UPDATE IN RADIOLOGY

Neuroimaging follow-up of cerebral aneurysms treated with endovascular techniques

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Abstract There are no specific recommendations in clinical guidelines about the best time, imaging tests, or intervals for following up patients with intracranial aneurysms treated with endovascular techniques. We reviewed the literature, using the following keywords to search in the main medical databases: cerebral aneurysm, coils, endovascular procedure, and follow-up. Within the Cerebrovascular Disease Group of the Spanish Society of Neuroradiology, we aimed to propose recommendations and an orientative protocol based on the scientific evidence for using neuroimaging to monitor intracranial aneurysms that have been treated with endovascular techniques. We aimed to specify the most appropriate neuroimaging techniques, the interval, the time of follow-up, and the best approach to defining the imaging findings, with the ultimate goal of improving clinical outcomes while optimizing and rationalizing the use of available resources.

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PALABRAS CLAVE
Aneurisma cerebral;
Espirales;

Resumen No existen recomendaciones específicas en las guías de práctica clínica sobre el tiempo, prueba de imagen ni intervalo para controlar la evolución de los aneurismas


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Introduction

Subarachnoid hemorrhage (SAH) is considered to be one of the most serious acute cerebrovascular diseases and causes 5% of all hospital strokes. Its most important cause is the rupture of an intracranial aneurysm.

Prevalence of intracranial aneurysms in the overall population is 0.4% in retrospective studies of autopsies, 3.6% in retrospective angiographical studies and 6% in prospective studies.\(^1\) The incidence of SAH ranges from 2 to 22.5 cases for every 100,000 person-year\(^6\) with great variations among different regions. It is more common in women and it is associated with the consumption of tobacco, alcohol and cocaine, family syndromes and predisposing genetic diseases (Ehlers–Danlos, dominant autosomal heptorenal polycyst disease).\(^3,4\) Patients diagnosed with aneurysms have an annual risk of bleeding of 0.4% per year.\(^7\)

The overall population mortality rate is 50% and hospital mortality rate depends directly on the clinical state at the moment of admission, the Fisher scale, the size of aneurysm and on the type of therapy used.\(^7\) The mortality rate of a ruptured untreated brain aneurysm is 60% being the dependency rate close to 15–20%. The main prognostic factor is the rate of re-bleeding around 20–30% during the first month and 3% afterwards.\(^8\)

The surgical management of ruptured aneurysm started back in the 60’s improved significantly the prognosis of these patients when reducing the rate of hospital mortality to 8–20% and the rate of dependent patients to 20–37%.\(^9\) Both the endovascular procedures with platinum coils and assisted procedures have improved the excellent results of surgical therapy leaving a mortality rate of 7–15% and the rate of dependent patients close to 20%.

In the year 2002 the International Subarachnoid Aneurysm Trial Collaborative Group (ISAT)\(^10\) multicenter randomized study was published; this study comprising 2143 patients in 43 centers compared surgical management to endovascular therapy. The manageable ruptured aneurysms through endovascular and surgical approaches were randomized leaving those aneurysms that were more accessible for each one of these arms of treatment under-represented. When it comes to disability-free survival at 1 year this study showed that the outcomes of endovascular therapy were way better than those of surgical management. The reduction of relative and absolute risks at 1 year in dependence or death of the endovascular group vs the surgical group was 22.6 and 6.9%, respectively. Still the rate of re-bleeding from surgical management is lower and the percentage of closed aneurysms is significantly greater even though the ongoing analysis of the ISAT study through the years has shown that yet despite these inconveniences protection in terms of survival to endovascular therapy stays the same with the passing of time.\(^11,12\) Many prospective and retrospective studies have confirmed these findings.\(^13\)

Literature shows that intracranial aneurysms can reopen and grow after therapy.\(^14\) This growth or recurrence of aneurysms is due to compaction of the coil mass, growth of the residual aneurysmal neck, or expansion of the back of the aneurysm.\(^15\) There are also two (2) different types of aneurysms: (1) early—during the first six (6) months after therapy and (2) late—due to a regrowth of the aneurysm treated or to the appearance of a new aneurysm in the same location.\(^16\)

There are no specific recommendations in the guidelines of clinical practice on the time, image modality or interval used to do a follow-up of the aneurysms treated through endovascular approach.\(^27\) The only consensus is that such a follow-up is a must and that it needs to be a long-term follow-up. In the guidelines of clinical practice published by the American Heart Association (AHA) in 2012 there is a class I-level-of-evidence B-recommendation for the follow-up of aneurysms treated through endovascular or surgical approach. This very general recommendation establishes that aneurysms treated need to be followed through an image modality and that both the time and the image modality need to be individualized.\(^28\)

The goal of this study is to establish recommendations and guideline protocols based on scientific evidence for the neuroimaging follow-up of intracranial aneurysms treated through endovascular therapy including more adequate neuro-image modalities, the interval, the time of follow-up and the most adequate way of defining radiological findings all in an attempt to improve clinical outcomes and rationalize the resources available. To that effect we looked for in the most important journals available in the last 10 years published in the most important medical databases (PubMed, EMB reviews, Cochrane Database of Systematic Reviews) using keywords like: brain aneurysm; coils; endovascular proceeding; and follow-up. We did a thorough review of clinical trials, meta-analyses and systematic reviews published for the last 10 years.\(^10-26,29-62\) Both the outcomes and the recommendations aimed at the assistance practice but not at research studies or the monitoring of clinical trials. These are the variables collected: author, journal, year of publication, number of patients treated, number of aneurysms treated, diagnostic proceedings used
Figure 1  45-year old woman with a subarachnoid hemorrhage due to broken aneurysm of the anterior communicating artery treated with coils through endovascular approach (A). Two (2) months later she had a new event of subarachnoid hemorrhage accompanied with morphological changes and reimpaction of coils (B, arrow). 3D digital subtraction angiography (DSA) with coils represented in white (C and D, arrow).

(CTA, 3D TOF angioMR, angioMR 3D with intravenous contrast [IVC angioMR], digital subtraction angiography [DSA] and 3D rotational angiography [3DRA]), and times of use, grade of blockade according to the Raymond' classification and type of therapy (coils, assisted technique yes/no, balloon, endoprosthesis) and time of follow-up of aneurysms. In the articles reviewed the sum of aneurysms published was 18,234. The most common diagnostic technique used to monitor the aneurysms treated with endovascular therapy was brain angiography (with >65% of patients) followed by contrast angioMR (34.7%) and angioMR TOF (32.8%). The average time of follow-up for the aneurysms was 10.0 months (range: 1–60 months).

Image modalities to follow-up aneurysms treated with coils

The resolution of several image modalities available to follow-up brain aneurysms treated with coils are: angioMR 0.6–1 mm; CTA 0.4–0.7 mm; DSA 0.2 mm; and 3DRA 0.15 mm. Therefore the image modality with greater resolution is 3DRA. Due to its high spatial resolution DSA is considered the technique of the image of reference even though they have an index of complications of 0.43%, 53,64

Simple X-ray

Some studies confirm that the follow-up of aneurysms treated through endovascular approach with simple X-rays while assessing the morphological change of coils (Fig. 1) show a correlation close to 90% with DSA, a sensibility of 60–80% and a specificity of 70–95%. 53

Computerized angiotomography

CTA (Computerized angiotomography) is not appropriate for the follow-up of endovascular therapy of aneurysms due to the artifacts caused by coils. 59,60

Digital subtraction angiography and 3D rotational angiography

These are the reference modalities today for the follow-up of aneurysms treated with coils. 54-56

3DRA (Fig. 2) consists of the 3D volume reconstruction of data acquired during rotational angiographic exploration. It gives us very detailed information on the situation of platinum coils and the relation between these coils and vascular structures and shows multiple projections of the aneurysmal neck. It has certain limitations other than being an invasive
proceeding like being associated with a greater dose of radiation and a greater dose of contrast in just one injection. These two (2) issues usually solve themselves with the arrival of more modern equipments capable of doing the acquisition of images in shorter times (3 s instead of 7 s) and fewer shots (40 instead of 100) in each rotation. The link cost-efficiency in the monitoring of aneurysms treated with coils is the same of the angioMR despite this technique has a lower cost. 41-45

3D TOF angioresonance

This is an alternative low-morbidity non-invasive modality with causing no discomfort to patient. It does not use ionizing radiations or agents of contrast either (Fig. 3). 46

The most common parameters of the 3D time-of-flight (3D TOF) sequence are TR 36; time of echo (TE) 6.9; FOV 18 cm × 16.2 cm; 25° of inclination; 256 × 224 matrix; 46 partitions; thickness cut of 0.7 mm; and a 6 min-acquisition time. 50

The sensibility for the diagnosis of recanalization taking DSA as the standard of reference is 80–85%, specificity is 90–100%, VPP is close to 100%, and VPN is 90%. 47

One of the advantages of 3D TOF angioMR is that because it does not use gadolinium it is a more cost-efficient modality without running the risk of nephrogenic systemic fibrosis in sensitive patients. 48,49 Its greater limitations are that it is a relatively long modality, spin mismatch and signal saturation. Since the TOF sequence is insensitive to slow or

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**Figure 2** 36-year old man with a subarachnoid hemorrhage and a mirror aneurysm in both carotid bifurcations. Reimpaction of coils after 4 years in the 3D arteriography (A, thin arrow) with aneurysmal growth of left carotid bifurcation (A, thick arrow) and non-subtraction negative image (B). Control after endovascular therapy with coils (C).

**Figure 3** 46-year old woman with a subarachnoid hemorrhage and an aneurysm of the posterior communicating artery (A, arrow) treated with coils for complete closure (B, arrow). 3D TOF angioMR after 6 months showing the complete closure of the aneurysm both in the reconstruction (C) and the source image (D, arrow).
There are no significant statistical differences between both modalities 3D TOF angioMR and IVC angioMR when it comes to doing follow-ups of brain aneurysms and yet concordance among readers is greater with the IVC angioMR (Fig. 4). The most common parameters of the IVC angioMR sequence performed in the coronal plane are TR 6.6; TE 2.4; FOV 22 cm × 22 cm; 45° of inclination; 259 × 224 matrix; thickness cut of 1.4 mm; and a 58 s-acquisition time.

IVC angioMR is faster and more independent from flow than TOF is (Fig. 5). It may have a problem in the uptake of vasa vasorum or the organized thrombus which might lead us to think of the remainder of the aneurysm. Also it allows us to see small arteries so it is way better to assess distal aneurysms like bifurcation aneurysms of the pericallosal artery and the callosomarginal artery and better study the recanalization of giant aneurysms capable of showing thrombosis among the coils, the artifacts due to coils and a slow flow at neck level (Fig. 6).
Neuroimaging follow-up of cerebral aneurysms

3-Tesla equipments

The main advantage of 3T angioMR\textsuperscript{25} is that they duplicate the signal-noise link which allows reduction of TE and improvement of spatial resolution – $1.024 \times 512$ matrices and 1 mm cut thickness. They also increase T1 relaxation times which in turn enhances the contrast in blood turning them into an alternative to DSA when it comes to efficiency.\textsuperscript{22} However sensibility seems to be similar to 1.5 T equipments.\textsuperscript{47,51-56}

There are special cases to be taken into consideration

Certain coils like Nexus\textsuperscript{8} (ev3, Irvine, CA) cause more artifacts above all on the 3D TOF angioMR,\textsuperscript{57,58} probably due to the platinum–iridium alloy of these coils compared to the platinum–wolframium alloy of others.\textsuperscript{69}

On the other hand endoprostheses can cause artifacts capable of simulating stenosis complicating the adequate assessment of the aneurysmal neck.\textsuperscript{55} The endoprosthesis Enterprise\textsuperscript{6} (Codman, MA) can produce more artifacts than Neuroform\textsuperscript{6} (Stryker, Neurovascular, Fremont, CA), at least with 3D TOF angioMR.\textsuperscript{60} With flow-diversion endoprostheses control is recommended through DSA until more reliable data on the period of neoendotzelization\textsuperscript{56} become available. If we have used Onyx\textsuperscript{6} (ev3, Irvine, CA) to treat the aneurysm this material is hypointense in all angioMR sequences and it barely causes artifacts. On the angioCT it causes artifacts due to the energetic rush of radiation (beam hardening).\textsuperscript{57}

Definition of findings in neuro-image modalities

Using the ISAT\textsuperscript{10} study as the guideline together with new prospective studies from non-consecutive patients like The Clinical and Anatomic Results in the Treatment of Ruptured Intracranial Aneurysms Study,\textsuperscript{14-17} and The Cerebral Aneurysm Re-rupture After Treatment Study\textsuperscript{20} the following concepts need to be taken into consideration:

1. Degree of closure of aneurysms after the initial therapy (DSA) (Fig. 7).
   b. Closure with residual aneurysmal neck. Closed aneurysm with residual aneurysmal neck to preserve the origin of a branch. Both the full closure and the closure of the residual aneurysmal neck can be grouped in "correct closure" of aneurysm.
   c. Remainder of aneurysm. When the closure of aneurysm is partial you can only close the point of rupture or we will not achieve a good density of coils inside the aneurysm.

2. Degree of closure of aneurysms during follow-up (DSA and/or angioMR) (Fig. 7).
   a. Stable therapy. When aneurysm has not changed its degree of closure with respect to previous controls.
   b. Improvement of therapy. When the degree of closure has improved with respect to a prior study.

Figure 7 Categorization of the degrees of closure of aneurysms treated through endovascular approach. (A) Complete closure. (B) Incomplete closure. (C and D) Residual neck.

Follow-up time of aneurysms treated with coils

Long term clinical follow-up has shown that aneurysms treated with coils have a very low rate of a re-bleeding. In some series with long-term follow-up\textsuperscript{10} the rate of re-bleeding was <0.1% even though in the endovascular group of ISAT\textsuperscript{10,11} it got to 2.6% during the first year. In the Cerebral Aneurysm Re-rupture After Treatment Study\textsuperscript{20} the rate was directly dependent on the degree of closure of the aneurysm and reached 17.6% when the closure was <70% of aneurysm.

The series coincide in that re-bleeding after therapy occurs mainly during the first 6–12 months and it is associated with the degree of closure of the aneurysm.\textsuperscript{20} Worsening of the degree of closure of the aneurysm occurs mainly during the first 6 months. In long-term follow-ups some series have shown a rate of regrowth of aneurysms <2% after the first year up to 10 years. Both bigger aneurysms with incomplete closure and posterior circulation aneurysm usually recanalize. Some authors say that one aneurysm completely closed after 6 months does not need to be followed anymore.\textsuperscript{20,21} Stable morphological outcomes at 1 year suggest that the chances of recurrence are extremely low.\textsuperscript{14}

Patients with SAH have a higher risk of having a new aneurysm of which one third will be true aneurysms and the rest aneurysms already present misdiagnosed in the angiography. "De novo" or early-onset aneurysms are usually defined aneurysms growing round a primitive aneurysm. In the ISAT\textsuperscript{17,12} 11 of the 24 re-bleed aneurysms were due
to other aneurysms 4 of which were already present and the rest being completely new. Today we usually think that aneurysms represent a form of vasculopathy ("aneurysmatic disease") requiring long-term follow-up. The rate of appearance of these new aneurysms is very low around 0.75–1.54% after 5 years of follow-up. This is why some authors do not recommend screening new aneurysms in patients with SAH due to costs and complications derived from angiography. These same authors say that it is necessary to have more information on the possible factors of risk in the occurrence of new aneurysms in patients with SAH to be able to identify those that can benefit screening.

Therefore there is no consensus on what is the advisable time for an adequate follow-up of aneurysms treated via endovascular approach. Some authors recommend follow-up during the next 3 years, while others only recommend 1 year when the occlusion has been stabilized. There are groups that have followed these patients even 10 years after therapy. They are usually followed at least during the two first years when there is a higher rate of worsening in the degree of closure in an effort to spot partially closed aneurysms and early recanalizations and reduce re-bleeding and similar values to those of surgical series. In the series the rate of re-treatment is between 6 and 11%.

Security of coils and endoprostheses in magnetic resonance studies

The composition of coils–platinum, nitinol or platinum and iridium has been evaluated and the control of aneurysm can be done through the MR.

New coils and endoprostheses need to be evaluated in advance to assess security in magnetic fields.

Used platinum coils do not interact with the magnetic field and they do not cause artifacts preventing the MR-follow-up of aneurysms to happen. In vitro studies show that the increase of temperature is minimum during this MR-follow-up.

The security of platinum coils and intracranial endoprostheses has been evaluated in vitro in 1.5 T-MR. In 3T-MR not all coils and endoprostheses have been evaluated.

The responsibility of interpreting image modalities

When it comes to interpreting aneurysms non-interventional neuroradiologists do it the same way as interventionalists. Inter-observer concordance to determine the degree of closure of the aneurysm through magnetic resonance is good so there are no noticeable differences in the assessment of endovascular therapy.

General recommendations for the follow-up of aneurysms treated via endovascular approach

1. Time and follow-up interval of aneurysms treated via endovascular approach.

   According to the immediate outcome of endovascular therapy it is recommended at least one initial control through DSA during the first year depending on the degree of closure of aneurysm (Fig. 8):
   - In patients with complete closure of aneurysm–DSA between 6 and 12 months.
   - In patients with residual aneurysmal neck–DSA between 3 and 6 months.
   - In patients with incomplete closure of aneurysm–DSA between 1 and 3 months.

The duration of follow-up of aneurysms treated through endovascular approach will be established according to:

a. Its shape and form of presentation:
   a.1 Broken aneurysms.
   - Aneurysms with complete closure – at least 3 years (recommended: 5 years).
   - Aneurysms with residual aneurysmal neck: if stable all the way until 5 years.
   - Aneurysms with incomplete closure: they need to followed-up indefinitely.
   a.2 Not-broken aneurysms.
   - Aneurysms with complete closure: 3 years.
   - Aneurysms with residual aneurysmal neck: 3 years.
   - Aneurysms with incomplete closure: Indefinite follow-up.

b. According to size:

   Big size aneurysm (giant aneurysm) need and ongoing follow-up given its high rate of re-growth. Here is what we recommend:

   With complete closure of aneurysm: follow-up of at least 5 years.
   Residual aneurysmal neck and incomplete closure: indefinite follow-up.

c. According to the patient’s age: Young patients with aneurysms treated with coils need to be followed-up indefinitely due to risk of new aneurysms.

2. The ideal image modality for the follow-up of aneurysms treated with coils.

   Today DSA and 3DA are considered to be the chosen modalities for aneurysms treated with coils. But because they are bloody and risky modalities they are not recommended for long follow-ups so a DSA control is recommended during the first year to later use non-invasive image modalities. A new DSA is indicated before any changes in the morphological characteristics of the aneurysm.

   Aneurysms treated with endoprostheses or flow-diversion endoprostheses need to be controlled through DSA due to flow artifacts caused inside the endoprostheses. Non-invasive tests will only be used when we are positive of the endotetilation and stability of the aneurysm.

   AngioCT is not a valid test to follow-up aneurysms treated with coils.

3D TOF AngioMR and IVC angioMR are adequate for the follow-up of aneurysms. There is no evidence as to which one of these two modalities is the best and there are no randomized trials comparing them to the DSA. There is no
Brain aneurysm managed with endovascular techniques

DSA-Assessment of immediate outcome

Montreal scale

Complete closure  Remainder of the neck  Remainder of aneurysm

DSA 6-2 months  DSA 3-6 months

Stable closure  Worsening of the degree of closure

Worsening of the degree of closure

3D TOF angioMR - IVC angioMR 12-24 months

Stable closure  Worsening of the degree of closure

Follow-up through MR  Re-therapy?

Early DSA? Multidisciplinar decision

Figure 8 Algorithm for the follow-up of aneurysms treated with coils.

There is a great variability of protocols and experiences in every center in the follow-up of brain aneurysms treated with coils. When it comes down to control and monitoring it is recommended to use the same equipment and sequence. Both the experience and capabilities of each center are crucial to indicate a new DSA when suspicious about growth; follow-up needs to be done by experienced neuroradiologists though.

Conclusions

There is a great variability of protocols and experiences in every center in the follow-up of brain aneurysms treated with coils. The first control modality after follow-up to assess the efficacy and stability during the first year will be the DSA to later jump into angioMR for long-term control. A new DSA will be indicated when the morphological characteristics change or when the degree of closure gets worse.

Whether for the follow-up the use of contrast in the angioMR or 3 T images is better remains to be confirmed.

The image modality-follow-up of patients with aneurysms treated with coils especially MR needs to be done under the supervision of a neuro-radiologist and under adequate technical homogeneous conditions that will allow us to compare studies according to the availability and experience of each center.

**Ethical responsibilities**

**Protection of people and animals.** Authors confirm that no experiments have been done with humans or animals during this research.

**Confidentiality of data.** Authors confirm that in this report there are no personal data from patients.

**Right to privacy and informed consent.** Authors confirm that in this report there are no personal data from patients.

**Authors**

1. Original Idea of the Study: All the group members.
2. Study Design FD, AS, AH, EM, LSRM, AGG.
3. Data Mining: All the group members.
Conflict of interests

Authors reported no conflicts of interests.

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References


