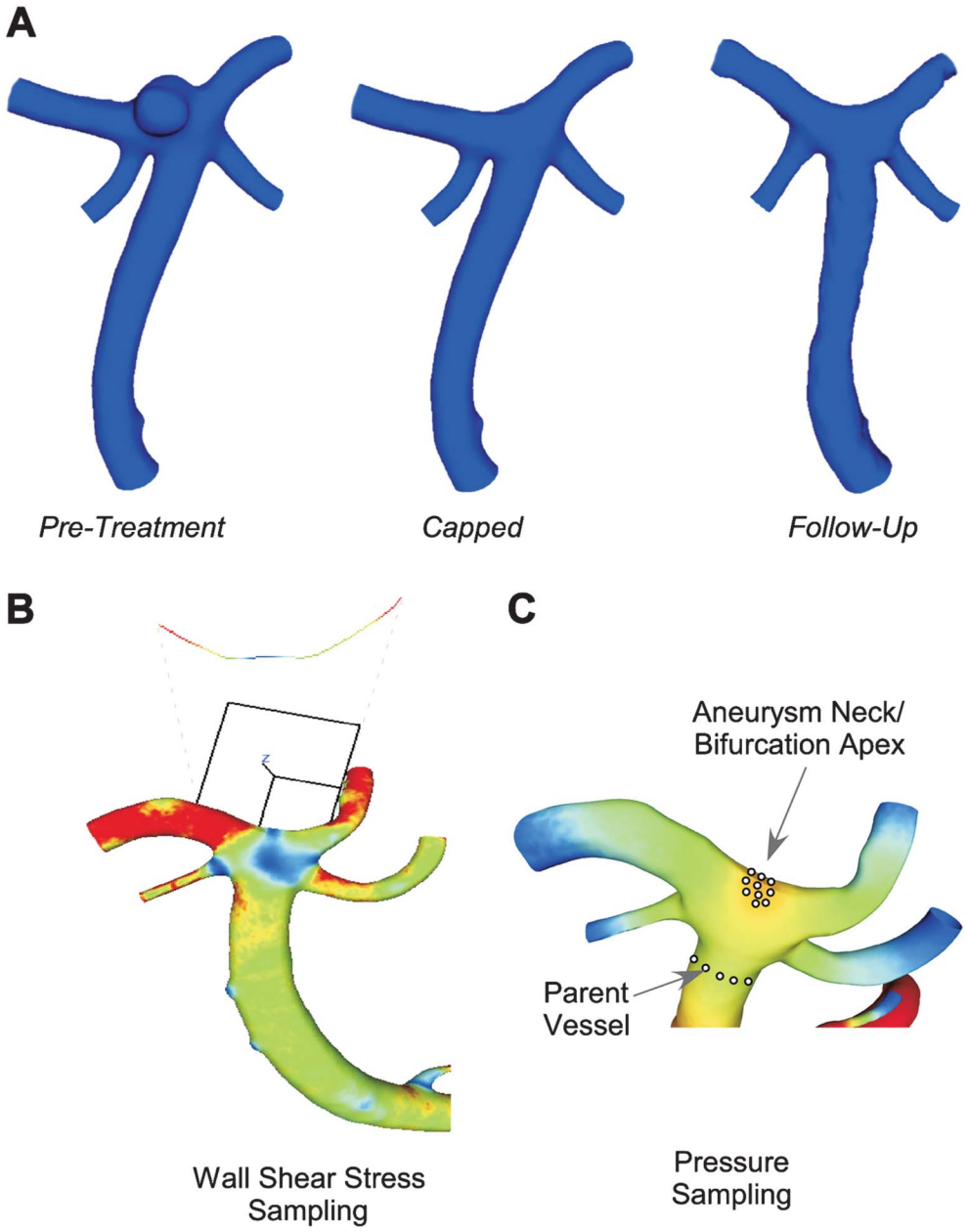


FIGURE 2. **A**, *volume rendering of a basilar bifurcation aneurysm (**left**) was virtually coiled (capped, **middle**) and the aneurysm neck closed by using meshing software to isolate the effect of angular change between pretreatment and latest follow-up (**right**).* **B**, *method of wall shear stress sampling at the apex: a cutline is created on the distal wall of the bifurcation apex and both daughter branches for shear stress measurement.* **C**, *method of pressure sampling: 10 points on the flow impingement zone (FIZ) at the bifurcation apex and 10 circumferential points at the distal end of the parent vessel were acquired for measurement of extent of pressure increase at the FIZ.*

Stent-Induced Hemodynamic Changes at the Bifurcation Apex

Stent-deployment-induced angular changes in the parent vessel as well as the distal branch of the bifurcation led to significant straightening and important alteration in the apical WSS pattern (Figure 5). A consistent pattern emerged whereby the FIZ (arrowhead, Figure 5A) was noted to be deflected away from the stented daughter vessel. D_{FIZ} (FIZ distance) increased from a mean

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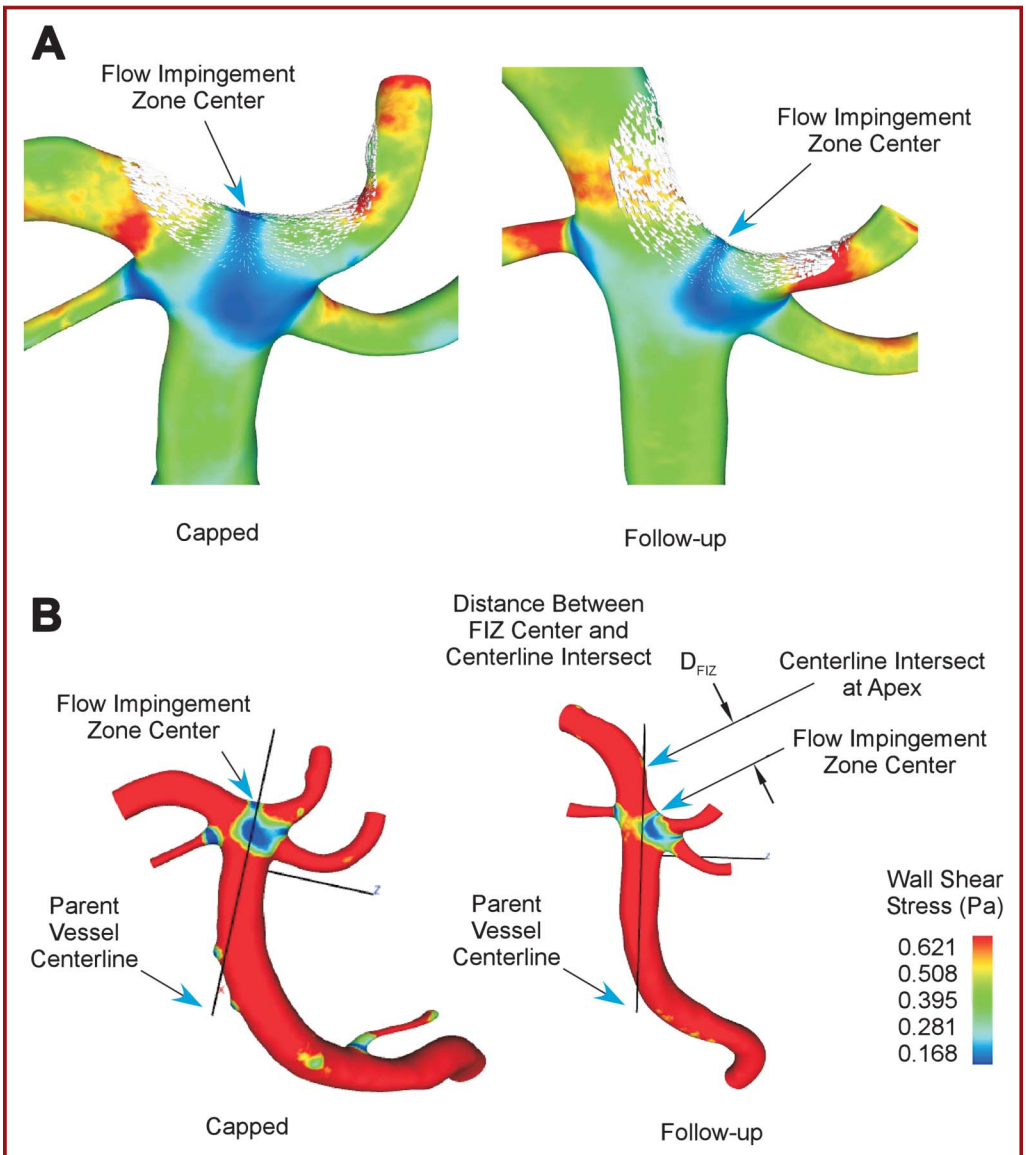


FIGURE 3. A, *WSS-shaded volume rendering of a stent-coiled basilar bifurcation with focal WSS vectors at the FIZ show stagnation at its center and WSS vectors emanating away toward each daughter branch. Note the migration of the FIZ center at follow-up away from the stented and straightened branch.* **B**, *in order to assess FIZ migration with stenting, the distal parent vessel centerline and its intersection with the bifurcation apex were used as references.* D_{FIZ} *is the distance between the FIZ center and the intersect of the parent vessel centerline at the apical wall (***right***). WSS, wall shear stress; FIZ, flow impingement zone.*

of 0.045 ± 0.20 mm to 1.53 ± 0.21 mm ($P < .001$) for a mean migrated distance of 1.48 mm away from the stented daughter branch (Figure 5B).

Comparison of the pressure on the vessel wall (Figure 6A) revealed that latest follow-up values showed significant decreases in both the distal parent vessel pressure from 26.13 ± 1.55 Pa to 22.37 ± 1.14 Pa ($P = .007$) as well as pressure at the FIZ from 38.15 ± 1.93 Pa to 32.31± 1.46 Pa ($P = .002$) (Figure 7A). Most importantly, the pressure difference between the distal parent vessel and the FIZ was decreased by stent-induced remodeling from 12.02 ± 0.69 Pa to 9.89 ± 0.56 Pa, consistent with a blunting of the relative pressure at the stasis region on the bifurcation apex ($P < .003$).

We then evaluated the effect of the angle change on WSS and its distribution on the apex (Figure 6). WSS trough value decreased from 0.43 ± 0.10 Pa to 0.30 ± 0.07 Pa, although without reaching significance at follow-up. The peak values of WSS in either daughter branches were not significantly altered with stent-induced remodeling changing for WSS_1 from 1.56 to 1.90± Pa and for

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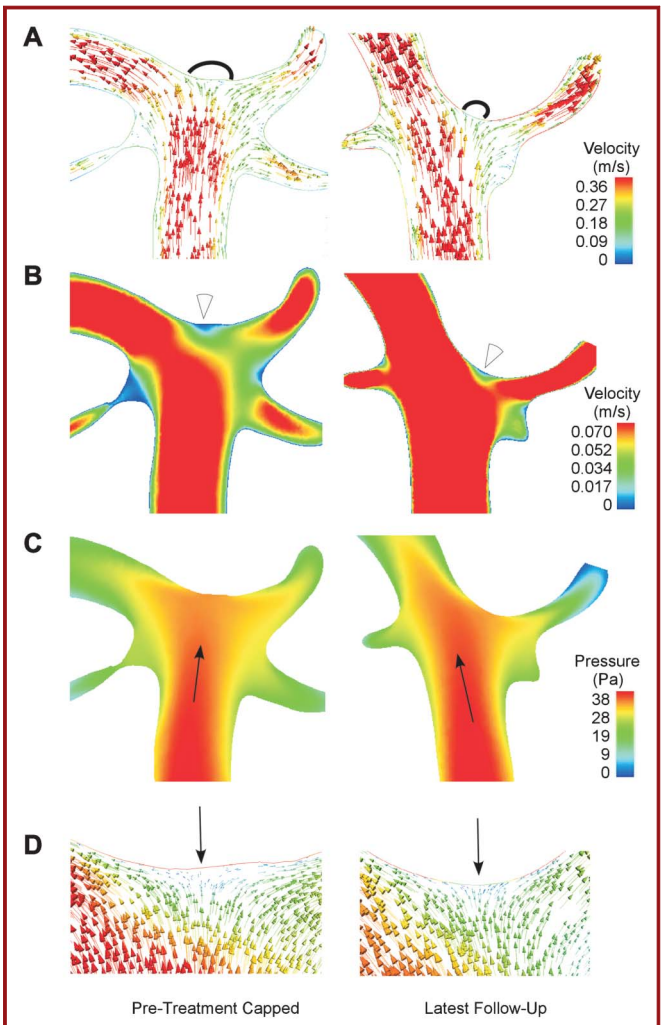


FIGURE 4. *Representative hemodynamic changes as a result of stent-induced angular change in a basilar bifurcation.* **A**, *sagittal cross-sectional flow vector representation color-coded by Velocity with half-ellipse representing the flow-impingement zone (FIZ).* **B**, *cross-sectional Velocity profile illustration focal region of stasis at the FIZ (arrowhead).* **C**, *cross-sectional pressure profile.* **D**, *magnified view of the velocity vectors.*

WSS_2 from 1.76 to 1.63 Pa. Similarly, peak-through differences before and after stent-angular remodeling were not significantly different from 1.22 ± 0.13 to 1.46 ± 0.29 Pa.

More importantly, the width of the FIZ (W_{FIZ}), defined as the region between the peaks of WSS (Figure 6B), was noted to be significantly reduced in size from 3.4 ± 0.3 mm to 2.5 ± 0.2 mm (P = .004) with decreases in both D_1 (1.7-1.3 mm, P = .003) and D_2 (1.7-1.2 mm, P = .018) (Figure 7B).

Bifurcation Angle-Dependent Location and Width of the FIZ

In a quest to determine whether a predictive relationship could be established between the aneurysm-bearing bifurcation angle

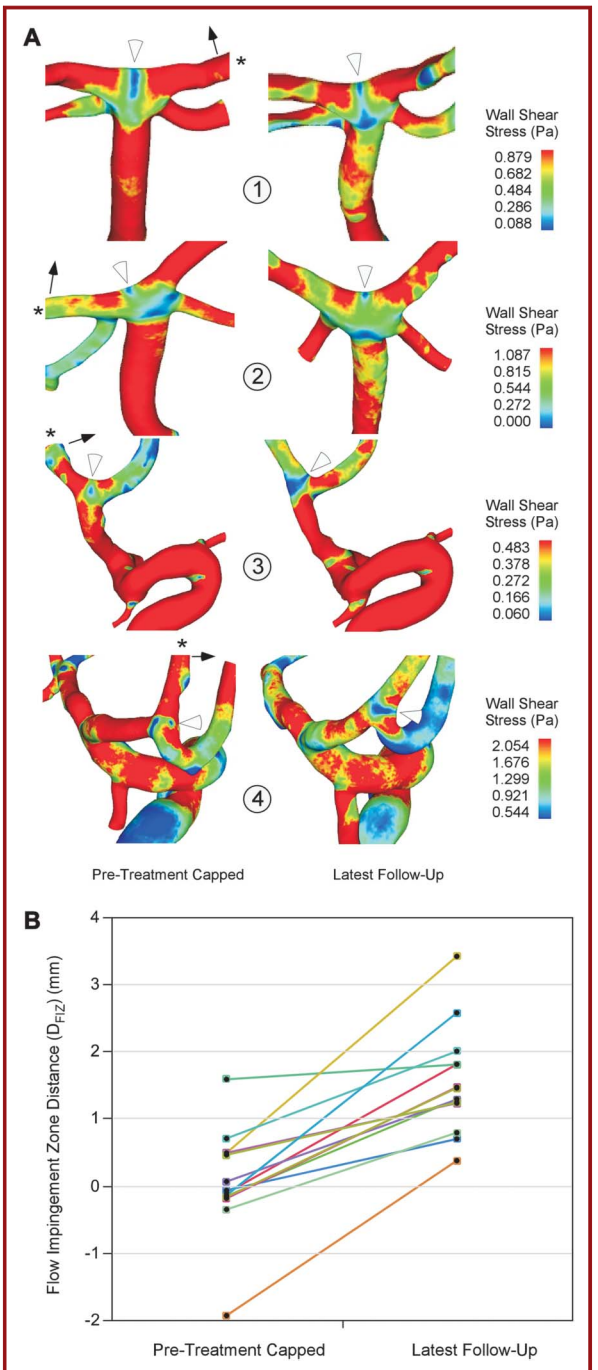


FIGURE 5. **A**, *wall shear stress profile of 4 representative bifurcation aneurysms treated using stent coiling illustrating the change in the pattern of shear forces at the apex including migration of the flow impingement zone (white arrowhead) as a result of the movement (arrow) of the stented daughter vessel (star) and straightening of the parent-daughter transition: basilar bifurcation (1, 2); middle cerebral bifurcation (3); anterior communicating bifurcation (4).* **B**, *comparison of the flow impingement zone distance D_{FIZ} between pretreatment and latest follow-up, with the D_{FIZ} increased and moved away from the stented daughter branch at the latest follow-up.*

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and the properties of the FIZ, linear plots were performed of D_{FIZ} and W_{FIZ} with respect to bifurcation angle δ (Figure 8) by using the Pearson correlation test. Measurement of the distance of the FIZ from parent vessel centerline shows significant linear correlation with a coefficient $r = 0.58$ ($P < .002$) (Figure 8A). Conversely, flow impingement width W_{FIZ} demonstrated a negative linear correlation of coefficient $r = .46$ ($P < .02$) with respect to bifurcation angle. These findings confirm the effect of the bifurcation angular remodeling on the displacement and narrowing of the FIZ.

DISCUSSION

Stent-mediated coiling has been associated with a number of changes to the underlying parent vessel, including in-stent stenosis and, more recently, angular remodeling. The current study

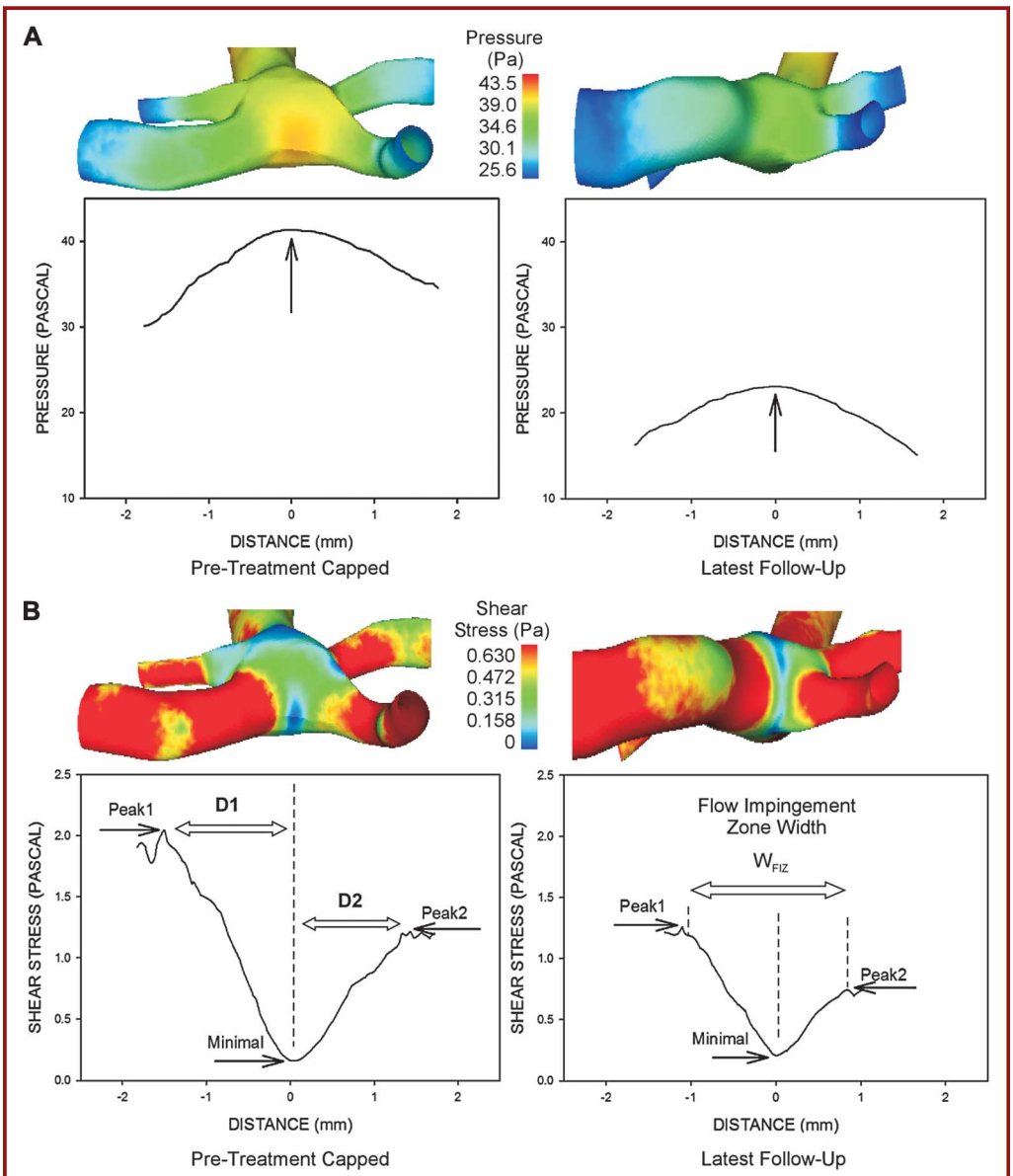


FIGURE 6. *Comparison of pressure and WSS plotted against the distance on the apical centerline after virtual aneurysm removal (pretreatment capped) with latest follow-up.* **A**, *pressure: upward arrow indicates the summit of the pressure at the center of the FIZ.* **B**, *WSS: D1 indicates the distance between the minimal and peak 1 of WSS, whereas D2 indicates the distance between the minimal and peak 2 of WSS. The dashed line demonstrated the minimal WSS at the center of the FIZ, which corresponds to the impingement center at the bifurcation apex wall. The sum of D_1 and D_2 yields the width of the FIZ, W_{FIZ}. WSS, wall shear stress; FIZ, flow impingement zone.*

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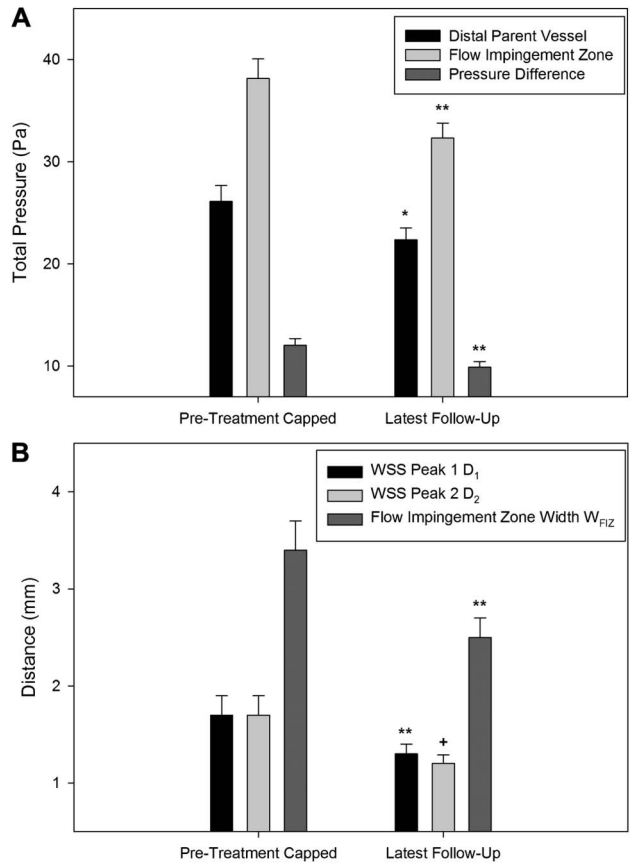


FIGURE 7. **A**, *bar graph of pressure at the bifurcation apex shows decreased pressure difference at the center of the flow impingement zone following stent-induced angular remodeling.* **B**, *analysis of width of the flow impingement zone (W_{FIZ}) as measured by distance from FIZ center to either WSS peaks on daughter branches D_1, D_2. (+, P < .02; *, P < .01; **, P < .005). WSS, wall shear stress; FIZ, flow impingement zone.*

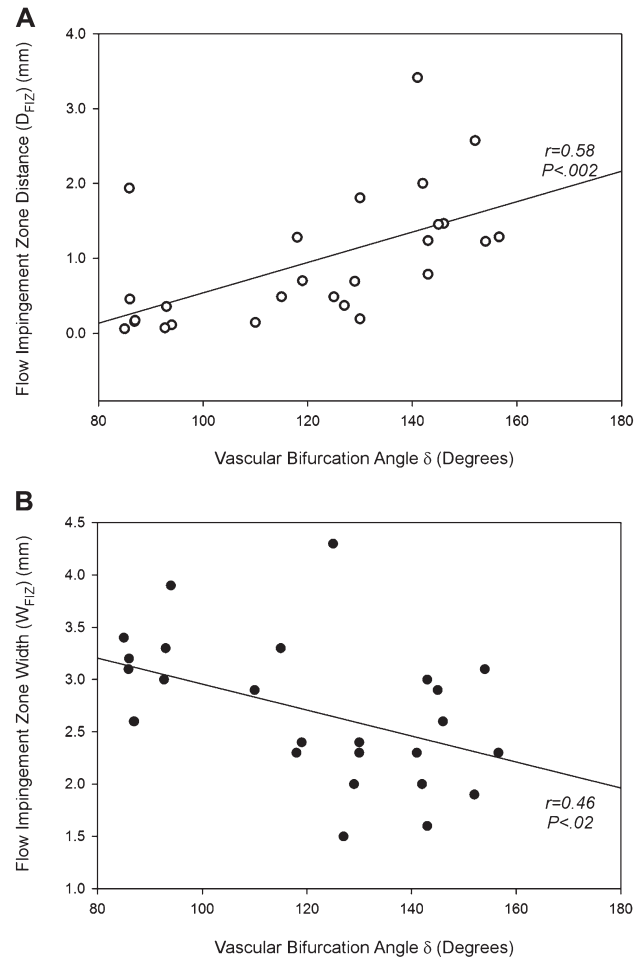


FIGURE 8. **A**, *linear correlation between flow impingement zone distance from parent vessel centerline (D_{FIZ}) and bifurcation angle δ at the target parent-daughter bifurcation consistent with increasing migration of the FIZ with stent-induced vessel straightening.* **B**, *inverse linear correlation between flow impingement zone width (W_{FIZ}) consistent with FIZ narrowing with vessel straightening. FIZ, flow impingement zone.*

showed for the first time that stent-induced angular remodeling of intracranial vascular bifurcations was associated with statistically significant hemodynamic alterations at the apical region, specifically at the FIZ. The central finding of the study is that the isolated stent effect of straightening the target parent-daughter vessels resulted in statistically significant migration of the FIZ as well as a narrowing of its width, in effect, fundamentally altering the underlying wall shear forces and attenuating the pressure at the apex. It is important to note that our method did not take into account the microhemodynamic and mechanical changes induced by the deployment of the stent into the vessel wall nor any resulting flow-diverting effect from the stent struts on the vessel wall or additional resistance to flow on the unstented daughter branch. Nonetheless, the hemodynamic changes resulting from the stent-induced angular remodeling should be considered in addition to the other known stent-mediated effects such as flow diversion[14] and intimal hyperplasia.[1,3]

With the major blood flow directed toward the stented daughter vessel branch, the direct FIZ on the bifurcation apex wall was reduced, the flow impingement center was noted to move toward the nonstented side, and the total pressure on the bifurcation apex wall was decreased. The distance between the 2 peaks of WSS created by flow on the bifurcation apex wall also decreased statistically significantly, which indicates not only the reduction of the direct FIZ, but also a more focused region of both WSS peaks on the impingement zone. These important hemodynamic alterations should be expected to have important effects on the underlying aneurysm-inducing forces as has been recently shown.[11,15] Meng et al demonstrated that apical regions exposed to a high product of WSS and its spatial gradient undergo destructive remodeling akin to that seen in regions undergoing

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aneurysm genesis. The stent-induced FIZ migration and narrowing would be expected to lead to statistically significant changes in this process, specifically moving these forces to a new region away from the stented segment.

The momentum per unit volume of flow is greatest in the central velocity stream, because of their relatively high flow velocity.[16] The impact and sudden deflection of central streams at the apex result in the transmission of a pulsatile impulse to that region of the bifurcation, and, at the moment of impact, a portion of the kinetic energy of the moving blood is converted to pressure energy (stagnation pressure) at the apex. This was seen to decrease in the current study as a result of the angular remodeling induced by stenting. The current study simulated constant systolic flow input; pilot studies using pulsatile conditions showed the same pattern of change induced by the angular alteration (data not shown). Nonetheless, it is possible that, under certain pulsatile conditions, additional phenomena not detected in the current study may become evident; these will require a more detailed and computation-intensive pulsatile analysis in the future. Stehbens[9] studied flow in glass models of arterial bifurcations with different bifurcation angles varying from 30° to 180° and berry aneurysms at low Reynolds numbers and found that the model with the bifurcation angle of 30° and sharp apex seemed to disturb the laminar flow least. For a given angle of bifurcation, it was found that the blunter the apex, the lower the velocity that was required to initiate major vortex formation. Similarly, he reported that the wider the bifurcation angle, the lower was the velocity required to initiate major vortex formation. Consequently, the stent-induced angular remodeling and vessel straightening would be expected to counteract these deleterious features of wide-angled and blunt bifurcation apices.

Although the stent-induced FIZ migration can be beneficial if it moved toward less vulnerable regions of the apex that are less likely to progress,[9,18] it is also plausible that the FIZ migration could also lead to conditions favoring aneurysm progression or recanalization. In addition, it is possible also that the FIZ could be migrated into less biologically active endothelialized regions of the apex, such as the coil mass, away from the vulnerable neck inflow-zone. This angle remodeling-induced hemodynamic remodeling could either compete with or complement the beneficial effects of intimal hyperplasia and flow diversion of the stent struts.

One additional factor that should not be neglected is the effect of parent vessel straightening proximal to the actual bifurcation; this is likely to be the only effect seen in the waffle-cone stent-coiling technique[17,19] that has not been studied in the current study. The waffle cone technique allows the placement of coils in some cases, but it is hard to reckon that this changes the hemodynamics in a favorable way, because all the flow is directed into the coil package. In addition, although it is possible that coiling itself, especially in large and giant aneurysms, can lead to changes in the parent vessel geometry that were not accounted for by the dome removal approach used in the current study, in none of the cases used here were the domes so large that coil packing alone would have led to noticeable distortion of the bifurcation apical anatomy. The assumption of zero distal vascular resistance at the outflow zones of the modeled bifurcations is an accepted simplifying construct in CFD modeling, because it is currently difficult to estimate or measure directly. This simplification led to an artificially small, although statistically significant, change in pressure at the FIZ; the actual real value is likely larger.

CONCLUSION

With the increase of the stented angle and the decrease of the bifurcation angle seen in response to self-expanding intracranial microstents, blood flow is deflected toward the stented branch and less toward the bifurcation apex, consequently leading to a migration and narrowing of the FIZ and a decrease in apical pressure. This novel response to intracranial stenting should be added to intimal hyperplasia and flow diversion properties of stents used in stent-mediated coiling. Further study is needed to evaluate the clinical effects of this angular remodeling process, such as altered recanalization, aneurysm recurrence, or improved durability.

Disclosure

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COMMENT

The authors describe the angular component of vascular remodeling resulting in straightening of the bifurcation angle in an immediate and delayed fashion after deployment of the stent.

This is an interesting and well-written paper and I congratulate the authors for their continued efforts to understand the hemodynamics of coil embolization. The authors argue based on their data which is derived from a synthesis of measurements of the vascular anatomy before and after coiling and stent deployment and computational fluid dynamic (CFD) analysis to evaluate the hemodynamic alterations that the altered geometry of the vascular tree has number of effects: stent-induced angle remodeling leads to migration and narrowing of the flow impingement zone with blunting of the bifurcation apical pressure which would be responses predicted by CFD analysis should be considered in addition to the known intimal hyperplastic and flow diverting properties of intracranial stenting.

If we accept the numerous assumptions and limitations of this study, and the authors do point these out whenever indicated, then the results are indeed very interesting. A few assumptions are more complex and should be pointed out to the reader: The pre-treatment system was simulated by removing the aneurysm virtually from the geometry and performing CFD simulation in order to predict the effect of coiling without stent deployment. This leaves us wondering about the effect of the coils on the geometry alone, since there is a certain variability in packing density, changes in wall stress due to placing of a coil that is slightly too large compared to one that is slightly too small, that cannot be accounted for. On the other hand it is difficult to make the case that this has any significant impact on the results. Additionally the stent itself is not modeled, again it is difficult to even estimate whether this would translate to a second-order effect or could this affect the primary order of magnitude effects described here.

The authors uncover a range of changes that are predicted to occur after stent-assisted coiling of bifurcation aneurysm which the authors attribute by way of virtual deduction to the stent placement. It may be a consideration to attempt validation of a part of this study by looking at aneurysms that fit the inclusion criteria for this study and where the aneurysm was coiled first and then the stent placed. This may not be the senior authors' clinical preference but it is possible that some other aneurysms were treated in this order rather than the order of events described in the paper and could be analyzed the same way.

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