Endovascular Management of Cerebral Aneurysms

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During the last decade, the field of endovascular surgery for the treatment of neurovascular disorders in general, and for cerebral aneurysms in particular, has undergone tremendous growth. As new technologies are developed and more experience is gained by trained endovascular therapists, more and more lesions will be able to be treated by less invasive methods. Improvements in catheter, guidewire and delivery system design, the development of various embolic agents and the technical advancements in imaging equipment have all contributed to the advancement of the field.

Today, the endovascular treatment of cerebral aneurysms is a reliable, reproducible and well-accepted technique. Presently, most endovascular aneurysm treatments involve the use of detachable balloons and/or metallic coils. Detachable balloons are primarily used for deconstructive procedures or aneurysm neck protection. Detachable coils varying in size, length, flexibility, and configuration can now be reliably placed within an aneurysm and detached either mechanically or by electrolysis in a controlled fashion.

The evolving techniques of endovascular aneurysm treatment including the development and use of precipitates, stents of various designs, neck protection and remodeling, aneurysm liners, liquid polymers, hydrogels, aneurysm

neck protection, micro-anastomoses, bio-active manipulations to endovascular devices as well as real-time three-dimensional imaging will be discussed.

Aneurysms Treatment

The present state of the art in endovascular aneurysm treatment consists of endovascular coiling of the aneurysm lumen using the 3rd generation Guglielmi detachable coil (GDC3) system. This technique allows access to the great majority of aneurysms and the placement of electrically detached coils, thus excluding the lesion from the circulation. Endovascular GDC treatment has been available since 1991.

During this time, it has become apparent that the GDC technique decreases the incidence of aneurysm rehaemorrhage at 6 months after rupture¹⁰. Clinical results seem to support protection from bleeding in aneurysms for up to 5 years after treatment⁴. Data is currently being collected beyond 5 years.

Early series however demonstrate close to 10% aneurysm recurrence due to suboptimal coil stability over time. Stability depends on several factors including the density of coil packing, the aneurysm's relationship with the parent vessel, the aneurysm's location in relation to flow and shear forces, and the size of the aneurysm and its neck as well as the dome-to-

neck ratio. Recurrence from coil packing has been observed in aneurysms that lie in the direct linear path of blood flow (i.e., "end aneurysms"), in aneurysms with a wide neck, and very large aneurysm^{9,11}.

In "side aneurysms", the treatment has been more stable. Some end aneurysms, particularly those with a narrow neck, remain stable. Those aneurysms with favorable flow dynamics such as side inflow and outflow remain stable even if terminal, probably due to blood flow distortion. Additional techniques including 3-D framing, neck framing, balloon remodeling and stent assisted coiling as well as the availability of soft, and shortly, ultrasoft coils are enhancing our ability to offer endovascular treatment for wide necked aneurysms¹³.

Aneurysms in difficult high-risk locations, in older patients, and in-patients with high surgical risk may be better treated by endovascular means, as the GDC technique is safe and appears to offer good protection. If long-term follow-up of present technology supports the current endovascular experience, future management of cerebral aneurysms may consist primarily of endovascular techniques.

In particular, aneurysms with a small neck at any location may best be treated using endovascular techniques. The true importance of the GDC technique, however, is that it provides a treatment alternative to surgery which is considered to be reliable and safe. Endovascular coiling with GDCs, in appropriate cases, is as effective as surgery, and is overall safer, even considering those patients that need to be re-treated. For this reason, the GDC technique is currently readily available and being employed with increasing frequency throughout the world.

Remodeling Technique

Balloon remodeling¹² allows for the treatment of wide-necked aneurysms that were initially regarded as uncoilable, because the GDC coils could not conform to the lesion and subsequently herniated out the open aneurysm neck, jeopardizing parent vessel patency.

The technique uses two delivery systems: the conventional two-tipped GDC microcatheter to deliver coils and a balloon-tipped catheter with or without a guide wire.

The balloon is inflated across the aneurysm neck, and the coil being inserted adopts the flat surface presented by the balloon and retains that memory. After coil placement but before detachment, the balloon is deflated and the coil is observed. If the coil is stable, it is then detached.

This technique also can increase the density of aneurysm packing, which may improve long term stability of the coil structure. Balloon remodeling is potentially associated with slightly higher morbidity because of the additional balloon-tipped catheter and the manipulation required to position and subsequently inflate and deflate the balloon with each coil placed.

The technique, however, gives more security from coil herniation and migration, and in the case of aneurysm rupture, the balloon is immediately available for vessel occlusion. In many respects, balloon-assisted aneurysm coiling is similar to reconstruction of an aneurysm neck using multiple clips.

Alternatively, direct neurosurgical clipping to create a different dome-to-neck ratio can be performed before coiling.

Revascularization

Large and giant aneurysms pose treatment difficulties to both endovascular and neurological surgeons. Treatment of these lesions can be either constructive or deconstructive. In a deconstructive procedure, the parent vessel feeding an aneurysm is occluded or trapped either surgically, endovascularly, or by a combined technique.

Individuals with giant aneurysms who have failed balloon test occlusion and require parent vessel occlusion should be considered for alternative therapies such as bypass. Once a vessel is anastomosed into a normal vascular segment either proximal or distal to the lesion, either a microsurgical or endovascular technique can be used to eliminate the abnormal segments of vessels. Bypass procedures using current techniques are limited by temporary occlusion times, vessel caliber and flow mismatch, and the risks of delayed graft thrombosis.

Successful bypass in carefully selected patients, however, can offer an alternative method of preserving flow distal to an aneurysm after parent vessel occlusion. Microsurgery is likely to evolve primarily in the areas of microanasto-

moses, vessel transposition, and microvessel grafting and this evolution will play a main role in the development of open microneurosurgical techniques in the management of cerebrovascular disease. Improvements in the speed and accuracy of vessel anastomosis by using laser technology, laser soldering, or microanastomotic devices (D. Newell, personal communication, 1998) should reduce the duration of temporary occlusion of vessels and should further advance bypass safety and efficacy. In addition, tissue adhesives may be used on smaller vessels to permit greater success of distal anastomosis.

Further improvements in our understanding and manipulation of the coagulation system should also help prevent early thrombosis of bypass grafts. This understanding of the coagulation cascade may also be relevant to the management of patients with any endovascularly placed device.

Functional Rearrangement

It may become possible to redesign the cerebral circulation with improved ability to perform microanastomoses and knowledge of the anatomical basis of the vascular territories. For example, an endovascular device may be used to occlude a vessel at a certain segment, and leptomeningeal or larger anastomotic arteries may then be permitted to reconstitute that segment by flow reversal³.

This strategy could also be used to disconnect a vascular bed, allowing isolation of a territory within the cerebral circulation.

We use rearrangement of the circulation to treat selected cases of brain arteriovenous malformations or to provide superselective administration of chemotherapeutic or cytotoxic agents. Vascular isolation also may permit assessment of the physiological correlates of vascular territories. Endovascular catheterization to different areas of the brain and the injection of either a depressant of neurological activity (amobarbital or lidocaine) or of a neurological stimulant (amphetamine) can reproduce an epileptic focus or alter neurological function.

Subsequent injection of an embolic agent, when appropriate, may then be performed to obliterate a vascular lesion or even a seizure focus.

Vasospasm

Vasospasm is a significant cause of morbidity and mortality after subarachnoid haemorrhage³. The onset of vasospasm is usually between days 4 and 8 after aneurysm rupture. Early intervention using balloon angioplasty and selective papaverine infusion using interventional techniques in symptomatic patients who have failed medical management can significantly improve their outcome^{5,7}.

In these patients, the diagnosis of vasospasm is confirmed by angiography. Both treatments can reverse vessel narrowing; however, balloon angioplasty provides a longer effect^{5,7}. Current research into vasospasm treatment may be helped by our ability to navigate in the cerebrovasculature. For example, by using interventional techniques, administration of newer generations of calcium channel blockers or manipulation of rheological factors may be achieved in regions of focal spasm.

The local introduction of genetically engineered vasodilatory genes such as endothelial nitric oxide synthase (eNOS) using endovascular techniques may also play a role in vasospasm treatment. eNOS expression has been documented in human cerebral vascular smooth muscle after transfection with both the *Escherichia coli* Lac Z gene and eNOS cDNA¹. Evidence of eNOS expression can be found by assaying for the metabolic products of the nitric oxide synthase reaction i.e., nitrate and citrulline. In the future, endovascular techniques may be used to introduce eNOS or similar agents in patients with symptomatic vasospasm or prophylactically in all subarachnoid haemorrhage patients during their initial angiogram. This type of early genetic therapy may allow early transfection and vector exposure and may theoretically result in rapid gene expression and prevention of vasospasm. Transvenous catheterization using endovascular techniques may also evolve and make retrograde reperfusion a reality. This technique may be applied in the treatment of cerebral ischemia from vasospasm.

Coil Design

The development of bioactive coils may improve the ability of the endovascular surgeon to treat aneurysms. Bioactive surface designed coils that stimulate the coagulation cascade

have recently been introduced. Potential manipulation of clot stability may be more useful in endovascular aneurysm treatment than enhancing thrombogenicity³. Pretreated or coated coils may eventually use genetically engineered coagulation factors or promoters of coagulation to enhance aneurysm occlusion. In particular, improved coil design combined with techniques such as balloon remodeling may help coil treatment of aneurysms located at the end of laminar flow patterns or end aneurysms. Similarly coated coils may be useful in giant aneurysms. Other coil coatings such as angiogenic coatings, antivasospastic coatings, or endothelial promoters should eventually become available and may play a major role in aneurysm treatment.

These therapies could conceivably all be combined in a single coating on an endovascular coil. In the future, a patient presenting with an acute subarachnoid haemorrhage could undergo immediate diagnostic angiography with induction of prophylactic therapies for vasospasm or ischemia and could receive definitive treatment of his/her aneurysm in one minimally invasive procedure.

Future Endovascular Devices

The most immediate breakthroughs or technologies that develop for endovascular aneurysm treatment will probably be therapies based on reliable detachable devices with or without biological complements.

Coils suitable for better aneurysm volume filling which promote thrombosis or endothelialization can be expected within the next few years. Different metal alloys, and the use of combined metallic devices and liquid polymerizing agents are being explored at present and should further enhance mechanical aneurysm occlusion and improve long term structural stability.

Intracranial Stents

Intravascular stents are currently available for use in coronary vessels and the peripheral vasculature. They have been used extensively for arterial stenosis, repair of vessel ruptures or fistulas (covered stents), and, most recently, in the experimental treatment of abdominal aortic aneurysms.

Their use is rapidly expanding into the cerebrovascular system. For example, stenting has been used for carotid atherosclerosis or distal internal carotid artery aneurysms^{8,13}. Stent design continues to be refined, and delivery systems are more flexible and of lower profile.

Consequently, microstenting of intracranial vessels has become a reality. Endovascular stents are a major research area for industry and many investigators. Endovascular stents may also be used to incorporate growth factors and endothelial growth promoters. These agents may be used to treat cerebral ischemia or permit an orderly healing process of a damaged vessel. The goal of this technique is growth of an endothelial lining to seal defects in the blood vessel wall, which may be particularly useful in the endovascular repair of giant aneurysms, where vessel reconstruction is required.

Conclusions

Many exciting possibilities in the field of endovascular surgery still lie ahead of us. The treatment of cerebral aneurysm should evolve in a multifactorial fashion and should include areas such as liquid embolics and their delivery, three-dimensional imaging, vessel transposition and microanastomoses, endovascular aneurysm neck protection, microcatheter and microguides, stent technology and bioactive manipulation.

In the field of imaging, major advances already available include three-dimensional selective and superselective angiography and endovascular imaging by which the inner vessel lumen and the origin or face of an aneurysm can be seen from the inside, measured, and assessed before and after treatment. A combination of endovascular aneurysm neck protection, biological modifications such as local application of endothelial growth factors and manipulation of the coagulation cascade, and microanastomoses or vessel transposition should permit us to safely treat aneurysms that currently cannot be treated or for which treatment is associated with significant morbidity. In addition, our knowledge of cerebral vascular anatomy and physiology, particularly our understanding of the venous system in brain function and of the plasticity of the vascular territories, should continue to expand.

The management of cerebral vascular disease also should be further enhanced by our ability to navigate within the venous system. Finally, microcatheter and microguide wire designers continue to provide us with more flexible, hydrophilic-coated, and variable stiffness devices for more controlled and subtle

navigation in the vascular system and for flow-directed and propelled catheterization techniques.

These various techniques and our improved understanding of the cerebral vasculature should carry endovascular treatment of all cerebral vascular lesions into the next century.

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