

## Original Investigation

# Comparison of TOF MRA, Contrast-Enhanced MRA and Subtracted CTA from CTP in Residue Evaluation of Treated Intracranial Aneurysms

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This study has been presented at the 16<sup>th</sup> World Congress of Neurosurgery in Istanbul, Turkey, between 20 and 25 August, 2017.

**ABSTRACT**

**AIM:** To compare effectiveness of contrast-enhanced magnetic resonance angiography (CE-MRA), 3D-Time-of-flight magnetic resonance angiography (3D-TOF-MRA) and subtracted computed tomography angiography from computed tomography perfusion (sub-CTA) in residue evaluation of intracranial aneurysms treated either with coiling or clipping.

**MATERIAL and METHODS:** Sixteen treated aneurysms, which were evaluated with three methods within two weeks after the operation, were enrolled. The success of each imaging technique in the demonstration of residue aneurysm and nearby vessels was compared by Fisher's Exact Test. The differences among the three methods were evaluated by Cochran's Q test ( $p \leq 0.05$ ).

**RESULTS:** Perfusion abnormality was noted in 81% of clipped and none of coiled patients. Vessel visualization in the vicinity of aneurysm was better in sub-CTA, followed by CE-MRA. In clipped aneurysms, sub-CTA revealed residue aneurysms in 16.7% of the patients while 3D-TOF-MRA and CE-MRA revealed none. In coiled aneurysms, CE-MRA revealed residue aneurysms in 100%, and TOF-MRA in 33.3% while sub-CTA revealed none. Although dramatic differences were noted in the evaluation of residue aneurysm as well as nearby vessel visualization, no statistical significance was noted due to very few patients in the subcategories.

**CONCLUSION:** This is the first study comparing the effectiveness of CE-MRA, 3D-TOF MRA and sub-CTA in residue aneurysm evaluation although our results were suggestive, not conclusive. Vessel visualization in the vicinity of the aneurysm was better in sub-CTA in all cases regardless of coiling or clipping. Residue aneurysms were more commonly revealed by CE-MRA in coiled patients and more commonly and better shown by sub-CTA in clipped patients in addition to showing perfusion abnormality that was more common in clipped patients.

**KEYWORDS:** Aneurysm, CE-MRA, TOF-MRA, CTA, CTP, Intracranial

**ABBREVIATIONS:** **CE-MRA:** Contrast-enhanced magnetic resonance angiography, **CTA:** Computed tomography angiography, **CTP:** Computed tomography perfusion, **MRA:** Magnetic resonance angiography, **3D-TOF-MRA:** Three dimensional time-of-flight magnetic resonance angiography, **Sub-CTA:** Subtracted computed tomography angiography from computed tomography perfusion, **MCA:** Middle cerebral artery, **ICA:** Internal carotid artery, **CT:** Computed tomography, **MRI:** Magnetic resonance imaging.



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## ■ INTRODUCTION

Assessment of treated aneurysms is critical and needs effective method to reveal any residue. However, this assessment is speculative as to how long, how often and by which technique the treated aneurysms need to be followed and which subgroups carry a higher or lower risk for reopening. This study compared contrast-enhanced magnetic resonance angiography (CE-MRA), three dimensional time-of-flight magnetic resonance angiography (3D-TOF-MRA) and subtracted computed tomography angiography from computed tomography perfusion (sub-CTA) for the follow-up of treated intracranial aneurysms either with coils or clip.

Intracranial aneurysms are treated either with microneurosurgical clipping or endovascular procedures, e.g. coiling (13,18). Intraarterial digital subtraction angiography (DSA) is considered to be the gold standard for the detection and treatment following of intracranial aneurysms, but this technique is invasive, irradiating and associated with a risk of thromboembolic complications as well as complications related to contrast media injection (14). In many institutions, magnetic resonance angiography (MRA) and computed tomography angiography (CTA) are usually preferred in the follow-up of treated cerebral aneurysms due to their non-invasiveness. However, on control images, these non-invasive imaging techniques become much more challenging in the vicinity of the treated aneurysm owing to the interaction of the various therapeutic devices (i.e., aneurysm clips, embolic coils, and/or stents) with the proton relaxation signal intensity of magnetic resonance imaging (MRI) or photon flux of computed tomography (CT). Coil- or clip-related artifacts hinder the evaluation of possible residue aneurysm as well as vessels in the region of the treated aneurysm. Therefore some institutions still prefer using standard catheter based DSA for evaluation despite its invasiveness (10). In some, DSA is still the primary imaging modality in residue evaluation in the 3 months following clipping of aneurysms in patients with subarachnoid bleeding.

In patients with aneurysmal subarachnoid bleeding, early detection of vasospasm is critical for the treatment and survival of patients. Although DSA is invasive, it is still preferred since it allows intraarterial treatment during imaging of vasospasm. Nowadays, non-invasive imaging to visualize vasospasm and the associated perfusion deficit has become possible via CT perfusion (CTP)(2,15). In new scanners, CTA views can be created from CTP data by subtraction via post-processing. Both perfusion deficit and vasospasm can be evaluated only by CTP imaging without increasing radiation dose. In the literature, TOF-MRA is suggested for residue imaging in aneurysms treated by coiling. TOF-MRA is non-invasive imaging with no need for contrast agent for visualization of brain vessels. Contrast enhanced MRA (CE-MRA) is not routinely used for brain vessel imaging. However, it shows brain vessels much better than TOF-MRA because of intravenous contrast injection. Some institutions prefer CE-MRA for residue evaluation in aneurysms treated by coiling (17). In our institution, we prefer CE-MRA to TOF-MRA in routine imaging if we use contrast agent for another reason.

In our institution, TOF-MRA, CE-MRA, CTP and DSA can be done for residue evaluations of treated aneurysms.

We retrospectively collected the patients that had undergone TOF-MRA, CE-MRA or CTP within two weeks for residual aneurysm evaluations following treatment either by coiling or clipping, or for another reason such as vasospasm and perfusion deficit. We compared the three imaging modalities in terms of residual aneurysm evaluation.

## ■ MATERIAL and METHODS

All patients harboring ruptured or unruptured intracranial aneurysms were treated by our endovascular team with microneurosurgical clipping or endovascular coiling procedures at our center. Our endovascular team includes neurosurgeons, radiologists, neurologists and anesthesiologists. All patients' examinations were performed by a neurosurgeon (TTD) with 10 years of experience and radiological evaluation was performed by a fellowship educated neuroradiologist (AA) and an interventional neuroradiologist (HO), both with 20 years of experience. They reviewed the cases together and reached a consensus in any disputed case. Approval of the ethical review board of the hospital was obtained for this retrospective study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

### Study Population

Treated aneurysms, which were evaluated with TOF-MRA, CE-MRA and CTP within two weeks after the operation, were taken into consideration. CT angiography views were created from CT perfusion views by the subtraction method.

Fifteen patients with saccular aneurysms were enrolled into the retrospective study from April 2013 to November 2016. One patient had two treated aneurysms. A total of 16 treated aneurysms were taken into consideration. These cases consisted of 11 females and 4 males. Their ages ranged from 25 years to 82 years with a mean of 52.8 years. Among them, 7 had hypertension and 2 had both hypertension and diabetes mellitus as co-morbidities. The location of the aneurysms and their treatment modalities are shown in Table I. Of the 16 aneurysms, 3 were coiled (2 x Neuroform™, Boston Scientific, Natick, MA; 1 x Driver™, Medtronic Inc., Minneapolis, MN). The other 13 aneurysms were surgically clipped (Sugita Titanium Aneurysm Clip. (Mizuho Ika Kogyo Co., Tokyo, Japan) (Table I).

### Radiological Imaging

MRI was performed on a 1.5 Tesla system (Avanto; Siemens Medical Solution, Erlangen, Germany) with an 18-channel body coil and high performance gradients (maximum gradient, 45 mT/m; maximum slew rate, 200 T/m/s). All examinations were performed with a standard head coil.

### TOF MR Angiography

3D-TOF images were acquired in the transverse plane with the following parameters: TR/ TE, 25/7 ms; flip angle, 25 degrees;

**Table I:** Location of Aneurysms and Their Treatment Modalities

Aneurysm No	Location of Aneurysm	Clipped/Coiled
2443099	Supraclinoid ICA	Clipped
571805	Supraclinoid ICA	Clipped
1537755	Carotid Terminus	Clipped
291548	Carotid Terminus	Coiled
2322412	MCA trifurcation	Clipped
206481	MCA trifurcation	Clipped
2470446	M1 Saccular	Clipped
2390449	Anterior communicating artery	Clipped
2390449	Supraclinoid ICA	Clipped
2376613	Anterior communicating Artery	Coiled
1152900	Supraclinoid ICA	Clipped
2316786	Supraclinoid ICA	Coiled
168303	Anterior Communicating Artery	Clipped
1576940	MCA trifurcation	Clipped
99555	MCA trifurcation	Clipped
2264928	MCA trifurcation	Clipped

**ICA:** Internal carotid artery, **MCA:** Middle cerebral artery, **M1:** Part of the middle cerebral artery from the origin to bifurcation/trifurcation.

matrix, 211×256; field of view (FOV), 200×170 mm; slice thickness, 0.7 mm. Source images were then reconstructed using a maximum intensity projection (MIP) algorithm. Multiple projections using a large FOV were obtained every 15 degrees over 180 in lateral and anteroposterior views, providing 12 views in total.

#### Contrast-Enhanced MR Angiography

A CE-MRA fast imaging with steady-state precession (FISP) sequence with a rectilinear k-space sampling (flip angle, 30°; FOV, 230 mm; matrix, 259×384; TR, 3.44; TE, 1.39; slice thickness, 1.0 mm) was acquired in the coronal plane with an acquisition time of 40 seconds. A bolus of 0.2 mmol/kg of gadolinium chelate (gadoterate meglumine; Dotarem, Guerbet, France) was injected at a rate of 2 mL/s using an MRI-compatible power injector. Source images were then reconstructed using a MIP algorithm. Multiple projections using a large FOV were obtained every 15° over 180 in lateral and anteroposterior views, providing 12 views in total.

#### Volume CTP-CTA

CTP was performed on a 128-row CT scanner (SOMATOM Definition, Flash; Siemens Healthcare, Erlangen, Germany). CTP covered the whole brain. The CTA data set was recovered from whole brain coverage CTP.

Volumetric CTP was performed in an adaptive 4D spiral mode (tube voltage, 80 kV; tube current-time product, 180 mAs; collimation, 128 × 0.6 mm; rotation time, 0.3 seconds; CT dose index volume, 74 mGy). The coverage in the z-axis included 13 cm from the skull base. Thirty spiral scans were performed within 45 seconds. In the adaptive 4D spiral mode, the table continuously performs a smooth, periodic motion between 2 end positions while acquiring spiral scans. This generates multiple 3D scans that are sequential over time. The effective dose was 2.29 mSv. 45 mL of iodinated contrast iohexol (Omnipaque, 300 mg/mL of iodine; Amersham Health, Princeton, NJ) followed by 50 mL of saline flush, injected via an 18-gauge cannula into a cubital vein at a rate of 4.7 mL/s using a power injector (Ulrich, Missouri). The Volumetric CT scan was initiated after a start delay of 4 seconds; 30 consecutive 3D datasets were reconstructed with the parameters described above. The time point with the highest opacification in vessels was selected from the dataset. These images were subtracted from first images in which there is no contrast material in the vessel. With subtraction, bone and artifact were removed. CTA data and their MIP reconstructions were created using the CT scanner workstation (Syngo; Siemens).

#### Data Analysis

Clipped or coiled aneurysms were evaluated by the 3 imaging techniques in terms of residue aneurysm and nearby vessel visualization. Perfusion abnormality was evaluated by CTP.

Scoring was used for visualization of vessels in the vicinity of aneurysms among the 3 imaging techniques. The best technique in depicting vessels nearby an aneurysm was scored as three points; the second best was scored as two points and the third one as one point. The highest total score belonged to the best imaging technique.

In the evaluation of residual aneurysms, the 3 imaging techniques were used to show the presence or absence of residual aneurysms. DSA was further performed in the presence of residual aneurysms.

#### Statistical Analysis

Measurements were entered into SPSS (ver. 19) and statistical analyses including Fisher's Exact Test and Cochran's Q were carried out. Among the imaging techniques, the success of each imaging technique in the demonstration of residue aneurysm and nearby vessels was compared by Fisher's Exact Test. In each imaging technique, the differences among the three imaging techniques were evaluated by Cochran's Q test. A significance level was set to 0.05 or lower.

## RESULTS

A perfusion abnormality was revealed only by CTP. Following treatment by either coiling or clipping, a perfusion deficit with hypoperfusion, was present in 57% and hyperperfusion in 7% of the patients. The remaining 35% of the patients showed normal perfusion. Perfusion abnormality was much more common in clipped patients, of whom 72% showed hypoperfusion and 9% hyperperfusion while the rest (18%) of the clipped patients and all coiled patients showed normal perfusion.

Among the three imaging techniques, vessel visualization in the vicinity of the aneurysm was best in sub-CTA, followed by CE-MRA and TOF-MRA, respectively.

In patients with clipped aneurysms, sub-CTA revealed residue aneurysms in 16.7% of the patients while TOF-MRA and CE-MRA revealed none in the same population (Figure 1A-F). In patients with coiled aneurysms, CE-MRA revealed residue aneurysms in 100% and TOF-MRA in 33.3% while sub-CTA revealed none in the same population (Figures 2A-E, 3A-F). Subsequently, residue aneurysms were all confirmed by DSA.

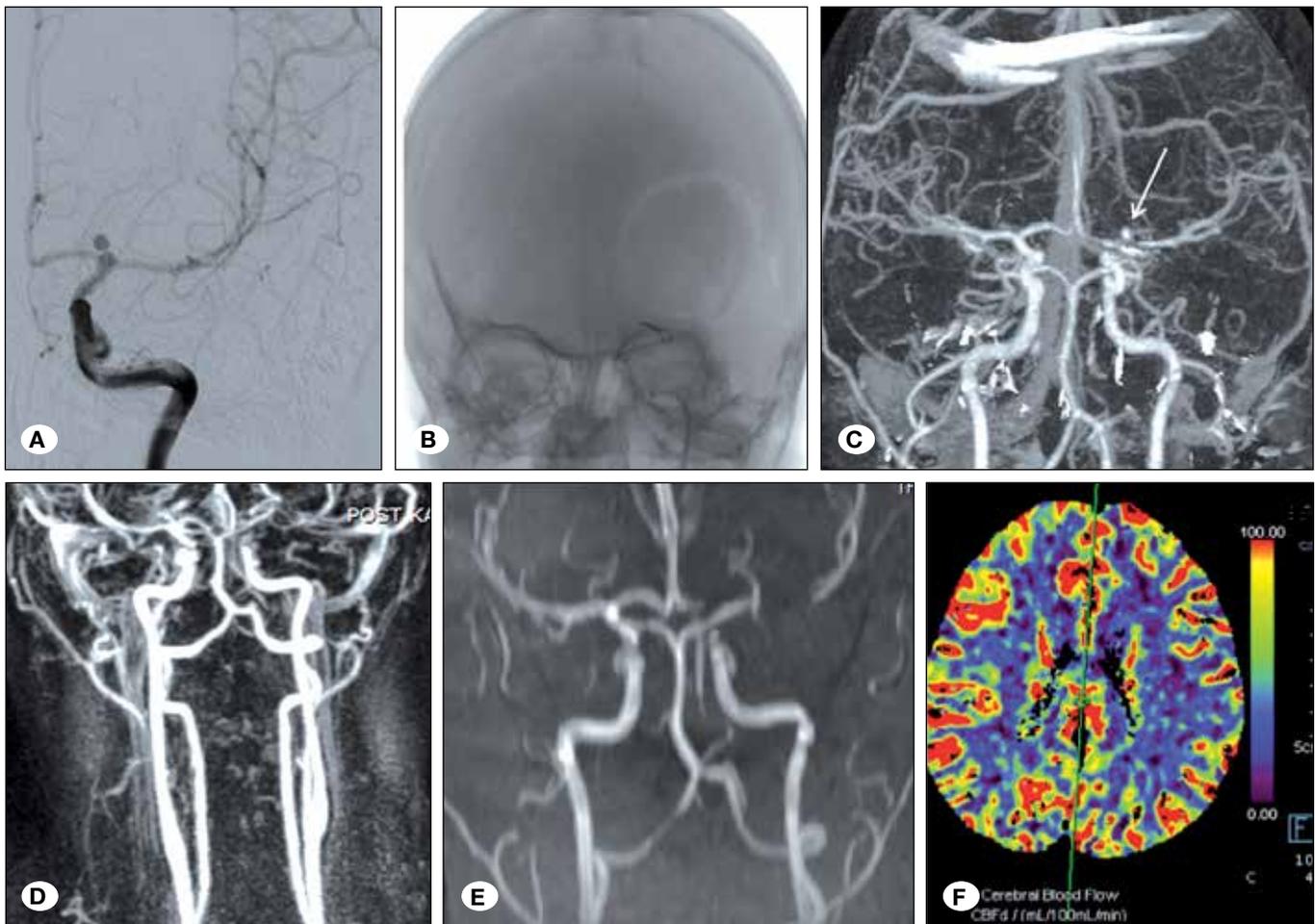
Although dramatic differences were noted in the evaluation of residue aneurysm as well as nearby vessel visualization, we could not find any statistical significance for either of them due to very few patients in the subcategories.

### DISCUSSION

In the assessment of treated aneurysms, the imaging technique to be chosen should be non-invasive, easy and repeatable. Until recently, the gold standard technique has been catheter-based DSA that is usually performed at either 3

to 6 or 12 to 15 months depending on the institution's policy. However, DSA is invasive and carries a measurable degree of morbidity. Moreover, the technique of DSA includes patient discomfort, cost, and radiation exposure (17). In the literature, timing for evaluation of residue aneurysm by DSA is not clear, repeatability of DSA is not easy, and new non-invasive imaging techniques challenge the need for DSA. Therefore, DSA is not routinely used in the follow-up assessment of treated aneurysms at several institutes (1).

Recent studies have suggested non-invasive imaging techniques such as CT or MRI modalities (24,26,27). Lately, the use of these modalities, such as CTA, 3D-TOF MRA and CE-MRA have increased but artifacts resulting from clip and coil cause a problem in determining the exact occlusion rates in treated aneurysms. High-attenuation platinum alloy coils causes marked beam hardening and streak artifact on CT and CTA, which typically obscure not only the aneurysm but also the adjacent parent and branch vessels as well as the surrounding brain parenchyma. Platinum alloy coils create relatively little distortion of the local magnetic field and, therefore, cause much less dramatic disruption of the MRI and MRA signal intensity (3,22,23,25,26).

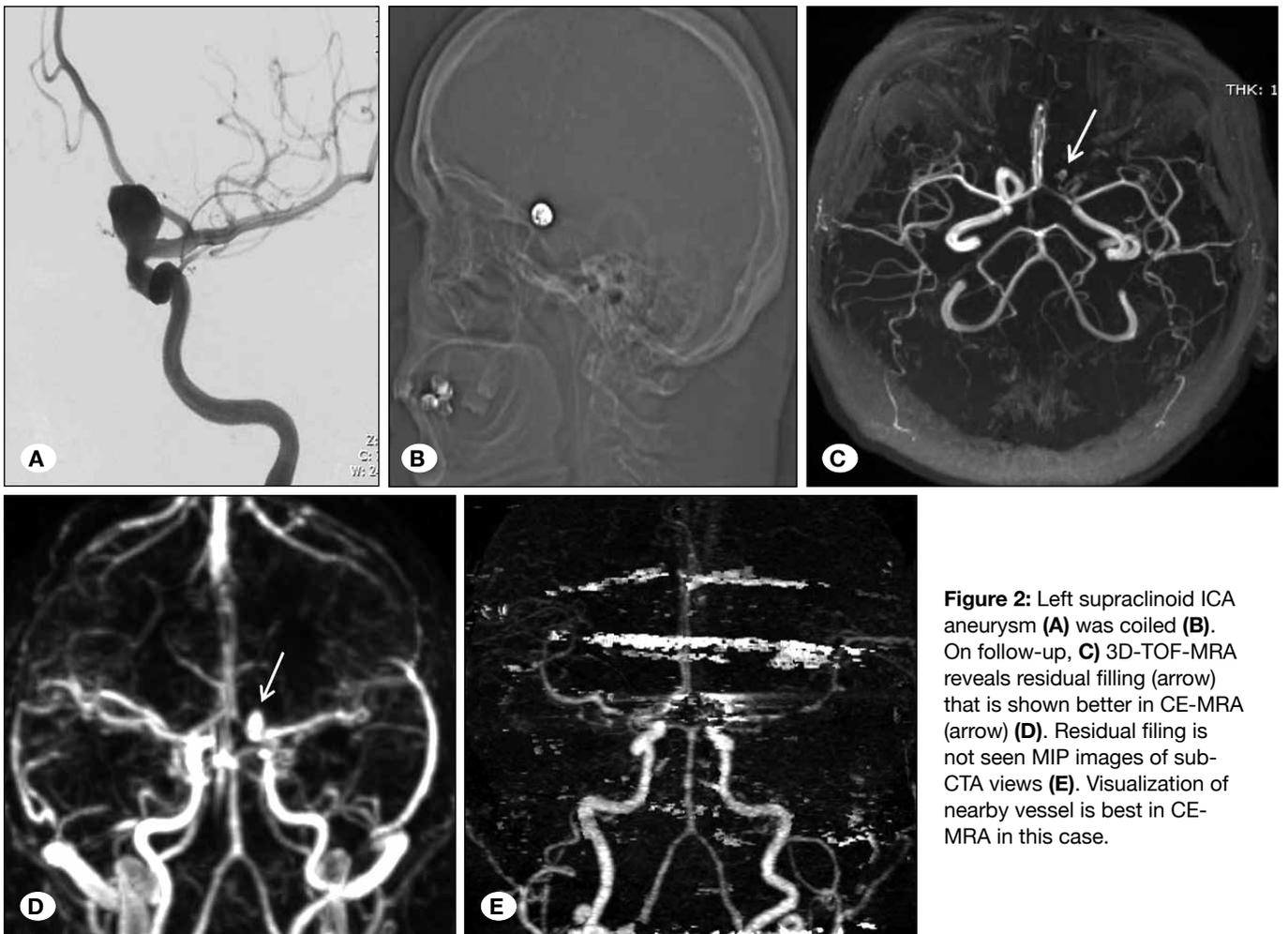


**Figure 1:** Left carotid terminus aneurysm (A) was clipped (B). On follow-up, (C) sub-CTA reveals residual filling (arrow) that is not shown on CE-MRA (D) or 3D-TOF-MRA (E). Visualization of nearby vessel is best on sub-CTA in this case. Additionally, cerebral blood flow is decreased on left middle cerebral artery territory on CTP (F).

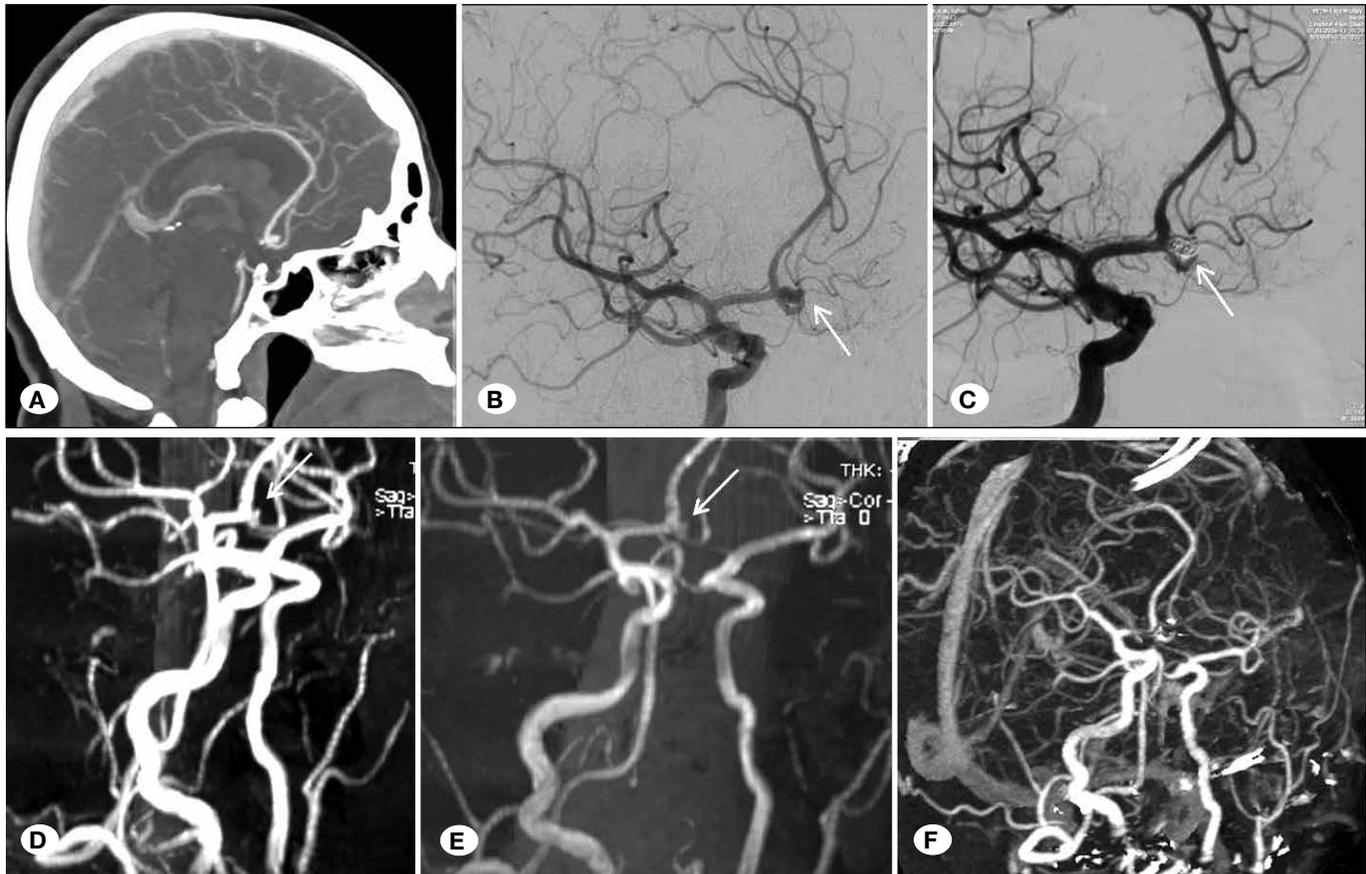
In follow-up of intracranial aneurysms treated with endovascular coil occlusion, two different MRA techniques (3D-TOF-MRA and CE-MRA) are discussed (18). Most have reported the superiority of CE-MRA (3,12). CE-MRA has been shown to be as accurate as conventional catheter-based cerebral angiography. CE-MRA has replaced DSA for this purpose in many institutions. Several studies have compared CE-MRA to DSA and have shown that CE-MRA is an accurate technique to reveal aneurysmal remnants and re-canalization after endovascular coiling (12,17,21). On the other hand, some studies also showed lower sensitivities of CE-MRA compared with the TOF-MRA for the detection of residual neck or residual aneurysm. Furthermore, TOF-MRA provides better spatial resolution than CE-MRA that is inherently not susceptible to saturation effects (6,11,21). Some could not find any statistical difference between accuracies of 3D-TOF-MRA and CE-MRA with no added benefit of contrast administration (5,8,12,20). Moreover some show that CE-MRA and 3D-TOF-MRA were less accurate than DSA in the detection of aneurysm remnant (12). Some reported that MRA is better than DSA because of artifacts resulting from subtraction methods and opaque coil packages limiting DSA. Finally, MRA has begun to replace DSA for the detection of residual or recurrent aneurysms in follow-up of aneurysms treated with endovascular coil occlusion (7), although some studies were still suspicious for MRA (11,20). Furthermore, endovascular coil mass has high hyperdense artifact on CT techniques. These coils are designed to allow optimum visibility during endovascular treatments performed under fluoroscopic control. The coil-related artifacts typically obscure not only the aneurysm but also the adjacent parenchyma and branch vessels as well as the surrounding brain parenchyma on CT, CTA imaging. CT techniques also have radiation exposure hazards (7).

Technical advancements have made MRI techniques more effective. Several studies have reported 3T to be superior to 1.5 T when utilized for follow-up of coiled intracranial aneurysms, and although artifacts are more pronounced in 3T than 1.5T, remnant aneurysm are better shown in 3T (7,15,22,23). MRI techniques, such as short TE acquisition and doubled receiver bandwidth, are used to decrease coil-related artifact in both CE-MRA and TOF-MRA (21,22). CE-MRA carries a risk of nephrogenic fibrosis due to gadolinium -containing contrast agent in patients with chronic renal diseases (17).

In the follow-up of intracranial aneurysms treated with clipping, CE-MRA and TOF-MRA have been of limited value due to susceptibility artifacts of clips obscuring the region of interest. Some studies have shown that CE-MRA and TOF-MRA



**Figure 2:** Left supraclinoid ICA aneurysm (A) was coiled (B). On follow-up, C) 3D-TOF-MRA reveals residual filling (arrow) that is shown better in CE-MRA (arrow) (D). Residual filling is not seen MIP images of sub-CCTA views (E). Visualization of nearby vessel is best in CE-MRA in this case.



**Figure 3:** Anterior communicating artery aneurysm on CTA (A) was coiled with pre- (arrow on B) and postcoiling DSA views (arrow on C). On follow-up, MIP image of CE-MRA (arrow on D) and 3D-TOF-MRA (arrow on E) reveals residual filling that is not seen on MIP view of sub-CTA (F). Visualization of nearby vessel is best in CE-MRA in this case.

are of use in assessment of patients in whom artifacts were reduced by using titanium alloy clips (6,9). Imaging after surgical aneurysm clipping has traditionally been evaluated with DSA. CTA may provide an acceptable alternative in many cases, particularly for long-term postoperative follow-up (16,19,27). Recent studies reporting the role of CTA for postoperative evaluation of aneurysmal occlusion rates after surgical clipping suggest that CTA might be considered valuable in patients treated with titanium clips (19,27,28). CTA was reported to have a higher sensitivity and specificity in the detection of residue-recurrent aneurysm, when compared to DSA, and especially residue-recurrent aneurysm larger than 2 mm (19). Artifacts from clips on CTA can also be reduced by using titanium alloy clips instead of cobalt alloy clips to detect small residual-recurrent aneurysms (1).

CTP is also a non-invasive technique. Nevertheless, residue aneurysm evaluation by CTA and CTP is not commonly used in clinical practice. CTP quantitatively evaluates cerebral hemodynamics to identify regions of potential ischemia due to vasospasm (1,15). In our study, we evaluated remnant aneurysm with subtracted CTA from CTP. During CTP, consecutive images were taken as contrast agent went through the brain. If we subtracted the image with contrast in

arterial vessels from the image with no contrast in the brain yet, only the arterial vessel can be seen. By subtraction, artifacts resulting from the clip can be erased. Our study is first study using sub-CTA from CTP in remnant aneurysm evaluation in clipped patients. We noticed that residue aneurysms of clipped patients being well depicted on sub-CTA comparison to the CE-MRA and TOF-MRA.

In the literature, many studies have compared MRA techniques with each other or MRA and DSA or DSA and CTA (4). Our study is first study comparing all three non-invasive imaging techniques (CE-MRA, TOF-MRA and sub-CTA from CTP) in the same population as well as sub-CTA from CTP, a new technique that has never been studied in the follow-up of treated aneurysms so far. We suggest that the sub-CTA from CTP should be used in the follow-up of clipped patients due to its success in artifact removal and demonstration of residue aneurysm.

Our study has some limitations. First, the few patients in subcategories hinder the statistical analysis although dramatic differences are present in the evaluation of residue aneurysm as well as nearby vessel visualization in subcategories. Second is we compared three imaging modalities with each other. We could not use DSA as a gold standard for all cases.

However the cases with residual aneurysm were all confirmed by DSA. Third, based on the limitations mentioned above, our results were suggestive not conclusive.

## ■ CONCLUSION

In the follow-up of treated aneurysms, the choice of imaging technique to be used should be made on both a patient-by-patient and clinical experience basis. However, we noticed that residual aneurysms were more commonly revealed by CE-MRA in coiled patients and they were more commonly and better shown in sub-CTA from CT perfusion in clipped patients. In addition, perfusion abnormality is more common in clipped patients compared to coiled ones. These non-invasive techniques can reduce or eliminate the need for conventional catheter-based angiography. Further studies with larger series comparing the effectiveness of CE-MRA, 3D-TOF-MRA and sub-CTA from CT perfusion in the evaluation of residual aneurysm are needed to enhance our results.

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