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CONTEMPORARY ENDOVASCULAR TREATMENT OF INTRACRANIAL ANEURYSMS

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In the past twenty years we have witnessed a revolution in the treatment of intracranial aneurysms. Endovascular technique and materials have rapidly developed since the approval of Guglielmi detachable coils in 1995 which now allow successful treatment of most aneurysms. The development of intracranial stents and balloons for stent-assisted coiling and balloon-remodeling technique further expanded the spectrum of aneurysms treatable with endovascular technique. For these reasons, the aim of this review was to describe endovascular technique and materials which we use in our daily practice, to show benefits of endovascular treatment and to discus complications of endovascular treatment and surgical treatment of intracranial aneurysms. Endovascular treatment is more comfortable for the patient not only because it is minimally invasive but also because it does not require long hospitalization equal to that after surgical treatment. It is a fact that with further development of endovascular materials, this a procedure will have even a more significant place in the treatment of intracranial aneurysms. *Acta Medica Medianae 2015;54(2):63-70.*

Key words: *aneurysms, endovascular treatment, coil embolization*

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Introduction

Aneurysms represent pathological dilatation of arteries and can be broadly classified as secular, fusiform, or dissecting. Even though sometimes asymptomatic, they can cause symptoms by compression to the adjacent brain or cranial nerves (1). Rupture of intracranial aneurism causes subarachnoidal hemorrhage (SAH) which is accompanied by a high rate of mortality and morbidity (2). Microsurgery has been firmly established as the "gold standard" for the treatment of intracranial aneurisms. However, over time, the endovascular treatment of intracranial aneurisms has become the treatment of choice in cases of surgically difficult or inoperable aneurysms. Moreover, with improvements in both materials and endovascular technique the spectrum of treatable aneurysms with endovascular technique is expanded. This review describes modern endovascular technique and materials, discusses complications and outcomes of coiling and surgical clipping in the relevant literature.

Pathophysiology, prevalence and risk factors

Data from autopsy studies indicate that 1% to 5% of adults have cerebral aneurysms (3). Mechanisms of formation of intracranial aneurysms are complex and appear to result as a consequence of compound factors including hemodynamic stress, vascular remodeling and inflammation (4-6). However, alteration in the expression of numerous genes in aneurysm walls has been identified (7). Valk MH et al. (8) in their systematic review and meta-analysis of unruptured intracranial aneurysms found that the prevalence of aneurysms in adults is approximately 3.2% and male/female ratio is approximately 1:1.3. Prevalence is higher in older age, peaking in the 60-79 year age group. Furthermore, prevalence is higher among patients with polycystic kidney disease, atherosclerosis, brain tumor, and the family history of intracranial aneurysms (8). Cerebral aneurysms are most often located in or near the Circle of Willis at arterial branch points where there is a gap in tunica media and internal elastic lamina (9), although significant percentage is not associated with a branching vessel. The anterior communicating complex (30–35%) is the most common location, followed by the internal carotid artery (30%). The basilar apex represents the most common location in the posterior circulation

and accounts for 10% of all intracranial aneurysms (10). Aneurysms are also classified by size into subgroups of small (<10mm), large (10–25mm), and giant (>25mm) in diameter. Intracranial aneurysm can be single as well as multiple. Multiple aneurysms are found in 15-30% of patients (11). Risk factors for multiple aneurysms include female gender, postmenopausal state, cigarette smoking, hypertension and a family history of cerebrovascular disease (12).

Patient selection

Technique of endovascular aneurysm treatment varies from case to case. It is wise to review all the available imaging procedures (MRA, CTA, DSA) in preparation for particular intervention. This will enable appropriate strategy and device selection in order to permit smooth and efficient performance during the procedure.

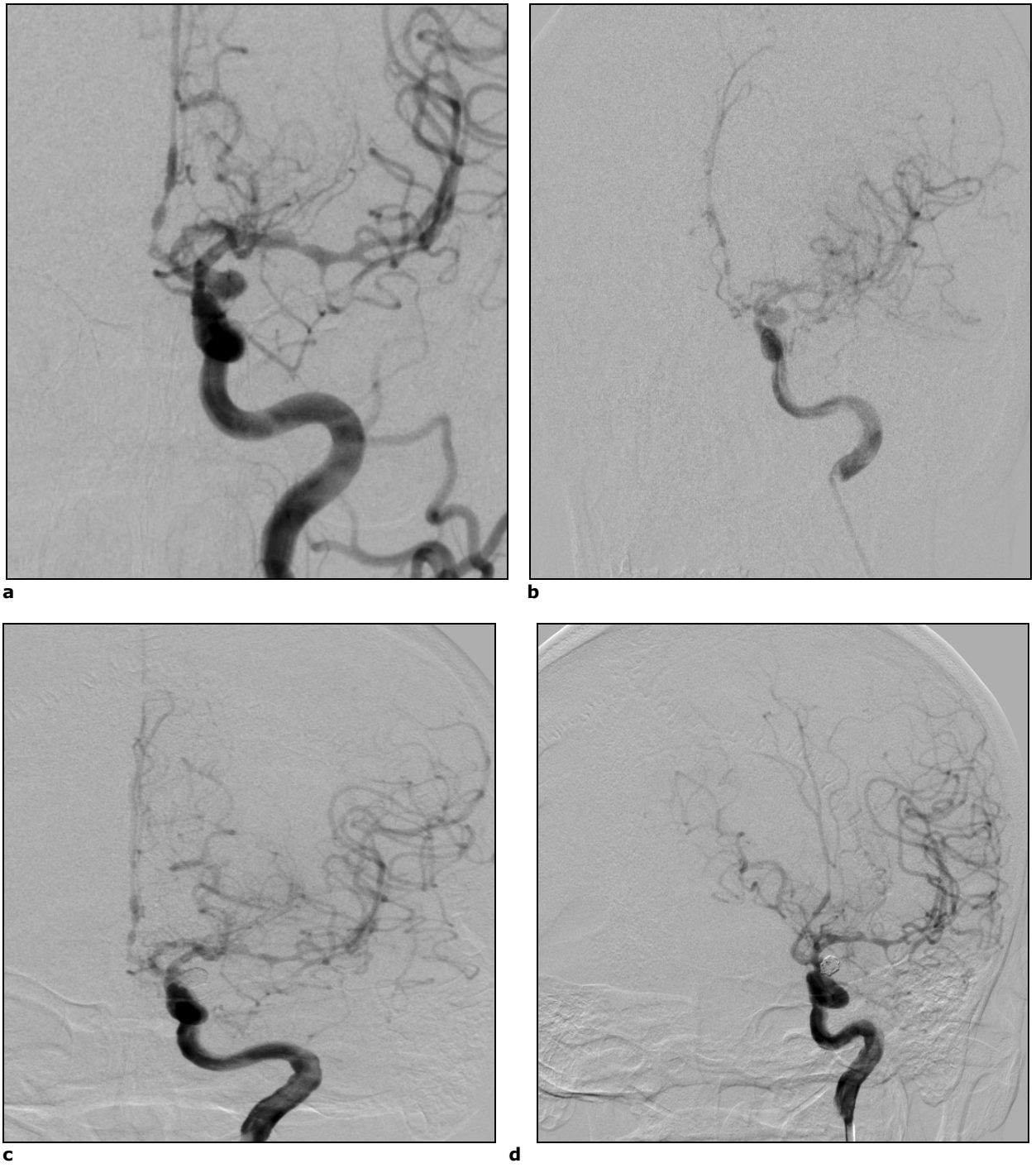


Figure 1: DSA revealed ruptured aneurysm at ICA sin and spasm at ACA and MCA sin (Figures 1a and 1b). It was successfully completely excluded from circulation with simple coiling (Figures 1c and 1d).

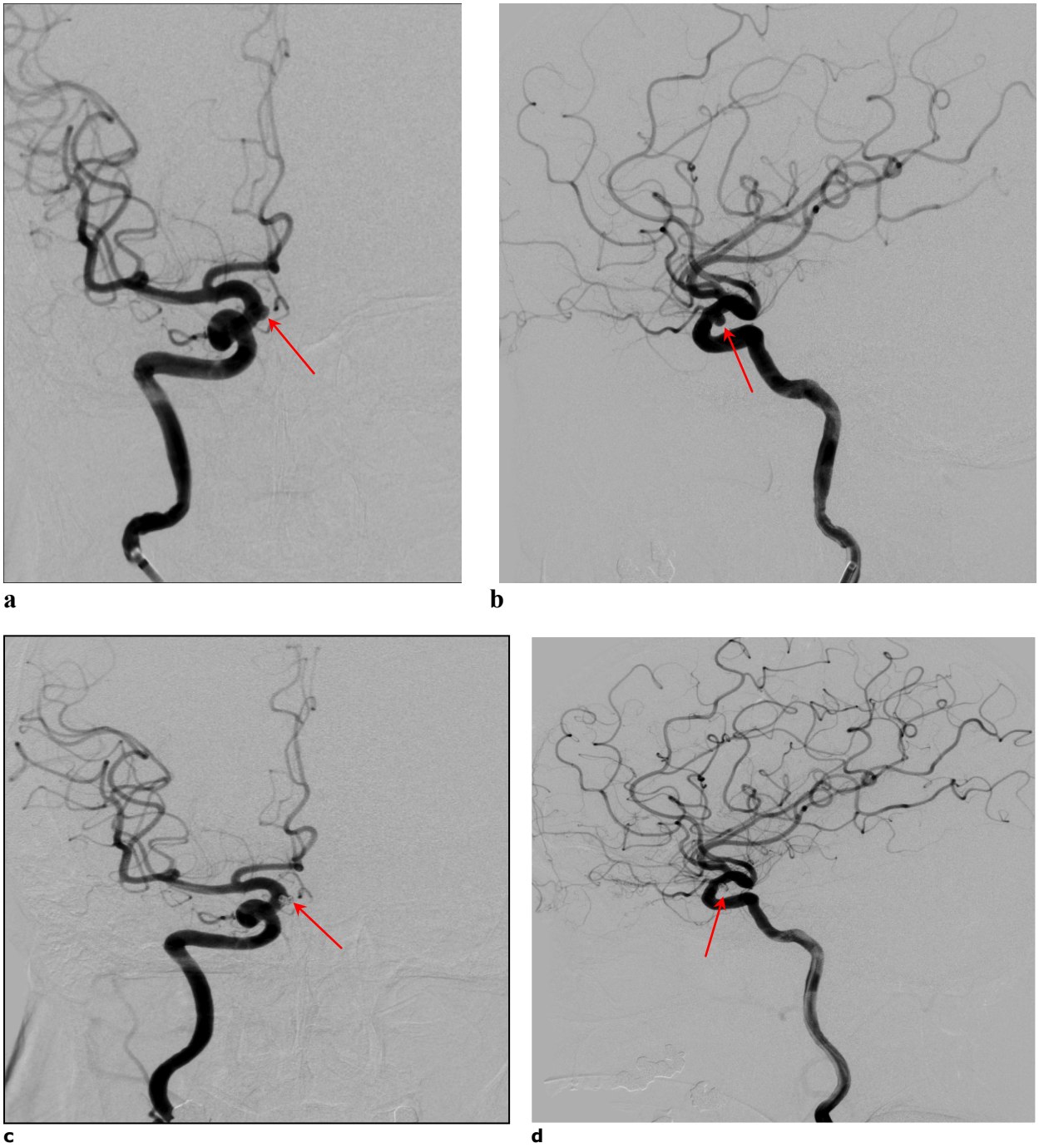
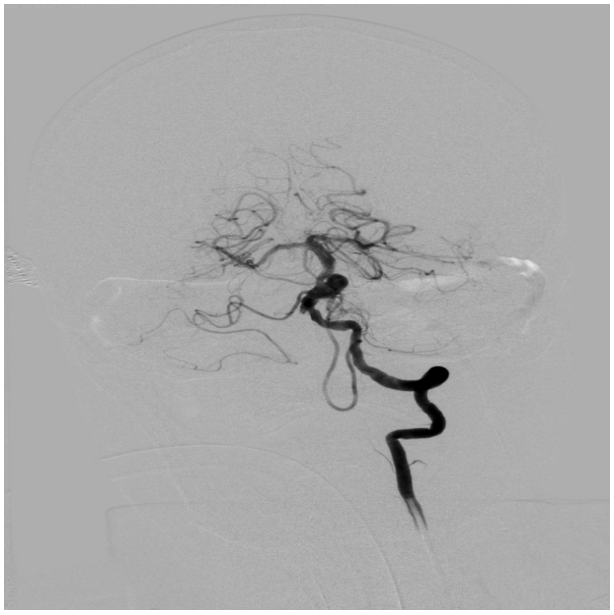


Figure 2: Small (less than 4mm) unruptured aneurysm at ophthalmic segment, posterior wall ICA dex aneurysm (Figure 2a and Figure 2b, red arrows). Aneurism was completely excluded from circulation with one coil (Figure 2c and Figure 2d, red arrows).

The geometric characteristics of the aneurysm are the first criteria to be considered in order to choose whether the intervention will be performed only with coils (Figure 1 and Figure 2) or stent-assisted or balloon-assisted coiling. Fusiform aneurysms or aneurysms with wide neck can be threaded with flow diverters as well (13). The ideal dome-to-neck ratio (Figure 3a) for coiling must be more than 2. The diameter of the neck should not be wider than the diameter of the parent vessel, and slightly smaller than the diameter of the aneurism (14).The use of stents or balloons was generally indicated for wide-necked aneurysms (>4mm) or those with an unfavorable dome-to-neck ratio (<1.5) (15). Stents may also be used in rescue procedure when coils prolapse into the parent vessel.

Endovascular technique

Guido Guglielmi, an Italian neurosurgeon who had been working with engineers at Target Therapeutics, Inc, developed the Guglielmi detachable coil (GDC, Stryker Neurovascular, Fremont, CA) (16,17). Clinical use of GDC coils began in



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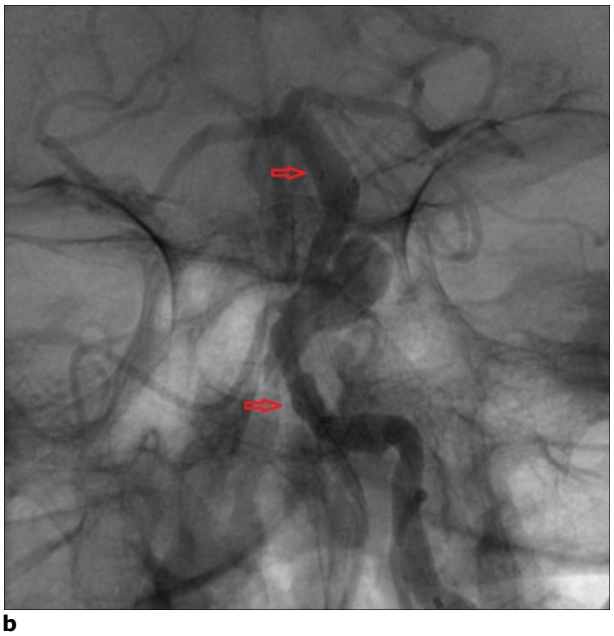

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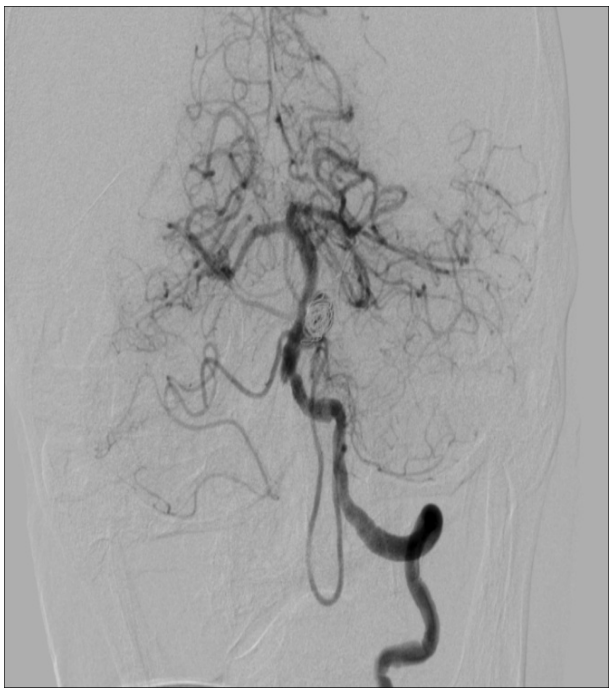
Figure 3: DSA revealed unruptured aneurysm at proximal BA with wide neck (Figure 3a). Enterprise stent was placed (arrows in Figure 3b) and then the aneurysm was filled with coils (Figure 3c).



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1991, and in 1995 the FDA granted approval of GDC coils for the treatment of high-risk, inoperable, or ruptured intracranial aneurysms. In the last 20 years, huge progressional and technical refinements in the design of aneurism coils have been made. A range of shapes, sizes, design, stiffness, presence or absence of "bioactive" material, and detachment systems of coils have been introduced on the market. On the other hand, the first case of intracranial stenting for treating a brain aneurysm was reported by Higashida et al. in 1997 (18). At present, stent has become one of the most important tools in treating difficult aneurysms not feasible for simple coiling (19)(Figure 3). There are currently five types of intracranial stents (Neuroform EZ, Solitaire, Enterprise, Leo plus and LVIS) which are used for assisting coiling and one type of stent (Wingspan) for the treatment of intracranial atherosclerotic disease available worldwide. Detailed description of endovascular procedures using these materials is out of scope of this review and the following is a general outline of the procedure used by the authors for most patients. Patients with aneurysms, either ruptured or unruptured, are treated under general anesthesia. Every procedure is divided into a vascular access phase and an intervention phase.

A vascular access consists of placing a guide catheter in the internal carotid artery (ICA) or vertebral artery (VA) which provides stability for further supraselective catheterizations and high quality angiographic images of aneurysm dome, neck and parent vessel. The authors of this review prefer to use the Neuron International Access System (Penumbra, Inc., San Leonardo, CA). We use Neuron 0.053 in. guide catheter for most primary coiling cases or Neuron 0.70 in. or Neuron MAX 0.088 in. when balloon remodeling is anticipated, or when high quality angiograms are necessary. To prevent thromboembolic complications which may occur during the coiling we use IV heparin loading dose of 5000I.J. or 70I.J./kg for unruptured aneurysms, and for ruptured aneurysms we withhold heparin until enough coils have been placed in the aneurysm; then we give the loading dose of 70I.J./kg. In cases of unruptured aneurysms when intracranial stent are planned, double antiaggregationclopidogrel 75mg as well as 100 mg of acethyl-salicic acid PO QD is administered for five or more days. If a stent has to be deployed urgently and the patient has not been prepared with antiaggregation agents, we prefer

using a GPIIb/IIIa inhibitor. A bolus of 0.025 mg/Kg of intravenous abciximab is administered just before stent placement and it is followed by infusion at the rate of 10mcg/min for 12 hours (20-22). Evidently, this strategy should be used with caution and not as a routine regarding well-known hemorrhagic side effects of intravenous GPIIb-IIIa inhibitors.

When the guiding catheter is in the adequate position, the interventional phase may begin. A good "working view" must be obtained and it should demonstrate the aneurysm, parent vessel, and guide catheter tip clearly. For this purpose, a 3D angiogram is done and the image of the aneurysm is rotated on the workstation monitor to obtain the best view and the corresponding position of the x-ray tube.

The next phase consists of supraselective catheterization using microwire and microcatheter and placing the microcatheter tip in the aneurysm. Microcatheres have two radio-opaque markers at the distal end which are always 3cm apart to align with the marker of coil pusher wire. They come in several prepared shapes (straight, 45°,90°, "J" and "S") or they may be steam-shaped. An "S" shaped microcatheter often works best for superiorly directed aneurysms, while pigtail shape may be helpful in case of superior hypophysial aneurysms. Navigation of microcatheter over the microwire must be done under "roadmap" guidance. In case of end-artery aneurysms (e.g., basilar apex aneurysm), the microwire can usually be carefully advanced directly into the aneurysm, followed by the microcatheter. Great care must be taken in using the hydrophilic wires, because they may allow the microcatheter to advance suddenly and rapidly, creating a risk of perforating the aneurysm dome. Sidewall aneurysm (e.g., ophthalmic segment ICA aneurysms and SCA aneurysms) can be accessed by guiding the microwire and microcatheter tip beyond the aneurysm's neck and then microwire is pulled back into microcatheter, and the microcatheter is slowly pulled back, allowing the tip to flip into the aneurysm. Stable position of microcatheter is when the tip of microcatheter is several millimeters in the aneurysm. Ideally, the tip of the microcatheter should be at the center of a spherical aneurysm, not against its wall. During the introduction of coils the side to side motion of the microcatheter tip is an indication that the microcatheter tip is in the good position.

Some general rules in coil selection are that the first coil is a framing the 3D coil which is meant to "ovalize" or "sphericize" the aneurysm with gentle outward radial force and also extend across the neck of the aneurysm, helping to narrow the effective neck area and facilitate further coil deposition. The selection of the first coil is important because it determines how densely the aneurysm can be packed. The diameter of the first coil should be 1mm wider than the maximum diameter of the aneurysm. Pear-shaped aneurysms, however, are treated as though they were two aneurysms of different sizes (the dome and the proximal tubular portion). In these cases, the diameter of the first coil should be 1mm wider than the maximum diameter of the dome of the aneurysm. After one or more 3D coils are deployed to frame the aneurysm, filling coils are deployed, and at the end of the procedure the finishing coils are placed. Filling coils are intended to occupy the space within the aneurysm after framing. They usually have helical shape and are of intermediate stiffness. Finishing coils are the softest coils and they are designed for final packing of the aneurysm and "finishing off" of the neck of aneurism.

As we have already mentioned, five stents (Neuroform EZ, Solitaire, Enterprise, Leo plus and LVIS) which are used for assisting coiling are now available in Europe. All stent cells are made of nitinol and they can be divided according to design into open-cell (Neuroform, Wingspan) and closed-cell (Enterprise, Solitaire, Leo plus, LVIS) types (20). The diameter and length of each device is chosen according to the diameter of the native vessel and the extension of the pathological segment (20). It is particularly important to detect potential irregularities due to other vascular p-athologies such as atherosclerosis or fibro-muscular dysplasia and tourtuosity of the parent artery, which influences the type of stent that is going to be used. When stent-assisted coiling is performed, the technique of catheter tip placement into the aneurysm sac can be divided into two methods, catheter jailing and the strut stenting technique (21). The choice between the two methods may depend on the physician's experience.

Discussion

Thirty years ago, the treatment of intracranial aneurism was exclusively surgical. During the last 20 years with improvements in materials and technique, treatment has been shifted from exclusively surgical to predominantly endovascular; aneurysm morphologies once considered untreatable endovascularly are now treatable with coils, stents, flow divertors. Several large clinical trials have demonstrated the safety and efficacy of endovascular treatment of intracranial aneurysms. Data from the prospective International Study of Unruptured Intracranial Aneurysms (ISUIA) study showed that the 30-day morbidity and mortality rate with surgery is 13.2% and the one-year morbidity and mortality is 12.2% in patients with unruptured aneurysms. The 30-day morbidity and mortality rate with endovascular treatment is 9.3% and after one year 9.8%. Mean duration of follow-up after surgical treatment was 4 years and 3.7 years for patients who had endovascular treatment. Risk factors for complication with surgery include older age (>50 years), aneurysm size (>12mm), posterior circu-lation aneurysms localization (23). The Inter-national Subarachnoid Aneurysm Trial (ISAT) is considered to be the largest and longest of all trials conducted

regarding endovascular coiling vs. surgical clipping in selected patients with ruptured intracranial aneu-rysms considered suitable for either therapy (24). A total of 9.559 patients were screened, and 2.143 (22.4%) were randomly assigned to either surgery (n=1.070) or endovascular treatment (n=1.073). Clinical outcomes were assessed at 2 months and 1 year. Recruitment was stopped after temporary analysis showed a significant advan-tage of endo-vascular therapy. The rate of mortality and dependence at 1 year was 23.5% in the endo-vascular group versus 30.9% in the surgical group (24). Subgroup analyses showed significant benefits with endovascular therapy for patients aged 50-69, all Fisher grades, aneurysm lumen size <10mm and ICA aneurism location (25). No subgroup showed a significant benefit with surgery. The number of patients with rebleeding was slightly greater in the endovascular group at year 1 as well as late rebleeding after one year; however, five-year mortality was 11% in the endovascular group and 14% in the surgical group (25). Moreover, Brilstra EH et al. in systematic review of 48 studies found a rate of permanent complications with embolization of 3.7% (26). In spite of this, complication rates are somehow higher in stent-assisted coiling comp-ared to simple coiling as well as at the endo-vascular treatment of aneurysms <3mm. M. Shapiro et al. in their literature survey of stent-supported aneurysm coiling found that the overall procedure compli-cation rate was 19%, with periprocedural mortality of 2.1%. Approximately 45% of aneurysms were completely occluded at first treatment session, increasing to 61% on follow-up. Approximately 3.5% of in-stent stenosis and 0.6% of stent occlusion were observed atangiographic follow-up. Delayed stroke or transient ischemic attack was reported in 3% of subjects (27). Conclusion of the study is that complete occlusion rates remain somewhat low. For this reason, long-term angio-graphic follow-up information is needed to understand delayed stent-related issues and to better define the durability of treatment. Further-more, Brinjikji W at al. in their systematic review of endovascular treatment of very small aneu-rysms (<3mm) found procedural rupture rate of 8.3% and a combined rate of periprocedural morbidity and mortality of 7.3% (9). Based on the facts stated above and personal experience, the author of this review suggests an endovascular treatment with simple coiling in cases of older patients, aneurysm lumen size less that 10mm and paraclinoid ICA aneurism location, but also in cases of aneurysms in posterior circulation. Stent-assisted coiling is reserved for wide-neck aneurysms and it requires additional caution and longer period of follow-up due to higher rate of complications.

Conclusion

Experience with aneurysm coil embolization during the past decade showed that even though this is a safe and stable treatment method, there are still possibilities to improve the procedure. One of the improvements made in the management of wide-neck aneurysms was the introduction of stent-assisted techniques. The next-generation endoluminal devices will certainly impact further effectiveness of endovascular aneurysm treatment in the future.

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SAVREMENI ENDOVASKULARNI TRETMAN INTRAKRANIJALNIH ANEURIZMI

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U prethodnih dvadest godina bili smo svedoci revolucije lečenja intrakranijalnih aneurizmi. Endovaskularna tehnika i materijali su se dalje razvijali od 1995. kada je Guglielmijev koil uveden u lečenje intrakranijalnih aneurizmi. Razvoj intrakranijalnih stentova i balona koji se koriste kao potpora embolizaciji aneurizmi koilovima omogućio je proširenje spektra aneurizmi koje mogu biti lečene endovaskulrnim putem. Iz ovih razloga cilj ovog rada jeste da opiše endovaskularnu tehniku i materijale koje najčešće koristimo u svakodnevnoj praksi, da pokaže koristi endovaskularnog lečenja i da uporedi komplikacije edovaskularnog lečenja i klasične hirurgije. Endovaskularnina činlečenja kao minimalno-invazivan je komforniji za pacijenta, a i praćen je kraćim boravkom u bolnici nakon intervencije u odnosu na hirurško lečenje. Sigurno je da će daljim razvojem endovaskularnih materijala endovaskularna procedura imati još značajnije mesto u lečenju intrakranijalnih aneurizmi. *Acta Medica Medianae 2015;54(2):63-70.*

Ključne reči: *aneirizme, endovaskularni tretman, embolizacija spiralama*