



Current Status of Endovascular Therapy of Cerebral Berry Aneurysms

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Editorial

Autopsy reports have shown that cerebral aneurysms are present in roughly 5% of population [1-3]. Subarachnoid hemorrhage (SAH) is the most serious presentation of ruptured cerebral aneurysms. Estimated annual incidence of non-traumatic SAH ranges from 2 to 23 cases per 100,000, which translates to 6,500 to 74,000 annual cases of SAH in the United States. Approximately 80% of non-traumatic SAH cases are due to ruptured cerebral aneurysms [4-7]. Untreated ruptured cerebral aneurysms are associated with a high mortality and a risk of rebleeding [8]. The case fatality of cerebral aneurysm rupture is high (from 27% to 44%), but has decreased during the past 3 decades due to continuous improvements in patient management strategies [9].

The rupture risk of cerebral aneurysms is directly related to their size, shape and location [10-12]. Women and cigarette smokers are at increased risk for cerebral aneurysm formation and growth. Cigarette smoking in particular hastens this process in both sexes. Other independent risk factors for aneurysm formation and growth are hypertension and family history of stroke, with smoking and hypertension having an additive effect, whereas hypercholesterolemia, regular physical exercise and a healthy lifestyle reduce the risks of aneurysmal SAH [13].

The two main treatment strategies for obliteration of cerebral aneurysms are neurosurgical and endovascular. In neurosurgical approach, the operator gains access to the subarachnoid space via craniotomy to exclude the aneurysm from the blood circulation by microsurgical clipping. Harvey Cushing and Walter Dandy are credited with introducing microsurgical clips to treat cerebral aneurysms [14]. This method, with advancements in forms and types of microsurgical clips, was the standard of care for aneurysm treatment before mid 90s.

Endovascular therapy obliterates an aneurysm by occluding its dome with coils. Guglielmi et al. [15] introduced electrolitically detachable platinum coil – GDC. This device was approved by the FDA for the treatment of cerebral aneurysms in 1995, recognizing coiling as a competitive treatment strategy to microsurgical clipping.

The widespread acceptance of coiling has been hindered by the potential for cerebral aneurysm to recur over time after coiling [16]. This issue is even more relevant for large cerebral aneurysms for which angiographic recurrence is more likely than for smaller lesions [17]. The two most frequent complications of cerebral aneurysm coiling are thromboembolic events, which occur in 7.3% in unruptured and 13.3% in ruptured aneurysms respectively, and intraoperative rupture with prevalence of 2.0% in unruptured and 3.7% in ruptured aneurysms respectively [18,19]. Cerebral aneurysm coiling-caused mortality during their intraoperative rupture and thromboembolic events are observed in 3.7% and 16.7% cases respectively [19].

Durability of coiled cerebral aneurysms is assessed by their recanalization, which occurs in 20.8% of cases, requiring retreatment in 10.3% [20]. The risk of rerupture of initially ruptured cerebral aneurysms treated with coils runs in parallel with the degree of the initial occlusion of aneurysm cavity [21]. Due to the possibility of recanalization of coil-embolized aneurysms, their postoperative follow up by digital subtraction and/or magnetic resonance angiography became a necessary measure [21-23].

Significant advancements in imaging technologies and interventional tools for endovascular therapy of cerebral aneurysms, which include introduction of biplane flat panel digital and magnetic resonance angiography equipments, development of microcatheters, softer detachable coils, compliant balloons, stents and flow diverters contributed to improvements in management strategies for endovascular treatment of cerebral aneurysms [24].

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In order to improve the degree of coiling of wide-neck and complex cerebral aneurysms, neurovascular remodeling devices have been introduced. Moret et al. [25], described balloon assisted coiling (BAC) technique, in which a non-detachable single balloon placed in a parent vessel either across the neck of the aneurysm or a non-detachable double balloon placed distally and proximally to the aneurysm origin, is temporarily inflated during deployment of each coil in cerebral aneurysm [25]. Unfortunately, BAC method did not contribute to a better clinical outcome than unassisted coiling, but showed superiority of the former in anatomical results of endovascularly treated cerebral aneurysms and with improvements in balloon catheters they have been utilized with increasing popularity as a sentinel tool for intraoperative management of cerebral aneurysms that rupture during coiling [26-30].

Another approach for endovascular treatment of cerebral aneurysms, stent-assisted coiling (SAC), initially was described by Higashida et al. [31]. Since then several cohort studies comparing the SAC and coiling alone techniques have been published, however the results were controversial [32-41]. Two systematic reviews concluded that SAC seemed to have more adverse events than traditional coiling [42,43], but these studies were limited since only data on SAC was used. Hong et al. [44] recently reported results of meta-analysis of ten retrospective cohort studies that compared SAC with coiling of cerebral aneurysms. The study concluded that SAC has a significantly lower recurrence rate than conventional coiling (16.2% vs. 34.4%).

Analysis of complication events did not show any significant difference between the two methods. However, Bodily et al. [45] reported a qualitative, systematic review of 17 articles on SAC treatment of ruptured aneurysms, where they concluded that adverse events appear more common and clinical outcomes are likely worse than those achieved without stent assistance.

As stents were being developed for cerebral use, it was hypothesized that stents could be utilized to divert flow away from the aneurysm back into the parent vessel, and the concept of endovascular flow diversion was proposed [46-49]. Early *in vitro* and *in vivo* studies showed this concept to be valid, but clinical application was limited because of high porosity of first-generation cerebral stents. With technological improvements, cerebral flow diverters have become available for parent vessel reconstruction endoluminally and early clinical experiences have been encouraging. According to recently reported meta-analysis of 29 studies concluded that treatment of cerebral aneurysms with flow-diverter devices is feasible and effective with high complete occlusion rates [50]. However, the risk of procedure-related morbidity and mortality is not negligible.

Raymond et al. [51] have shown in preclinical studies that embolized aneurysms recanalize due to early endothelial invasion of a clot inside the aneurysm cavity [51,52]. These studies have also proved that de-endothelialization caused increased migration and proliferation of fibroblasts and macrophages at the denuded area, which lead to local deposition of collagen and thereby minimized chances of recanalization. Based on these observations Raymond [53] invented a device that would effectively remove parts of endothelial lining of aneurysm cavity mechanically, physically or chemically in a pin-pointed fashion. However, Raymond's [53] invention doesn't offer the removal of endothelial layer in a circumferential fashion at the origin of a vascular defect.

However, preclinical evaluation of another method and invention

in endovascular therapy of brain aneurysms introduced by Shengelaia has proved to achieve this task by application of RF energy at the origin of such vascular defects. The most active component of the device is embedded within the wall of a balloon at its center and has a zig-zag shape in a deflated position and changes its shape to a ring-form when balloon is inflated. Further studies of this device are under way.

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