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INTRODUCTION

Michael Forsting, Editor

For more than a decade this newsletter has tried to keep you informed with the latest literature, mainly regarding interventional therapy of intracranial aneurysms. International experts review recent articles on this topic and provide you not only with summaries of the results, but also with their personal opinions about the research. Obviously the readers like this format, currently 300 colleagues receive the newsletter electronically and the number is still increasing.

With this edition of the newsletter a minimal change has occurred. From the beginning Boston Scientific has sponsored this newsletter and I am very grateful that the company supported this kind of independent scientific information. Now Stryker has taken over the neurointerventional business from Boston Scientific. Sometimes this leads to tsunami-like changes in companies. Obviously not in this acquistion and I am very happy that Stryker has agreed to continue with the newsletter.

Part of this newsletter covers the first results of the MAPS™ Trial. My personal opinion is that this is one of the best ways to organize studies. Take notice of it!

Warm regards,

Michael Forsting

Contributions to this issue: Jorge Olier Arenas, Michael Forsting, Alejandro González García, Andy Molyneux, Laurent Pierot, Michel Piotin, Laurent Spelle

CRITICAL REVIEW OF LITERATURE
Intracranial Aneurysms

Clinical outcomes of ruptured and unruptured vertebral artery-posterior inferior cerebellar artery complex dissecting aneurysms after endovascular coil embolization

Lv X, Jiang C, Li Y, Wu Z
AJNR Am J Neuroradiol. 2010 Aug;31(7):1232-5

The endovascular team from Beijing, China reports the results of 22 consecutive patients with VA-PICA dissecting aneurysms. The diagnosis was based on clinical findings, MR imaging and cerebral angiography studies.

Six of these 22 patients had unruptured aneurysms, five of them had brainstem infarctions. Four of these were treated with stent-only or stent and coil embolization of the aneurysm, two with unilateral VA occlusion.

16 Patients presented with SAH. In this group 10 patients had selective aneurysm occlusion and six patients were treated with parent vessel occlusion.The author's conclusion is that favorable clinical outcome can be achieved with endovascular techniques.

Personal comment

I absolutely agree with the authors in the majority of the addressed topics. These dissecting aneurysms are a dangerous disease and should be treated. In most, if not all, patients endovascular therapy is possible and should be the first-line approach. Parent vessel occlusion – if possible from an anatomical point of view (or functional point of view) – is still probably the best endovascular option. My personal experience is that coils alone do not work and even the stent-coil combination does have a substantial risk of rebleeding. However, if parent vessel occlusion is not possible, stent plus coils may be the second therapeutic option.

I was a little bit surprised about the outcome of the patients. If you look at the result table in that paper you will find that all patients (100%) had a GOS of 5, meaning all were back to work. With the majority of patients (16/22) having had a SAH (six of them with HH of 3 and worse) this is hard to believe. I am convinced that this is a simple printing error. Even if procedure-related morbidity and mortality is very low, the SAH-related morbidity and mortality should be slightly higher than zero.

In summary, this is a nice paper about a rare vascular problem with good recommendations for the treatment options.

Michael Forsting, Essen, Germany

Better outcomes with treatment by coiling relative to clipping of unruptured cerebral aneurysms in the United States 2001-2008

Brinjikji W, Rabinstein AA, Nasr DM, Lanzino G, Kallmes DF, Cloft HJ.
AJNR Am J Neuroradiol. 2011 Jun;32(6):1071-5

Patient outcomes are better for unruptured cerebral aneurysms treated at centers that preferentially treat with endovascular coiling: A study of the national inpatient sample 2001-2007

Brinjikji W, Rabinstein AA, Lanzino G, Kallmes DF, Cloft HJ.
AJNR Am J Neuroradiol. 2011 Jun;32(6):1065-70

In the June/July edition of AM J Neuroradiol (on line April) two articles are published examining the risks associated with treatment of unruptured intracranial aneurysms (UIAs)[1, 2]. I wrote a commentary on those articles in the same edition[3]. The two articles use the National Inpatient Sample (NIS) database from the United States. This database samples one third of all non-federal hospital discharges in the United States. The total sample size for the first article was 64,043; this makes it a very powerful tool for examining broad clinical outcomes of hospital treatment because it provides such a large sample size. It enables the study of a wide variety of conditions and their treatment with the added ability to examine differences over time that reflect what is happening in the real world of day-to-day clinical care. The outcome measures used for the studies were in-hospital death and the surrogate endpoint for adverse outcome, namely non-home discharge, ie discharge to a long-term or rehabilitation facility. The study of Johnson et al[4] has shown that this measure correlates well with the clinical complications and adverse outcomes, when applied to the treatment of UIAs. The first article looked at the comparative outcomes of clipping and coiling of UIAs over a time period of 2001 to 2008, and the change in clinical practice over that time period. The rate of coiling went from 20% in 2001 to 63% in 2008.
The percentage of patients who were not discharged home after surgical clipping was 14%, (4,184/29,918) or one in seven and 4.9% (1,655/34,125), about one in 20 after coiling. The mortality was also significantly lower in the coiled patients. It was 1.2% after clipping and 0.6% after coiling. Given the very large sample sizes these results were highly statistically significant. (p= <0.0001). Overall the number of adverse outcomes from treatment decreased from 14.8% to 7.6%.

The second study examined the effect of hospital and physician volume and the effect of clipping and coiling on the morbidity, complications and mortality following treatment of a UIA. The study had hospital and physician volume data on 10,644 patients treated for UIA with 49% undergoing clipping. The coiling patients were significantly older (about 2.5 years on average).

There was a highly significant difference in the outcomes based on the proportion of patients coiled in a particular centre. In centres that only clipped aneurysms the non-home discharge was 16.8% compared with 5.9% in centres that coiled 75-99% of aneurysms.

Mortality also differed significantly, 2% in the purely clipping centres and 0.5% in those centres doing mostly coiling. The case volumes in clipping centres were also significantly lower, with the majority of surgical patients treated at centres undertaking fewer than 20 cases per year.

Personal comment

These two articles are very important. There can be no doubt of the veracity of the data given the very large sample size and that the results represent the real outcomes of current US clinical practice.

When a patient is independent, walks into a hospital well and neurologically intact any clinical outcome other than being in the same condition on discharge, able to return home, resume normal activities and go back to work after a short interval is a potential disaster for both the patient and the family.

The data from these studies shows that the probability of their non-home discharge and the need to be discharged to a rehabilitation facility after treatment by surgical clipping was one in seven (about 14%) and for the patients treated by coiling about one in 20 (about 5%).

These figures should give cause for serious concern. Does it spell the death knell for surgical treatment of unruptured aneurysms? Probably not but it should compel any neurosurgeon proposing the clipping of a coilable unruptured aneurysm to provide realistic surgical risks to patients.

Many neurosurgeons and interventionists might observe that these data do not accord with either the literature – be they case series, registries or meta-analyses – or their own clinical outcomes.

The literature, however, suffers from the inevitable biases, particularly publication and centre selection bias. Published studies frequently come from high-volume and academic centres, which tend to publish their own case series and participate in multicentre studies. Case series with poor results are seldom published. The NIS database provides a realistic picture across a broader healthcare environment from a wide range of hospitals as it reflects day-to-day practice in the US.

When the International Study of Unruptured Intracranial Aneurysms (ISUIA) published the clinical outcomes of clipping and coiling in the Lancet in 2003[5] the results came as a surprise to many Neurosurgeons. Those data came from many large International Academic Medical Centres, the one-year clinical outcomes were substantially worse than was expected. It showed that 12% of patients who were prospectively enrolled and underwent clipping were dependent or had a poor cognitive status one year following surgical treatment of an unruptured aneurysm. The data was collected between 1992 and 1998.

The dramatic shift to coiling over the period of these two studies, 2002 to 2008, from 16% to 63% of cases, had the effect of nearly halving the nationwide morbidity and mortality for UIA treatment from almost 15% to 7.6%. The time trends provide strong evidence that complications, morbidity and mortality decline in direct proportion with increased coiling rates in almost all the measured fields.

Nevertheless there is no reason to be complacent about the outcomes of coiling. The results of coiling in most published studies are, unsurprisingly, better than clipping with most articles and meta-analysis data suggesting morbidity rates of about 5%[6]. This is

in line with these articles suggesting approximately 5% discharge rate to continuing care facilities or rehabilitation. Caution has to be exercised in directly comparing the clipping and coiling data from these studies. The populations in the two groups are likely to differ and are thus not necessarily directly comparable. However, interestingly the surgical population had a mean age nearly three years younger than the coiling population, and it would also be reasonable to assume that most of the high surgical risk posterior circulation aneurysms were treated by coiling.

The effect of volume, both physician and hospital, is also clearly evident from this data – higher volume strongly correlating with improved outcomes. This supports the need to centralize care in larger regional and academic centres to obtain optimum results when treatment decisions are taken. Such regionalization can often present challenges, even in publicly organized health care systems, and this may be even more difficult in private health care systems, where individual economic interests may play a part in decision making.

The treatment risks observed in these studies must be balanced against the natural history risk of an UIA. It is likely that the majority of the patients having treatment had small or medium sized anterior circulation aneurysms, although the nature and size of the aneurysms is not available from such databases.

This immediately raises the question as to whether these treatment risks are too high to justify treatment on any reasonably balanced risk assessment. Even if one takes the upper end of the estimates for the annual rupture risk of a small anterior circulation aneurysm of less than 7mm at 1% (and ISUIA suggested much less than this), then a surgical clipping treatment is exposing the patient to more than14 years of natural history on the day of surgery, and for coiling the figure would be about 5 years. If the annual rupture risks are as low as 0.5% or as low as 0.1% then the treatment risks are unacceptably high.

The argument frequently used for surgical preference compared with coiling is that the former is the 'definitive cure' (whatever that means), without the need for further follow-up. In the context of an incidental UIA where the risk of rupture is likely to be low without treatment then a reduction of future risk from perhaps one in 100 or 1 in 500 per-year to 1 in 5,000 or 10,000 is irrelevant relative to procedural risks of 1 in 20 or 1 in 7.

It reinforces the fact that, when undertaking treatment of UIAs, the overriding priority is to minimise adverse events and clinical complications.

Striving for angiographic perfection at the expense of a clinical event may not be a good idea when we have no idea how much such anatomical perfection changes the long-term rupture risk (and something we will never be able to measure after coil treatment).

This, in my view, makes the overriding obligation to make the procedure as safe as possible. Extensive stent usage in association with coiling and the accompanying need for dual anti-platelet therapy, and the additional risks that it inevitably creates, has to be considered when balancing risks.

Great anxiety is created in patients by the fear of events with major impact (such as rupture of an aneurysm) but low probability. Patients in general and the public at large are often poor at assessing such relative risks in everyday life (as with the risks posed by radiation).

Sadly, answering the question 'should an UIA be treated?' remains a major dilemma for the neuroscience community and is likely to remain so for the foreseeable future.

The major efforts made by Jean Raymond and colleagues to address these questions in a systematic and scientific way with a randomised trial – Trial of Endovascular Aneurysm Management (TEAM)[7], failed for a variety of reasons which were well addressed in a recent article in Trials[8].

The authors are to be congratulated on succinct and powerful reminders of what we should all bear in mind is 'first do no harm' and the need to put the relative risks of treatment and rupture risk in proper context. This should be at the back of the minds of all physicians when advising and treating patients with unruptured aneurysms be they neurosurgeons, neuroradiologists or neurologists. One of the most important principles in neurosurgery, taught to me by one of my neurosurgical mentors, is the KISS principle, Keep It Simple and Safe. Interventionist should have this principle at the back of their mind whenever they treat unruptured aneurysms.

Andrew J Molyneux, Oxford, UK

1. *Better Outcomes with Treatment by Coiling Relative to Clipping of Unruptured Intracranial Aneurysms in the United States 2001-2008. Brinjikji W, Rabinstein AA, Lanzino G, Kallmes DF, Cloft HJ. AJNR Am J Neuroradiol. 2011 Jun-Jul;32(6):1071-5.*
2. *Patient Outcomes Are Better for Unruptured Cerebral Aneurysms Treated at Centers That Preferentially Treat with Endovascular Coiling: A Study of the National Inpatient Sample 2001–2007 Brinjikji W, Rabinstein AA, Nasr DM, Lanzino G, Kallmes DF, and Cloft HJ, AJNR Am J Neuroradiol 2011 32: 1065-1070.*
3. *Treatment of Unruptured Intracranial Aneurysms, Cause for Concern? Molyneux AJ AJNR Am J Neuroradiol 2011 32: 1076-1077.*
4. *Effect of endovascular services and hospital volume on cerebral aneurysm treatment outcomes. Johnston SC. Stroke 2000; 31:111-117.*
5. *Wiebers DO, Whisnant JP, Huston J, 3rd, Meissner I, Brown RD, Jr., Piepgras DG, Forbes GS, Thielen K, Nichols D, O'Fallon WM, Peacock J, Jaeger L, Kassell NF, Kongable-Beckman GL, Torner JC: International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: Natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet 2003, 362:103-110.*
6. *Naggara ON, White PM, Guilbert F, Roy D, Weill A, Raymond J. Endovascular treatment of intracranial unruptured aneurysms: systematic review and meta-analysis of the literature on safety and efficacy: Radiology. 2010 Sep; 256(3):887-97. Epub 2010 Jul 15.*
7. *Raymond J, Molyneux AJ, Fox AJ, Johnston SC, Collet JP, Rouleau I; TEAM Collaborative Group: The TEAM trial: safety and efficacy of endovascular treatment of unruptured intracranial aneurysms in the prevention of aneurysmal hemorrhages: a randomized comparison with indefinite deferral of treatment in 2002 patients followed for 10 years. Trials 2008, 9:43.*
8. *Raymond A, Darsault TE, and Molyneux AJ on behalf of the TEAM collaborative group. Trial on Unruptured Intracranial Aneurysms (the TEAM trial): Results, Lessons from a Failure and the Necessity for Clinical Care Trials Trials 2011, 12:64 doi:10.1186 /1745-6215-12-64.*

MAPS™ Trial Data Presented

The MAPS (Matrix and Platinum Science) Trial data was presented for the first time at the SNIS Annual Meeting in Colorado Springs, Colorado on July 27, 2011. The trial enrolled 626 patients at 43 sites in 11 countries and investigated primary outcomes of GDC™ Coils and Matrix2™ Coils using a new experimental clinical primary endpoint called Target Aneurysm Recurrence (TAR). TAR was defined as a clinically relevant recurrence resulting in a bleed/rebleed, retreatmentor a death from an unknown cause. Secondary outcomes of the trial include angiographic outcomes, Modified Rankin Scores, technical procedural success and long-term follow-up. One of the primary objectives of the trial is to compare angiographic outcomes to TAR and assess whether angiographic outcomes are predictive of clinical events. The trial included patients with a single, de-novo intracranial aneurysm, ruptured or unruptured, 4-20mm in size. Patients were excluded if they had a Modified Rankin Score or Hunt & Hess Score greater than 3. The trial proved its hypothesis and established that Matrix^2 Coils are not inferior to GDC Coils. In Intent to Treat (ITT) analysis, the TAR rate for Matrix^2 was 13.3% vs. a GDC TAR rate of 14.6%. That difference did not prove superiority. For Matrix^2 Detachable Coils, initial angiographic occlusion rates (assessed by the core lab using the Modified Raymond Scale) were found to be highly predictive of TAR rates out to 15 months. The analysis also found that Matrix^2 Detachable Coils are uniquely sensitive to acute occlusion rates compared to GDC Coils, with the post-procedural Modified Raymond Score having a larger impact on TAR than dome size or neck size in Matrix^2 patients. As such, in aneurysms with Raymond Score of 1 or 2 post-procedure, Matrix^2 Coils had a significantly lower TAR rate than GDC Coils (2.7% vs. 9.6%, p=.01). Conversely, in aneurysms with Raymond Score 3 post-procedure, Matrix^2 Coils had a higher TAR rate than GDC Coils (24.2% vs. 16.1%, p=.17).

The MAPS trial showed excellent neurologic outcomes in both ruptured and unruptured aneurysms that were much better than what would have been expected based on the ISAT* and ISUIA** trials. Using Modified Rankin Scores that were independently assessed by a clinician not responsible for the patient's treatment, 90% of ruptured patients and 96% of unruptured patients were alive and free of disability up to 15 months post-procedure, which is great evidence of the advancement of aneurysm coiling in the past decade.

Further analysis to come from the MAPS Trial includes a more robust assessment of the angiographic outcomes, complete analysis of the 145 patients treated with the Neuroform™ Stent System in the trial, and long-term follow-up of TAR rates at 2, 3, 4 and 5 years post procedure.

** ISAT was sponsored by the Oxford Radcliffe Hospitals NHS Trust, UK.*

*** ISUIA was sponsored by the Mayo Clinic, Rochester, Minnesota, USA.*

MAPS, GDC and Matrix² are trademarks of Stryker². The trial is sponsored by Stryker Neurovascular.

MAPS Trial
Matrix And Platinum Science

A Letter from the President of Stryker

When the news of Stryker's acquisition of Boston Scientific's Neurovascular business was announced last October, some in the Neurointerventional community may not have been familiar with Stryker and may have questioned why we would be making such a significant investment in the neurovascular market.

For us, this acquisition represents an exciting opportunity to lead the global neurovascular market, one of the fastest-growing segments in healthcare today and one that is having a profoundly important impact on patients' lives around the world. I would like to provide some context about who we are and why we are so excited to join you in your specialty.

Stryker has a rich history of customer-oriented innovation. Dr. Homer Stryker, an orthopaedic surgeon practicing in Kalamazoo, Michigan, founded the company in 1941 on the core principle of creating innovative approaches to help surgeons do their work more easily and effectively to improve patients' lives. We are keeping this same customer-oriented focus with our new Neurovascular division and plan to work closely with you to provide solutions needed to treat patients in the safest and most effective way possible.

As you may be aware, we are a broadly based medical technology leader, operating in the complementary neurosurgical market with our Neuro Spine & ENT (NSE), Interventional Spine (IVS), Spine, Navigation and Craniomaxillofacial (CMF) businesses. We are committed to expanding into new growth platforms, such as neurointervention, and building upon our core markets, as this approach has been central to our history.

Our new Neurovascular division will operate as an independent business within Stryker, led by the current president, Mark Paul. Our goal is to provide Mark and team with the resources and autonomy needed to work closely with the global leaders in neurointervention to deliver solutions-oriented technology to deliver the highest level of patient care possible. We have been impressed by the support and excitement expressed by so many of you with our decision to enter this specialty. We look forward to a long-lasting and mutually beneficial relationship in the years to come. Thank you for your continued support.

Warmest regards,

Stephen P. MacMillan
Chairman, President and CEO

International Subarachnoid Aneurysm Trial 2009: Endovascular coiling of ruptured intracranial aneurysms has no significant advantage over neurosurgical clipping

Bakker NA, Metzemaekers JDM, Groen RJM, Mooij, JJA, Van Dijk JMC
Neurosurgery 66: 961-962, 2010

This is a special commentary on the 5-year follow-up data of the ISAT* study, published in the May 2009 issue of Lancet Neurology. The final conclusion of this *study* was that death and severe disability five years after treatment of a ruptured intracranial aneurysm is not statistically different between endovascular and neurosurgical treated patients. However, the authors still favored coiling because mortality of the patients was still lower in the endovascular treated group.

The group from the Netherlands have now combined data from previously published ISAT publications with the 5-year follow-up data and made something like a "modified intent-to-treat" analysis of their data. The crucial point they make is regarding early rebleeding. Seven patients in the endovascular group and 19 patients in the clipping group died prior to the first treatment. If one were to exclude these patients and recalculate five-year mortality, then the significant advantage in terms of mortality in favor of the endovascular treated patients is no longer present. The Dutch group thinks that this is a more appropriate analysis because a reliable outcome analysis between two treatment modalities requires the exclusion of pretreatment events.

Personal comment

In general, this way of looking at a problem is not wrong. However, in this study the number of patients with pretreatment rebleeding can in fact be dependent on the intention-to-treat, because coiling is usually done earlier and faster than surgery. So if the reason for the larger number of rebleedings is not a delay in allocation to a specific treatment group, but simply the shorter interval between initial SAH and treatment in the endovascular group, then the exclusion of the pretreatment rebleedings would distort the results. At least in the real clinical setting, coiling is usually performed faster and earlier after SAH and thus can probably avoid a certain number of early rebleedings.

Finally, it is a fact that we do have two excellent methods to treat intracranial aneurysms. The success of each method is not only dependent on the material (clip or coil), but mainly on the person who does the procedure. It requires simply a certain amount of honesty to decide in each specific situation which is the best for the patient. And on one weekend, clipping may be the best way to treat an Anterior Communication Artery aneurysm (the most experienced neurosurgeon is on call and his counterpart is an interventionist, who is less experienced) and the next weekend the situation is the reverse: same aneurysm, but different people on call. So this is far beyond numbers and p-values.

Michael Forsting, Essen, Germany

** ISAT was sponsored by the Oxford Radcliffe Hospitals NHS Trust, UK.*

Late adverse events in coiled ruptured aneurysms with incomplete occlusion at 6-month angiographic follow-up

Ferns SP, Majoie CBLM, Sluzewski M, van Rooij WJ
AJNR Am J Neuroradiol. Mar 2010; 31(3):464-469

This paper assesses late complications in a large series of 713 ruptured aneurysms repaired by coil embolization and monitored by angiography for an average of 41 months. In 124 (17%) cases occlusion was incomplete six months after the procedure. In eight of these cases either aneurysm re-rupture occurred (four cases) or aneurysm size gradually increased, leading to mass effect symptoms (also four cases). All but one of the aneurysms that underwent late complications were 15mm in size or larger and most (62.5%) were located in the posterior circulation. The authors report that in the group of incompletely occluded aneurysms the observed frequency of rebleeding represented a 10-fold increase in the risk of post-embolization rebleeding reported in the latest ISAT* and CARAT** studies. The paper demonstrates that the risk of rebleeding or regrowth is related to large aneurysm size, aneurysm location in the posterior circulation, and aneurysm repermeabilization. The authors put forward a hypothesis with regard to the causes leading to aneurysm regrowth and increasing aneurysm size and advise angiographic follow-up and retreatment until complete aneurysm exclusion is achieved.

Personal comment

The authors raise a well-known fact, namely the risk of late complications in repermeabilized large aneurysms. The originality of this paper lies in the observation of the gradual regrowth of some of these aneurysms. Regrowth of this sort can cause neurological symptoms as a result of the mass effect on adjacent structures and, in the long term, may raise morbi/mortality rates more than rebleeding. While there have been relatively few communications dealing with events of this kind, many readers will have experience with similar complications, whose course is often fatal. The authors point to an inflammatory origin as the cause of regrowth and advocate treating patients in this category with steroids, which could become standard for large, coil-embolized aneurysms. Nevertheless, the issue of the pathophysiology of regrowth remains to be elucidated, with the embolization coils themselves possibly playing a prime role, as a result of either hemodynamic alterations in the aneurysm sac or an added traumatic effect on top of systolic pressure giving rise to a secondary inflammatory response.

Jorge Olier Arenas,
Pamplona, Spain

** Sponsored by the Oxford Radcliffe Hospitals NHS Trust, UK.*
*** Sponsored by an unrestricted educations grant from Boston Scientific Corp. to the University of California, San Francisco.*

High-profile flow diverter (Silk) implantation in the basilar artery: Efficacy in the treatment of aneurysms and the role of the perforators

Kulcsár Z, Ernemann U, Wetzel SG, Bock A, Goericke S, Panagiotopoulos V, Forsting M, Ruefenacht DA, Wanke I.
Stroke. 2010 Aug;41(8):1690-1696

This is a retrospective review of initial angiographic efficiency and clinical side effects of the first 12 patients from five neurovascular centers, treated with Silk™ (Balt Extrusion) flow diverter (Silk FD) for a basilar artery aneurysm. Silk FD could be placed in all patients. Seven out of 12 patients had their aneurysm occluded during short-term follow-up.

Interestingly enough, the Silk FD was placed so as to cover an emerging branch in most of the cases (P1 segment of the PCA and superior cerebellar artery in nine cases; AICA in three). At the end of the procedure, all of those side branches were angiographically patent, except in one patient. In this later patient, the P1 segment jailed by the Silk FD was no longer opacified and it was hopefully supplied by the PCom.

Thromboembolic events were encountered in five patients:

- In one patient there was an acute unexpected basilar artery occlusion a few hours after FD implantation. It occurred in a patient harboring a ruptured, uncoilable, tiny aneurysm who received a partial loading dose of antiplatelet drug only six hours before the procedure. Local administration of antiGPIIB/IIa led to rapid and complete recanalization without any clinical deficit.
- In one patient with severe neurologic symptoms due to brainstem compression and ischemia, there was, 12 hours after the procedure, a complete occlusion of the basilar artery that was treated endovascularly. This patient seems to have had a difficult procedure since after the first Silk FD, which got a suboptimal opening, a second Silk then an Enterprise™ (Codman Neurovascular) stent were deployed in a telescopic fashion. MRI performed five days later demonstrated extensive edema around the aneurysm, which was excluded from circulation.
- In three other patients focal thalamic ischemic lesions were seen on follow-up MRI.

Because of the absence of brainstem and / or cerebellar lesions on MRI in all 12 patients, the authors conclude that perforators arising from basilar artery remained patent after Silk FD deposition.

Personal comment

The use of intracranial stents with increased mesh density has raised both hope and fear. Indeed, their flow diversion capability could be responsible for the occlusion not only of the aneurysm, but also of putative side branches or perforators.

This paper is the first to address this important issue. The result is pretty good in otherwise untreatable patients. Silk FD was delivered in all patients with a pretty high rate of efficiency regarding aneurysm occlusion. There were no arguments that Silk FD could increase the risk of perforator occlusions. However, jailing a side branch may jeopardize its patency. The reader will benefit from an interesting discussion about the different hypothesis underlying potential occlusion of a side branch jailed with Silk FD.

It appears that adjunction of material and poor antiplatelet drug preparation may represent risk factors for thrombo-embolic events.

Laurent Spelle, Paris, France

Crescent sign on magnetic resonance angiography revealing incomplete stent apposition: correlation with diffusion-weighted changes in stent-mediated coil embolization of aneurysms.

Heller RS, Miele WR, Do-Dai DD, Malek AM.
J Neurosurg. 2011 May 27. [Epub ahead of print]

The authors performed post procedural (within three days of the procedure) 3-T MR diffusion-weighted imaging and time-of-flight angiography in 58 patients (58 aneurysms) undergoing stent-assisted coil embolization of aneurysms using the closed-cell Enterprise™ VRD (Codman & Shurtleff, Inc.) and the open-cell Neuroform™ (Stryker Corp.) self-expanding intracranial stents. All patients were pretreated with clopidogrel and aspirin for at least thee days prior to the procedure.

They found a distinctive semilunar signal pattern, identified using 3-T MR angiography, represented flow outside the confines of the stent struts in patients in whom Enterprise but not Neuroform devices were used. This pattern, designated as the crescent sign, was confirmed to correspond to incomplete stent apposition by use of high-resolution angiographic flat-panel CT scanning (Dyna CT) revealing flow in between arterial wall and external edge of the stent.

The presence of the crescent sign was seen in 18 of 33 Enterprise-treated but in none of the 25 Neuroform-treated cases, and was more likely in stents delivered in the tortuous internal carotid artery ($p = 0.034$). The crescent sign was strongly predictive of ipsilateral post-procedural lesions seen on diffusion-weighted imaging in the entire population (OR 18, 95% CI 4.33–74.8; $p < 0.0001$).

In the Enterprise stent subset, ipsilateral lesions were detected on diffusion-weighted imaging in 15 (45%) of 33 cases; the crescent sign was seen in 12 (80%) out of 15 patients with ipsilateral lesions on diffusion-weighted imaging, but in only 6 of the 18 patients without lesions (OR 8, 95% CI 1.61–39.6; $p = 0.006$).

The authors went on to conclude that incomplete stent apposition was detectable on 3-T MR angiography as a crescent sign, and was found to be highly prevalent in Enterprise closed-cell design stents used to assist coil embolization of aneurysms. Incomplete stent apposition was also associated with peri-procedural ipsilateral hyperintense lesions on diffusion-weighted images. These results identified an association between incomplete stent apposition and thromboembolic complications in stent-assisted coil embolization of intracranial aneurysms.

Personal comment

As the authors stated, the central finding of this study is that the presence of incomplete stent apposition, as evidenced by the 3-T MR angiographic crescent sign within the intracranial circulation, is highly associated with an increased procedure-related risk of thromboembolic complications as demonstrated on diffusion-weighted imaging. However, the authors did not know precisely how many patients in either Enterprise or Neuroform groups sustained a clinically obvious ischemic stroke. What is noteworthy is that none of the patients suffered an irreversible clinical deficit attributed to the lesions noted on diffusion-weighted imaging by the time of discharge. However, it would have been interesting to know about the clinical follow-up. Did crescent sign correlate with further delayed ipsilateral ischemic insult? Did the authors confront delayed in-stent thrombosis to the presence of the crescent sign?

Consequently, the time course of incomplete stent apposition, and any effect it may have on long-term thromboembolic events, remains unknown.

Both stents, the Neuroform and the Enterprise, have their respective advantages and drawbacks. The stent has a lower profile, which enables its delivery with a .021-inch inner diameter microcatheter, giving a better navigability than the Neuroform. The latter requires the use of a .027-inch inner diameter delivery microcatheter, subsequently limitating the navigability of the system to access distal lesions. Conversely, the open-cell design of the Neuroform allows a better conformation in tortuous arterial anatomy. Both stents are part of the armamentarium given to the neurointerventionists to treat complex aneurysmal lesions, such as lateral and bifurcation wide-necked aneurysms, and more and more data supports the fact that better angiographic outcomes are obtained with the stent-assisted technique[1]. However, it is obvious that the conclusions drawn from this original research should impact our daily practice regarding our stent choice to the best achievable compliance to the arterial anatomy.

Michel Piotin, Paris, France

1. *Lawson MF, Newman WC, Chi YY, Mocco JD, Hoh BL. Stent-Associated Flow Remodeling Causes Further Occlusion of Incompletely Coiled Aneurysms. Neurosurgery. 2011 Mar 23. [Epub ahead of print]. Neuroradiology, 2011; 38: 40 – 46.*

Management of anterior inferior cerebellar artery aneurysms: endovascular treatment and clinical outcome

Suh SH, Kim DJ, Kim DI, Kim BM, Chung TS, Hong CK, Jung JY
AJNR Am J Neuroradiol. 2011 Jan;32(1):159-64

The authors present a small retrospective series of nine anterior inferior cerebellar artery (AICA) aneurysms, seven (78%) of which were treatable endovascularly. One of the other two aneurysms was treated by surgical trapping, while the other underwent spontaneous thrombosis during catheterization. The condition presented as SAH in six patients and appeared as an incidental finding in three. The aneurysm presented as an AICA-PICA variant in five patients, and in the other two patients it was associated with Moya-Moya disease and an AVM. Aneurysm location was proximal in seven patients and distal in two. Clinical course was good in the patients treated endovascularly, and on long-term angiographic follow-up (seven patients) there was only one case of a small recanalization in one patient with a proximal aneurysm. The authors conclude that endovascular treatment is a safe and effective alternative to surgery.

Personal comment

The authors of this paper have put together a series of nine (not a small number) patients with AICA aneurysms and report good outcomes achieved by endovascular coiling. This small series is well presented; seven of the treated aneurysms were proximal, and five presented as an AICA-PICA variant, not just an academic question because the calibre of the proximal segment of the AICA increases in size. The two distal AICA aneurysms could not be repaired by coiling. This is what usually happens: ordinarily AICA aneurysms distal to the loop cannot be catheterized and have to be treated by occluding the parent artery using acrylic or coils.

The endovascular approach is clearly the first therapeutic option for both proximal and distal AICA aneurysms. AICA occlusion can be highly variable; as an endovascular treatment it tends to be asymptomatic in many cases, though it may lead to a range of clinical syndromes that can have important clinical translation. If the occlusion is distal to the internal auditory artery no deficits should arise, thanks to collaterals issuing from the PICA.

The authors have classified the AICA aneurysms as proximal or distal, but the proximal aneurysms should be subdivided into those involving the AICA origin and the rest. When repairing AICA origin aneurysms it is not uncommon to have to leave a short neck remnant, because the AICA may arise from the aneurysm neck. It is unusual to see that in one of the two cases described it was possible to deploy a stent measuring 4mm in diameter in an artery measuring less than 2mm without administering anti-aggregants until the following day. Arteries with such narrow lumens irrigating small distal territories are usually much more susceptible to thrombosis.

A literature search reveals that papers of this kind have been few and far between. We all know that these aneurysms are uncommon without being exceptional, and the authors have done us a service by having been able to put together this series for purposes of review. We will all have treated this type of aneurysm on occasion, but the fact is that, as the authors point out, before this paper only 17 cases of endovascular AICA aneurysm repair had been published, most treated by occluding the artery. Hence the saying what is not published does not exist. But they do exist, even though few have been published to date.

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Endovascular treatment using predominantly stent-assisted coil embolization and antiplatelet and anticoagulation management of ruptured blood blister-like aneurysms

Meckel S, Singh TP, Undrén P, Ramgren B, Nilsson OG, Phatouros C, McAuliffe W, Cronqvist M
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This paper is evaluating important issues regarding the management of the so-called "blood blister like aneurysms" (BBA). The authors describe 13 patients harbouring ruptured BBA mostly located on internal carotid artery (ICA, 11 patients), 2 of them being located on basilar artery (BA). All aneurysms were treated by endovascular techniques: parent artery occlusion in one ICA case, double stent in one ICA case and stent + coil in all other cases. Management of perioperative medications (anticoagulation and antiplatelet therapy) is very precisely described and is different from one patient to another.

Post-operative angiographic results are not so good with a residual aneurysm in 5/13 cases including the patient treated with a double stent, and dog ear or neck remnant in 4 cases. One patient with a residual aneurysm died from an early rehemorrhage. The other patients (12/13) had good clinical outcome. Three patients with ICA residual aneurysm, neck remnant, and dog ear experienced aneurysm regrowth and were retreated by parent artery occlusion in 2 cases and additional coiling in one case.

The (long but very interesting) discussion is focused on several important points: what are BBA? How to treat them? What is the appropriate perioperative treatment (anticoagulation and antiplatelet therapy)? Surgical treatment is difficult but the endovascular approach is also not so easy to perform due to the specific morphology of these lesions (small size and broad or ill-defined neck). Several endovascular options are discussed by the authors including parent artery occlusion, double stent, stent + coil, covered stent, and flow diverters.

For them, parent artery occlusion is a good option to treat the aneurysm but it will interfere with endovascular access for later vasospasm treatment if needed. Double stent seems to be associated with a high rate of residual or recurrent aneurysm requiring further treatments and is for this reason not really a good option. Experience with covered stents and flow diverters is limited and further evaluation is needed. According to perioperative medications, the authors suggest the use of a modified reduced antiplatelet regimen with a loading single dose of clopidogrel with maintenance ongoing ASA or in combination with a short course of heparinoids after the procedure.

Personal comment

The Mats Cronqvist team is as usual presenting a very precise and interesting analysis of a very important question: how to manage BBA aneurysms?

The definition of BBA is finally not so clear. If they are classically described as small, bleb-like, usually very broad-neck lesions at non-branching sites within the supraclinoid ICA, they can also have other locations, in particular the basilar trunk. Moreover the mechanism of these lesions is not so clear and most of them are probably the result of a dissection.

The treatment of these lesions is always very difficult due to their morphology and high risk of rebleeding including during the treatment. Clipping or wrapping is often associated with a poor outcome and endovascular approach is certainly the most appropriate treatment. Regular coiling is not feasible as the neck is generally very wide. Remodelling technique is feasible in some cases, but the risk of recanalization is probably high. Double stenting, Stent + coils, and Flow diverters are probably the best options with an adapted antiplatelet and anticoagulation regimen. As outlined by the authors, coiling of these aneurysms under the protection of a stent is not very easy and carries a relatively high risk of intraoperative rupture. The use of flow diverters is probably also a good option as recently reported[1] knowing that complete aneurysm occlusion is not always obtained at the end of the procedure[2].

Using stents and flow diverters, an important problem is the perioperative medications that have to be given to the patient. Our use of perioperative medications (anticoagulation and antiplatelet regimen) in the treatment of intracranial aneurysms singularly in case of stenting of flow diverter is quite empiric. Precise data regarding the risk of thromboembolic complications and intraoperative rupture according to the antiplatelet/anticoagulation regimen are missing. As suggested by the authors, the use of a modified reduced antiplatelet regimen is probably favourable, but must probably be evaluated in a large series of patients receiving different antiplatelet/anticoagulation regimen.

Finally this paper clearly illustrates that, in some specific situations, stenting of ruptured aneurysms is feasible during the acute phase, with reduced antiplatelet regimen, with a low rate of complications and good clinical outcome.

Laurent Pierot, Reims, France

1. *Kulcsar Z, Wetzel SG, Augsburger L, Gruber A, Wanke I, Rüfenacht DA. Effect of flow diversion treatment on very small ruptured aneurysms. Neurosurgery, 2010; 67: 789 – 793.*
2. *L. Pierot. Flow diverter stents in the treatment of intracranial aneurysms: where are we? Journal of Neuroradiology, 2011; 38: 40 – 46.*

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