The Potential of Flow Modification in the Treatment of Intracranial Aneurysms

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Abstract

Background and purpose: To summarize the theoretical background and existing technical achievements of flow modification techniques in the treatment of intracranial aneurysms.

The evolution of the concept of flow modification for aneurysm treatment is overviewed within the published literature on application of stents for aneurysms. The newest achievements using dedicated flow modifying devices is discussed.

Reconstruction of laminar flow within intracranial arteries harboring aneurysms is feasible. Reorientation of flow using dedicated flow modifying devices is a highly effective technique in the treatment of large, broad neck, otherwise untreatable aneurysms.

Introduction

The application of stents for the treatment of intracranial aneurysms has been first proposed in the early 90's [1-3]. During the early years of application of this technique the primary goal was the geometrical reconstruction of the parent artery in order to promote packing of the aneurysm. Flow conditions within the parent artery and the aneurysm itself have long been considered as playing an important role in aneurysm growth and rupture [4-11]. With the latest technologies, flow modification within and around the aneurysm became the primary objective of using stent-like flow modifying devices in aneurysm treatment. Preliminary results of the first clinical application of such devices will be discussed.

Experimental background

The therapeutic potential of intravascular stent technology has been raised and its technical feasibility assessed in animal experiments in the early 1990's [1-3]. It was hypothesized, that the effect of stents on endovascular aneurysm treatment may be influenced by three mechanisms. First, anatomical/geometrical reconstruction of the parent artery with stent across a wide necked aneurysm facilitates dense aneurysm packing without compromising the lumen of the parent artery. Secondly, a stent placed across the aneurysm neck may alter the local flow dynamics by diverting flow streams and reducing the free surface area of the orifice. These may result in slow flow and thrombosis inside the aneurysm cavity. Finally, the mesh of the stent may serve as a framework for the proliferating intima to cover the aneurysm orifice and permanently separate it from the lumen of the parent artery [1].

The potential hemodynamic effects of stents were further evaluated in laboratory experiments. It was demonstrated, that depending on their mesh density, stents are capable of reducing vortex flow within the aneurysm and flow interaction between the sac and the parent vessel [12]. It was also shown, that besides the porosity, the geometrical design of the stent also has an impact on aneurysm thrombosis, depending on the local flow patterns [13,14].

Clinical experience with morphological reconstruction of the parent artery using stents (stent supported aneurysm packing)

Clinical reports published to date mostly focus on the mechanical effect of balloon expandable and self expandable stents that makes aneurysm packing feasible even if the neck is wide. In 1997, Higashida reported a fusiform BA aneurysm that was treated with a Palmaz-Schatz stent and GDC coils 15. Since than, several case reports were published on successful combined stent implantation and coil packing. This technique was used to treat dissecting aneurysms of the cervical 16-18 and the intracranial ICA 19, 20 and rather frequently for dissecting and fusiform vertebrobasilar aneurysms 21-26. Some of these patients were treated in acute subarachnoid haemorrhage (SAH) [15,21,22,25,26].

In 2002 Lylyk reported a large series of intracranial stent implantations including 72 cases treated for aneurysms. They achieved complete or nearly complete occlusion of berry aneurysms in 97% and of dissecting aneurysms in 100% [27].

In 2003 Wanke reported 3 cases that were successfully treated with a self-expandable stent system [28]. The same system was used to treat a bifurcation aneurysm applying a kissing stent technique [29]. Following the application of modified, balloon expandable coronary stents [30], open cell, self expandable, dedicated intracranial stents became available for the morphological reconstruction of the parent vessel across the aneurysm's orifice [30-38]. More recently, closed cell design self expandable stents were added to the therapeutic arsenal. This system is supposed to provide better conformity and opposition to the parent artery's wall and better coverage of the aneurysm neck [39-41]. In recent years, the application of stent supported aneurysm packing became a standard procedure.

Early evidence of the flow modifying effects of stents

This experience demonstrated, that stents not only provide a possibility for coil packing of broad neck aneurysms, but significantly improve the long term stability of aneurysm treatment even in the case of lower packing density [30,36]. In addition, several aneurysms have been found to thrombose spontaneously after stent placement alone. Lylik found 5 small aneurysms among 72 cases [37] and Fiorella published another five dissecting aneurysms thrombosing without coil packing [36]. These results confirmed, that besides of the mechanical support of anatomical parent vessel reconstruction, stents either have an effect on the flow within the parent artery and/or facilitate intimal growth within the parent vessel. Other publications described complete aneurysm thrombosis of giant aneurysms following double stent coverage of the orifice without coil packing [30]. This highlights the significance of stent design as proposed by Lieber and Barath earlier in experimental studies [12-14]. These observations moved the concept from geometrical to functional reconstruction of the parent artery meaning remodeling not only the anatomy, but also the flow within the parent vessel.

The new concept: restoration of laminar flow within the parent artery as the primary goal of stent implantation

The most straightforward way of reconstructing laminar flow within the parent artery is the deployment of covered stents across the aneurysm orifice. Although as of today, no dedicated intracranial stent graft is commercially available, coronary and peripheral covered stents can be and have been successfully applied in proximal sections of the circle of Willis [42]. One paper reports on the successful application of a prototype intracranial covered stent [43]. Since covered stents block completely the flow through the entrance of the aneurysm, thrombosis of the sack is immediate. However, this technique is strictly limited to vascular sections, that do not give rise to important side branches or perforators, since their occlusion will certainly follow.

To broaden the application of flow modifying devices, special stent-like designs have been developed and tested. Stents consisting of multiple layers of braided wire-mesh tubes may have a porosity that is small enough to significantly reduce flow across the aneurysm orifice but without blocking the laminar flow towards side branches. In addition, unlike most covered stents, these devices reserve the flexibility that is needed for smooth intracranial delivery. The effect of such multilayer stents (Cardiatis stent, Cardiatis, Belgium) have been studied by flow simulation (www.cardiatis.com/images/

stories/info/fluid-19%28105%29_c.wailliez_g.coussement_fpms), in silicon flow models (www.cardiatis.com/images/stories/info/etude%20luca%20in%20vitro), in animal experiments (www.cardiatis.com/images/stories/info 06-aortic-vein-pig-model) and human peripheral aneurysms [44].

The first clinical experience with dedicated flow modifying devices

Alternately, high mesh density, woven wire mesh tube flow modifying devices can now be applied to treat human side wall intracranial aneurysms. Depending on the flow conditions, size of the aneurysm and that of the neck, these devices can be applied either as a single piece, or multiple devices can be deployed within each other in a co-axial fashion. In practice, a multilayer stent is created this way on site, that is specifically tailored to the specific flow and geometry of the aneurysm to be treated.

Clinical application of one such device, the Silk stent (Balt Extrusion, Montmorency, France) has been reported (Patrick A. Brouwer: Placement of the new silk stent. Presented at the 4th Intracranial Stent Meeting, 2008, Ankara, Turkey). Utilization of another high mesh density flow modifying device, the Pipeline Embolization Device (PED, Chestnut Medical Technologies, Menlo Park, CA, USA) has been tested experimentally and used clinically. This device is made of woven wire mesh tube with pore sizes ranging from 0,65-0,43 mm in diameter. Mathematical calculations demonstrate that one such device is capable of reducing the circulation by 61% and the average kinetic energy of the flowing blood by 81%. inside the aneurysm. Electron microscopic studies demonstrate full endothelial coverage of the aneurysm ostium and patency of the origin of side branches in animal experiments using the rabbit subclavian artery. This device has been tested in a multicenter, prospective, nonrandomized study, the PITA trial enrolling 31 patients with 31 aneurysms, 28 located on the internal carotid, 1 on the middle cerebral and 2 on the vertebral arteries. Half the cases was treated with PED only, and the other half of the aneurysms received additional coil packing. There was a 100% procedural success rate, 2 patients suffered stroke as a complication, the mortality was 0%. At 6 months, 2 aneurysms had residual flow, the rest was completely occluded.

In our own experience, we treated a total of 19 aneurysms in 18 patients, 7 of them as part the PITA trial. Three aneurysms were giant, 11 large and 2 were small. By angiography, significant reduction of flow was achieved in all cases following deployment of one or more PED. Clinically, one patient developed a small visual field deficit due to a retinal branch embolization, one patient had a serious contrast reaction, one had a minor stroke due to in-stent thrombosis that resolved completely and one patient died due to rupture of a coexisting aneurysm.

Out of the 19, a total of 18 aneurysms had 6 months follow up angiography so far. All but one was completely occluded and the parent vessel remodeled. One giant aneurysm had partial filling at 6 months. All symptomatic patients except one experienced clinical improvement of their cranial nerve symptoms.

Conclusion

Restoring laminar flow across the aneurysm orifice is a viable concept for the endovascular treatment of intracranial aneurysms. Currently available technology allows for the safe and effective application of flow modifying devices for the treatment of proximal intracranial side wall aneurysms. Acknowledgments: this work was partially supported a grant from the Hungarian National Scientific and Research Fund (OTKA 73773).

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