Chairman’s Message

ARUBA is a beautiful island.

Growing up in Venezuela, I could almost see the island of Aruba from the coast of my country. At its closest point, Venezuela is separated from this alluring island by a mere 17 miles. As a child I had the opportunity to visit Aruba on several occasions. It is a strikingly beautiful country with much to offer.

As you can imagine, this is not the latest edition of your favorite travel publication, the intent of this letter is not to offer a tourism editorial, but rather to offer an opinion of the clinical trial ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations). The purpose of ARUBA, essentially, was to compare treatment versus observation of unruptured AVMs.

The National Institute of Neurological Disorders and Stroke (NINDS) halted enrollment in the trial early last year due to the greater number of detrimental events in the treatment group as compared to the natural history group (at a pre-specified level and time). The mean follow-up time for the study was only 33.3 months. The difference was most marked in the higher Spetzler-Martin grade lesions as compared with the lower grade lesions. It would be very informative to dive into statistically valid subgroup analysis. However, the data is not available in the related literature to evaluate. I suspect the number of subjects is too small for adequate subgroup analysis.

ARUBA was an extremely challenging study to perform, and I commend the investigators for beginning to shed some light on the subject. Many questions are raised from the work. What is the cause of events following treatment of the lesions? How many of the lesions were completely obliterated? Why the high rate of events in the Grade I and II patients? Many other questions have been posed in current literature.

Given that the risk of an untreated AVM is life-long, it becomes evident that, if these patients are followed over an extended period of time—such as 10 to 40 years—then, and only then, will comparisons and results be valid. The problem is this is not a practical proposition. The ARUBA study suggests—not statistically at this stage—that in expert hands, a decision for the management of a grade I or II AVM is relatively straightforward. Similar to what occurred with the carotid endarterectomy studies, the benefit of an intervention is only realized if the surgeons had a complication rate below a certain threshold. There is no reason to believe that management of AVMs would be any different.

How do we move forward? It is urgently needed for neurosurgeons to lead studies of diseases where we are best equipped to understand the decision making process. Unfortunately, we have a paucity of neurosurgeons willing and able to undertake clinical trials of this magnitude. As a specialty, we must
attract and reward neurosurgeons who—with appropriate training and desire—can tackle clinical trials in cerebrovascular neurosurgery.

Neurosurgery leadership in particular—and the discipline of neurosurgery in general—must enthusiastically embrace and support such efforts. We can no longer point to the shortcomings of the ARUBA study. Rather, we need to strategically coordinate ongoing clinical trials and develop a plan to further a new generation of clinical trialists.

If non-neurosurgeons continue to lead the trials that we, as neurosurgeons, should be leading, we will face similar shortcomings over and over again.

This is an urgent call to action.

As we face value-oriented care initiatives, strong objective data will provide the results and insights needed to formulate decisive and beneficial courses of action. For the benefit of our patients, we must become more engaged with studies of this magnitude. Being complacent will lead us down a path beneficial to no one.

ARUBA—as with the strikingly beautiful country so near to my homeland—has much to offer as a learning experience. We must develop a strategy and support it as fully as possible. The benefits of action are substantial, the failings of complacency are tragic.

Robert M. Friedlander MD, MA

SECRETARY’S MESSAGE

The AANS/CNS Section on Cerebrovascular Surgery is proud to continue our efforts to be the neurosurgical voice in the rapidly evolving development and delivery of open surgical and endovascular management of cerebrovascular disease. Our primary goal has been to advocate for cerebrovascular patients and specialists as a collective voice of roughly 500 members and 1400 resident members guided by our executive council.

We look forward with great excitement to our annual meeting February 10-11, 2014 in San Diego, CA. The AANS/CNS Joint Cerebrovascular Section/ 4th Society of NeuroInterventional Surgery (SNIS) International Endovascular Stroke Conference is also fortunate to be partnering with the Society of Brazilian Neurosurgery. We trust that our continued collaboration with the SNIS will continue to improve our educational offering as well as strengthening our united voice for the future of
neurovascular care. Co-Chairs Nicholas Bambakidis and Michael Kelly have put together a fantastic program that is comprehensive, innovative, and thought provoking.

Our Executive Council will be meeting once again in San Diego to continue our work on policy development, education, research, and collaboration with numerous organizations and specialists focused on cerebrovascular disease. Our most recent collaborative effort is a formal response to the recent release of the preliminary results of the ARUBA Trial (A Randomised trial of Unruptured Brain Arteriovenous malformations) recently published in Lancet. Several criticisms of study design, implementation and interpretation are discussed in the effort spearheaded by Nicholas Bambikidis, and we look forward to the publication of this response which will represent a collaborative effort of the Joint CV Section, SNIS, and likely our colleagues from Neurology. Additional important projects include coding changes and insurance coverage issues supervised by Henry Woo, the N2QOD database project directed by J Mocco.

Drs. Bendok and Siddiqui continue their work on the development of a Cerebrovascular Subspecialty Module for the Maintenance of Certification Exam of the American Board of Neurological Surgery. This will also result in an updated Self-Assessment in Neurological Surgery (SANS) Exam and possibly a written manuscript as a study guide.

We also look forward to our next annual Endovascular Practicum, offering neurosurgical residents and fellows the unique opportunity to interact directly with neuroendovascular faculty and industry with both didactic and "hand-on" training with the latest technology. The courses have been successful beyond expectations and plans are in place to continue and expand the opportunity this year under the guidance of J Mocco and Adam Arthur.

Other exciting new opportunities include the development of a Clinical Trials Advisory Committee to aid our members in the development, approval, and implementation of new clinical trials drawing from the experience of our successful clinician researchers, headed by Robert Friedlander and Bob Carter. Additionally, we announce the appointment of our first International Liaison to the CV Section, Dr. Mika Niemela an academic open cerebrovascular surgeon at the University of Helsinki, Finland. Dr. Niemela will keep us informed of the educational and collaborative opportunities outside North America, and plans are already in the works for a joint venture with the ESMINT (The European Society of Minimally Invasive Neurological Therapy) in Nice, France September 4-6, 2014. Our website: http://www.cvsection.org/ continues progress towards a completely new design under the direction of Greg Zipfel. We are in the final stages of this revitalization process.

The CV Section is a vital, dynamic, progressive organization committed to adapting to the changes in the treatment of patients with cerebrovascular disease. We encourage all neurosurgeons and cerebrovascular practitioners to become involved in our educational, research and advocacy activities. It is only through the efforts of dedicated individuals that we will continue to provide these important opportunities.

Sean D. Lavine, M.D.
TREASURER'S MESSAGE

I am happy to report that the Joint Cerebrovascular Section continues to be in excellent financial standing. The JCVS/SNIS Joint Annual Meeting in Honolulu, Hawaii was a tremendous success, and our upcoming JCVS/SNIS Joint Annual Meeting in San Diego, CA is shaping up to be equally outstanding. Our net assets continue to show significant growth due to the strength of our long-term investment pool. We have already funded the Robert Dempsey Resident Award in Cerebrovascular Research, the Brain Aneurysm Foundation Christopher C. Getch Chair of Research sponsored by the JCVS, and the DePuy Synthes Cerebrovascular Research award for 2014 through generous corporate sponsorship, and have begun to develop funds for these awards for 2015. A special thanks goes to Ray Turner, MD and Mustafa Baskaya, MD for their critical roles in these fundraising efforts. As in previous years, the JCVS plans to contribute $10,000 to the Washington committee and $20,000 to the AANS NREF in 2014.

Greg Zipfel, MD

AANS/CNSJoint Cerebrovascular Section
Annual Meeting –

“Adaptive Ingenuity”

and the 4th SNIS International
Endovascular Stroke Conference (IESC)

International Partner –

Society of Brazilian Neurosurgery

February 10-11, 2014
MEETING UPDATES

CV Section Annual Meeting

Nicholas C. Bambakidis, MD *Annual Meeting Chairperson*
Jay Mocco, MD *Annual Meeting Co-Chair*

The CV Section Annual Meeting, “Adaptive Ingenuity”, is shaping up to be an outstanding event for our members. It is being held again in conjunction with the 4th SNIS International Endovascular Stroke Conference on February 10-11, 2014 in San Diego, CA. Located at the Hard Rock Hotel directly across from the San Diego Convention Center, the Annual Meeting again immediately precedes the International Stroke Conference (Feb 12 – 14). The Abstract Center opened August 18, and in addition to multiple didactic and abstract sessions the meeting includes two debate sessions and a session on complication avoidance and management. The Society of Brazilian Neurosurgery is joining us as our international partners for this outstanding program, which features Chris Ogilvy, MD, as the Luessenhop Lecturer. Please join us for the premier educational event of the Cerebrovascular Section in San Diego.

Members of the Scientific Program Committee
Ricardo Hanel, MD
Peter Nakaji, MD
Adam Arthur, MD
Michael Kelly, MD - Scientific Program Chairperson, 4th SNIS International Endovascular Stroke Conference

*Christopher Ogilvy MD, 2014 Luessenhop Lecturer*
CV Section Agenda at AANS Annual Meeting

J. Mocco MD, MS and Peter Nakaji MD

The CV Section has an exciting agenda planned at the upcoming AANS Annual Meeting in San Francisco this April 5-9. The theme is “Expanding Neurosurgery”, and the program has shaped up to be a fantastic one. Dr. Juha Hernesiemi will be giving the Donaghy Lecture, with an introduction by our Section President, Dr. Friedlander. Dr. Felipe Albuquerque will provide an interesting discussion on complication management – and how to get out of trouble when a complication occurs. In the second session, Dr. Adam Arthur will bring us up to date on how simulation is changing the face of open vascular surgery training, and we will enjoy a spirited debate on the best methods for AVM management between, Dr. Michael Lawton and Dr. Jacques Moret. Finally, we should not forget that throughout this outstanding selection of talks and debates, there will be ground breaking research presentations on new discoveries in cerebrovascular disease. We are extremely proud to be able to share this truly outstanding program with our membership.

Dr. Juha Hernesiemi, 2014 Donaghy Lecture
Technology Update: Flow Diverters

by Andrew Ducruet MD

Flow diversion technologies are rapidly changing the face of intracranial aneurysm treatment. Since the approval of the Pipeline Embolization Device™ (PED), a significant proportion of aneurysms in the United States are being treated with flow diverters. While numerous empiric reports as well as published case series attest to the remarkable efficacy of this device, deployment of the PED may be complicated by tortuous vascular anatomy. Additionally, device visualization can be difficult at times, particularly along the skull base. Furthermore, unlike many intracranial stents, the PED cannot be re-sheathed and must instead be removed and discarded if the operator is not satisfied with the position of a partially-deployed device. A growing appreciation of these and other limitations has informed the design of new flow diverters. For instance, a refined version of the PED, which allows for the device to be re-sheathed, is anticipated. The next generation of flow diversion devices is also on the horizon, with two such devices presently undergoing prospective evaluation in the US after obtaining CE approval for use in Europe.

First, the Surpass™ flow diverter (Stryker Neurovascular, Fremont, CA) is an investigational flow diverting device that is not currently available for sale in the United States. The Surpass™ device is designed to maintain high pore density coverage across a range of device sizes. The design of Surpass™ incorporates an increasing number of wires in the larger devices, ranging from 48 wires in the 2.5mm device to 96 wires for the 5mm device. In this way, Surpass™ addresses one of the limitations of existing flow diversion devices; that is, the variability in pore size that occurs when flow diverting devices are placed in vessels of different size. A single device may therefore be used rather than multiple telescoping devices, which theoretically may increase the risk of side branch occlusion. Surpass™ also incorporates 12 platinum wires in its mesh to increase visibility. These features are designed to facilitate both the ease of deployment, and the efficacy of the device. Surpass™ is currently under evaluation at several centers both in the U.S. and abroad [The Surpass™ Intracranial Aneurysm Embolization System Pivotal trial to treat Large or Giant Wide Neck Aneurysms (NCT01716117)].

The initial clinical experience using Surpass™ in the treatment of 37 patients harboring 49 aneurysms was recently reported [1]. Thirty-six patients were treated with a single device, and all devices were successfully delivered. Thirty-five aneurysms were of the side-wall variety whose necks were completely covered, whereas 14 bifurcation aneurysms were only partially covered by the device. Dual anti-platelet medications were maintained for 3-6 months. The authors report no major peri-procedural morbidity or mortality in this series. During a 6 month follow-up, 10.4% of patients experienced a transient neurological deficit and a single patient (3%) developed a small stroke associated with a persistent neurological deficit. At 6 months, 29 of 31 aneurysms with complete coverage of the neck were completely occluded (94%), whereas only 5 of 10 bifurcation aneurysms were occluded. These results attest to the risk of neurological deficit associated with placement of flow diverters, as well as to the fact that complete neck coverage is required to achieve consistent aneurysm occlusion.

A second device currently under investigation (not available for sale in the US) is the Flow Re-Direction Endoluminal Device (FRED™) (Microvention, Tustin, CA). FRED™ is a self-expanding nickel/titanium, compliant closed-cell device with a dual working mid-section layer. This dual-layer construction differs from prior flow
diversion devices and is designed to facilitate device expansion and wall apposition. Additionally, FRED™ can be re-sheathed following 80% deployment. The pivotal trial of FRED™ (NCT01801007) is underway at 16 United States centers.

Two recent case series report the use of FRED™ for the treatment of intracranial aneurysms[2, 3]. These studies included a total of 19 patients with 22 aneurysms, 21 of which were in the anterior circulation. A single device was used in each case, and no peri-procedural complications were reported. All aneurysms except one were in the anterior circulation. Dual antiplatelet medications were used in all cases. All 6 cases with available angiographic follow-up demonstrated complete aneurysm occlusion at 3 months. In one patient both the aneurysm and parent artery had thrombosed, but the patient remained asymptomatic. In this case, the distal tines were noted to be constrained, which may have contributed to this episode of device thrombosis. This remains the only report of complications associated with placement of this device.

The flow diversion landscape continues to evolve at a rapid pace. The development of new technologies as well as the refinement of existing devices informed by an ever expanding clinical experience promises to facilitate the safe application of flow diversion techniques.

TECHNICAL FORUM: BLISTER ANEURYSMS, A PERPETUAL DILEMMA
BY KETAN R. BULSARA MD

The seemingly simple appearance of a blister aneurysm on an angiogram can hide the fact that this is probably one of the most treacherous lesions we face as cerebrovascular neurosurgeons. Many creative ways to treat and optimize patient outcomes in the setting of the potential devastation caused by these lesions have been utilized. They range from direct clipping, parent vessel occlusion with or without bypass, self-expanding stent placement with or without coils, and more recently flow diversion. In the setting of subarachnoid hemorrhage, there are differing opinions on optimal management of these lesions.

For the purpose of this technical forum, three perspectives are presented. The senior authors are Dr. Pascal Jabbour from Thomas Jefferson University, Dr. Ricardo Hanel from Mayo Clinic, Jacksonville Florida, and Dr. E. Sander Connolly from Columbia University, New York.

Management of Blister-like Aneurysms
Mario Zanaty MD, Pascal Jabbour MD

INTRODUCTION
Blood blister-like aneurysms (BAs) are lesions from non-branching sites that can be found within the intracranial circulation at any location, but the terminal internal carotid artery (ICA) remains by far the most common one [1-5]. BAs are uncommon and account for 1% of all intracranial aneurysms [6] and 0.5-6.5% of ICA aneurysms [7-9]. They pose a challenge to treatment because of their morphology and small size. BAs are associated with higher risk of rebleeding, relapse, and perioperative complications [6, 10, 11]. No consensus has been made on the management of BAs.

MANAGEMENT

Diagnosis and clinical presentation
BAs are present more commonly in younger patients when compared to saccular aneurysms [11, 12]. They affect females more frequently and have a right-side predominance [11, 12]. Given their small size and particular morphology, BAs are hard to diagnose on CT angiogram (CTA) and even on Digital Subtraction Angiography (DSA) [5, 13]. In a recent study, 50% (6/12) of BAs that presented with rupture were missed on CTA and 25% (3/12) were missed even on the first DSA [13]. Multiple projections are therefore needed to
explore their presence. After their rupture, BAs might rapidly expand in volume, progress to saccular shape, and end up having high rebleeding risk\cite{13,14}.

**General principles of management**

Treatment of BAs can be surgical or endovascular. Timing between ictus and treatment depends on institutional preferences; while some prefer to wait and monitor for hydrocephalus and vasospasms, others prefer immediate treatment to prevent the risk of rebleeding. The characteristics that render the treatment complex and threatening are the friability of the vessel wall, the small size of the aneurysm, and the absence of a neck\cite{7,15,16}. Gonzalez and Colleagues\cite{13}, in their systematic review of patients who underwent endovascular or surgical treatment for BAs, reported an initial treatment failure rate of 28%, a mortality rate of 19%, and a morbidity rate of 17%. Even more, 82% of the patients received multiple treatments. Perioperative complications occurred in 24.5% of the cases. The most frequently encountered complications were rupture and ischemic events. These numbers reflects the gravity of treating BAs.

**Surgical management**

Clipping is the most common surgical procedure and is usually offered first-line when surgical treatment is considered. It has a failure rate of approximately 21% (Table 1)\cite{13}. Surgical clipping for BAs differ from that of saccular aneurysms in few specific aspects. The most important differences are: early brain relaxation before exposing the proximal ICA, exposure of the medial part in contrast to the lateral part of the supraclinoidal ICA, and parallel clipping to incorporate normal arterial wall as opposed to perpendicular clipping for saccular aneurysm\cite{15}. Parallel clipping creates a stenosis with complete exclusion of the aneurysm. The parent vessel should be assessed with intra operative angiogram to detect any major stenosis\cite{15}.

Other surgical options are: surgical trapping with or without bypass and surgical wrapping. In a systemic review of 268 surgically treated patients, the overall mortality and morbidity rates were 14% and 18% respectively (Table 1)\cite{13}.

Surgical management is usually indicated for patients with lesions difficult to catheterize, such as lesions circumscribing the artery, and for patients who failed endovascular treatment. Failure is usually defined in the literature as regrowth, rebleeding or inability to secure the lesion. Finally, some authors prefer surgical treatment as first-line therapy, especially if immediate vessel reconstruction is of concern\cite{13,15,16}.

**Endovascular management**

Traditionally, stent assisted coiling (SAC) was the modality of choice, but recently flow-diversion (FD) is gaining more grounds. Other treatment options are: coiling, deconstructive procedures, and telescoping stenting\cite{13}. Conventional coiling is hazardous given the absent or malformed neck\cite{15,16} and with the introduction of newer modalities, has become ineffectual\cite{14}. In a systemic review of 147 endovascular procedures, first treatment failed in 46% of patients (Table 1). However the morbidity and mortality rates were relatively low (3.4% and 11.5% respectively; Table 1). Of the endovascular techniques, coiling had the highest combined morbidity-mortality rate, and flow-diversion along with
PAO had the lowest one. However, given the small number of patients and the lack of long-term follow-up, the results cannot be generalized.

PAO offers the advantage of low complication rate. It is usually indicated when the aneurysm access cannot be obtained. Nevertheless, sacrificing side branches is not always feasible. Even more, occlusion of a large vessel after a SAH can be devastating if vasospasm occurs. The resultant cerebral ischemia would lead to a worst outcome [15, 17]. More so, PAO might hinder the treatment of the vasospasm. As previously discussed, BAs have a higher risk of intraoperative rupture [14] due to their friable nature. The use of FD stent or conventional telescoping stents offers the advantage of avoiding intrasaccular catheterization. In all of the studies, one or two flow-diverter devices (FDDs) were used per aneurysm to achieve complete occlusion. Self-expandable telescoping stents have also been used with good neurological outcome and complete aneurysm occlusion [18, 19]. Overlapping self-expanding stents can induce thrombosis and promote parent artery remodeling [20]. They are particularly useful when there is a need for vessel wall stabilization.

However, stenting in the acute phase is not without risks. It poses the problem of dual antiplatelet use, which can be devastating in case of rupture. It also increases the risk of complication and retreatment [21]. Therefore, the risk of hemorrhage has to be weighed against the risk of thromboembolic complication. Early endovascular treatment is gaining more grounds and endovascular management is now the first line treatment in many institutions [13].

CONCLUSION

The need for multimodality treatments, the high morbidity and mortality rate, and the absence of guidelines highlight the complexity of this disease. In conclusion, it seems that endovascular treatment has a lower morbidity and mortality rates, while surgical treatment is more successful at securing the lesion from the first attempt. Larger multicenter trials are needed for further investigation.

REFERENCE


Table 1. Surgical and endovascular treatment complications and indications

<table>
<thead>
<tr>
<th>Method</th>
<th>Morbidity rate</th>
<th>Mortality rate</th>
<th>Failure rate</th>
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<td>- Failure of endovascular management</td>
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<td>- Catheterization difficulties</td>
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<td>- Parent Artery Occlusion if problem with aneurysm catheterization.</td>
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<td>- Overall health status contraindicates surgery</td>
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Endovascular Treatment of Ruptured Carotid Blister Aneurysm

Jang W. Yoon, MD, MS, Ricardo A. Hanel, MD, PhD

Carotid blister aneurysms are unstable and fragile lesions arising from the dorsomedial wall of the non-branching supraclinoid artery. They typically arise from the supraclinoid segment of the internal carotid artery; however, they can also rarely originate from anterior communicating artery and basilar artery. Often described as an entity of pseudoaneurysm, characteristic friable wall and wide neck-to-dome ratio often makes open surgical and endovascular treatment of these aneurysms extremely challenging. Histologically, these aneurysms lack usual internal elastic lamina and media and are only covered by thin fibrous tissue and adventitia. The rate of intraoperative rupture during open clipping and wrapping of blister aneurysms is reported to be as high as 50%.1,2 Recent introduction of novel endovascular devices has provided neurosurgeons and neuro-interventionalist with new tools in their armamentarium. Although early experiences with these devices are promising, long-term clinical outcomes and exact post-operative management are yet to be defined.

Endovascular treatment of blister aneurysms with primary coiling alone can be problematic for several reasons. Due to the unique characteristics of the lesion wall and typical configuration of small size with unfavorable neck-to-dome ratio, primary or balloon assisted coiling of these lesions is not recommended, leading to an elevated incidence of intraoperative rupture. In addition, there are reports of aneurysmal wall perforation by microcatheters and coils during their deployment. Endovascular parent artery occlusion had been utilized as a definitive treatment for blister aneurysms, however this may not be a feasible treatment strategy in patients who do not have adequate collateral flow or have critical arterial branches proximal to the aneurysm.
Several endoluminal devices have been proposed for the treatment of intracranial aneurysms. The Neuroform stent (Stryker/Boston Scientific, Kalamazoo, MI, USA) is an endoluminal device used as an adjunct to coil embolization, not to induce primary closure of the aneurysm. Based on computational fluid dynamics (CFD) analysis of saccular and blister aneurysm models, Tanemura et al. demonstrated that the placement of EnterpriseTM VRD (Codman & Shurleff, Inc., Raynham, Massachusetts, USA) induced significant hemodynamic changes that lead to stagnant and disturbed blood flow. One series reported the ability of the Neuroform device to occlude small aneurysms without coils, but the ability of the Neuroform to treat other types of aneurysms without adjunctive coils is unknown. The JoStent (Abbott Vascular) is a covered stent and has been used to treat proximal intracranial aneurysms with excellent results. There have been several attempts at treating blister aneurysms with stents or stents with coils showing some success of aneurysm obliteration at follow-up. The overlapping stents at the aneurysm neck, or stent-in-stent approach, has also been reported with or without coiling with the rationale of creating better flow diversion than with a single stent. In fact, overlapping stents markedly decrease the flow into these aneurysms as frequently demonstrated on angiography. Unfortunately, this treatment alone is effective in only 50% of cases (three out of six patients did not need further treatment or showed aneurysm regrowth at intermediate follow-up). Lee et al. presented nine patients treated with endovascular reconstruction, including stent-assisted coil embolization and stent-in-stent technique for blister lesions, with good outcome in only 30% of patients.

The pipeline embolization device (PED) (Covidien, Irvine, CA) is a new and novel device that is a self-expanding, porous, endoluminal device that diverts the pulsatile flow into the aneurysm which causes stasis, thrombosis, and regression of the aneurysm, while still allowing the flow within the parent artery. Since FDA approval in the United States (April, 2011- FDA labeled for unruptured aneurysms greater than 10mm on the carotid artery, petrous to ophthalmic segment), the use of PED has significantly increased. Early results from the use of PEDs for the treatment of aneurysms with challenging morphologies have been promising. PED is still far from being a perfect tool and is not without some major drawbacks. Firstly, the aneurysm is not obliterated immediately unlike coiling or surgical clipping. However, the clinical significance of incomplete obliteration of blister aneurysm seen on follow-up angiography is still to be determined. Secondly, there is need for dual antiplatelet therapy during post-operative period to prevent stent thrombosis and distal thromboembolic complications related to intraluminal metal exposure. There is, however, neither consensus nor the scientific evidence for the use of specific type, initiation and duration of anti-platelet therapy or the ideal extent of platelet inhibition. This highlights the challenges of managing patients with PED. Despite the risk of bleeding, the patients with PED must be placed on dual antiplatelet regimen during peri-operative period. The length of dual antiplatelet agent utilization remains a controversial topic and warrants further clinical investigation.

The key to successful treatment of blister aneurysms with flow diverter lies with the peri-operative management of dual anti-platelet therapy. Currently, the most commonly used dual anti-platelet therapies are aspirin and a P2Y12 receptor antagonist such as P2Y12 receptor antagonist such as clopidogrel, ticagrelor or prasugrel. These agents are absolute necessity in patients who receive PED to inhibit the platelet aggregation on the exposed metal strut of the flow diverter. Without proper inhibition of platelet function, platelet plugs may form and impede normal laminar flow that lead to turbulent flow.
within parent artery, which can eventually cause thrombosis or distal thromboembolism. Our protocol for dual antiplatelet regimen for stenting and flow diverters is PAU <550-, PRU 30-210. When dealing with ruptured aneurysms, we typically have patients loaded on dual antiplatelet (Aspirin 650mg and Ticagrelor 180mg) once decision is made for intervention. Almandoz et al. recently reported PRU < 60 was an independent risk factor for all hemorrhagic event whereas PRU > 240 was for all thromboembolic events in patients treated with PED. This highlights the challenges of managing patients with PED. There is need to better characterize dual antiplatelet therapy during post-operative period in order to optimize clinical outcomes in this patient population. Yoon et al(16) recently presented promising results on a multicentric experience of 11 patients treated with PED for ruptured carotid blister aneurysms. In this series, although perioperative complications occurred, 10/11 patients had mRS 2 or better at 30 days with no aneurysmal rebleeding. 9 of 10 patients had complete aneurysm occlusion at follow up. (Figue 1)

There are several other flow-diverters such as SILK (BALT, Inc., Paris, France) and Surpass (Stryker Neurovascular, Fremont, CA) with which there have not been wide spread of use for the treatment of blister aneurysms. The main challenges remain the same for all endoluminal device; achieving an adequate platelet inhibition without causing hemorrhagic complications.

In conclusion, the endovascular treatment options for blister aneurysms have been expanded significantly with introduction of flow diverters with many challenges still remaining to be solved. Prospective data is needed to better assess results of older and newer treatment modalities.


Figure 1: 53 year-old female presented with subarachnoid hemorrhage, found to have a right carotid blister aneurysm (A), treated with PED placement with no complication; with complete occlusion at 6-month follow up angiogram (B)
Technical Forum: Ruptured Blister Aneurysm
Management Strategies of Ruptured Blister Aneurysms

Jason A. Ellis, Philip M. Meyers, E. Sander Connolly Jr

Introduction
Cerebral blood blister-like aneurysms or simply blister aneurysms have traditionally been defined as thin-walled, broad based bulges from non-branching sites of the supraclinoid internal carotid artery (ICA) (Figure 1). In contrast to saccular aneurysms, they are typically very small, friable, and have a poorly defined neck. Initially described by Sundt and Murphey in 1969 as a “small sessile aneurysm on the dorsal aspect of the carotid artery [1]”, it has since been recognized that blister aneurysms may be found on all facets of the ICA as well as on other cerebral vessels including the anterior communicating, middle cerebral, posterior communicating, and posterior circulation arteries [2]. Nonetheless, the anterior (dorsal) wall of the ICA or, more precisely, its antero-medial wall appears to be the predominant site of occurrence [3].

Blister aneurysms represent 0.3-1% of intracranial aneurysms and 0.9-6.5% of ICA aneurysms [2, 4]. The vast majority of these aneurysms present with subarachnoid hemorrhage (SAH) and are estimated to represent 0.5-2% of all ruptured aneurysms [4]. Ruptured blister aneurysms are characteristically unstable, presenting many diagnostic and therapeutic challenges owing to their small size and thin walls. They are easily missed on initial imaging studies, frequently rebleed, and have historically been associated with much higher rates of morbidity and mortality than saccular aneurysms. The optimal treatment strategy for these aneurysms has also not yet been defined. The absence of a well-defined neck as well as its friable walls renders both direct clipping and endovascular coiling difficult or impossible in many cases. Consequently, a number of alternative treatment strategies including clip-wrapping, trapping, stent-assisted coiling, and flow diversion have been advocated. In this paper we will briefly review the pathophysiology, the diagnostic evaluation, and a number of therapeutic strategies utilized in the management of these difficult aneurysms.

Pathophysiology
Hemodynamic stress and atherosclerosis are thought to be the main contributors to the formation of blister aneurysms. As blister aneurysms are found at non-branching sites on the parent artery it is not surprising that they are found in regions of low wall shear magnitude. Rather, the hemodynamic parameter of wall shear gradient appears to be high in areas of blister aneurysm development [2, 5]. Histologically there is a defect in the wall of the parent artery where both the internal elastic lamina and media have disappeared [6, 7]. The defect in the parent artery is merely covered by a thin layer of fibrinous tissue and adventitia. According to the classification of Frosen et al. blister aneurysms correspond to a D-type histology with an extremely thin, thrombosis-lined hypocellular wall [8, 9]. The presence of a focal wall defect in blister aneurysms have led some to categorize them as pseudoaneurysms and to postulate subadventitial dissection as an inciting event [2].
Diagnostic Evaluation
A recent systematic review of the literature found that 99% of reported blister aneurysms of the ICA presented with subarachnoid hemorrhage (SAH) [4]. Intracerebral hemorrhage (ICH) and headache without SAH accounted for only 1% of presentations. Non-invasive vascular imaging with CT angiography (CTA) is typically obtained when there is initial suspicion for aneurysmal SAH. Few studies have specifically evaluated the utility of CTA in the diagnosis of blister aneurysms. A small series of six patients found that only 67% of ICA blister aneurysms could be identified prospectively on CTA and concluded that catheter cerebral angiography should be utilized when CTA is unrevealing [10]. Interestingly, Andaluz et al. found initial catheter cerebral angiography to be diagnostic in only 20% of their series of 5 patients with anterior communicating blister aneurysms [9]. Thus, early follow-up angiography may be more important than the initial technique as blister aneurysms are unstable, often exhibiting rapid expansion and configuration change, sometimes taking on a saccular shape on repeat imaging [3, 11].

Treatment Options
The unstable nature of blister aneurysms makes them treacherous lesions to treat either by open microsurgical techniques or via an endovascular route. Blister aneurysms frequently rupture during initial dissection even as meticulous microsurgical techniques are employed. Alternatively, the thin walls render many blister aneurysms incapable of supporting even the softest coils. Thus, in addition to standard clipping and coiling, a number of alternative therapeutic options have been developed to obliterate blister aneurysms. A recent review by Gonzalez et al. indicates that nearly 30% of patients require more than one therapeutic approach to definitively treat their blister aneurysm [4]. Needless-to-say the optimal treatment strategy for these aneurysms is unclear and will depend on the expertise of the treating surgeon or interventionalist.

Direct clipping
Direct microsurgical clipping of blister aneurysms can be accomplished in many cases. Obtaining proximal and distal control with temporary clipping is critical for safely manipulating and subsequently clipping these aneurysms. Consideration should be given to obtaining initial proximal control of the cervical ICA as blister aneurysms often rupture early during dissection. Subpial aneurysm dissection may also be prudent for those stuck to the frontal lobe. Since these aneurysms do not have a well-defined neck, the surgical technique involves parallel clipping which incorporates the aneurysm and a portion of the parent vessel wall into the clip blades (Figure 2) [12]. In some cases the clip blades will be unable to occlude the aneurysm without either causing significant stenosis of the parent vessel or risk slippage by not incorporating sufficient normal wall. The technique of cotton-clipping as popularized by Barrow and Spetzler may be useful in these scenarios [12, 13].

Clip-wrapping
Clip-wrapping involves circumferentially wrapping the diseased parent artery segment with material such as Gore-Tex followed by securing the wrap by cinching it with a clip. Alternatively, an appropriately sized Sundt clip graft may be used to achieve a similar construct [1, 14]. Obviously this technique should only be used on a segment of parent vessel without branches or perforators as they will likely be occluded by the cinched wrap. Of note, wrapping without clipping has been used in the past
however it provides no useful protection against rebleeding and is associated with high mortality rates [3, 15].

**Trapping**

Aneurysm trapping may be accomplished either microsurgically or endovascularly. Microsurgical trapping may be favored in instances where precise clip placement is necessary to assure uninterrupted flow within the ophthalmic, posterior communicating, and anterior choroidal arteries. Regardless of the method chosen catheter angiography it is essential for making an assessment of the collateral circulation and the completeness of the circle of Willis. Adequate cross-filling of the ipsilateral middle cerebral artery (MCA) and anterior cerebral artery (ACA) through the anterior and/or posterior communicating arteries should be confirmed. Despite such an assessment, ipsilateral ischemia is still possible [16] and consideration should be given to EC-IC bypass prior to trapping [17, 18]. Balloon test occlusion (BTO) should be considered when deciding whether an EC-IC bypass is necessary however it may be impossible in the setting of poor grade subarachnoid hemorrhage.

**Coiling**

Although the literature contains many reports of conventional or balloon-assisted coiling of blister aneurysms, this is not thought to be a durable or effective treatment for this class of aneurysms. High rates of rebleeding and recurrence are seen after coiling blister aneurysms [2, 7, 19, 20]. Furthermore, the procedure is not technically feasible in many cases due to the small size and wall fragility of these aneurysms. Stent-assisted coiling increases the technical success rate for placing coils but is also associated with relatively high rates of rebleeding and regrowth (Figure 3) [2, 7]. The need for dual antiplatelet therapy with aspirin and clopidogrel also makes this a less attractive strategy.

**Flow diversion**

Early attempts at endovascular flow diversion for ruptured blister aneurysms utilized either covered cardiac stents such as the Jostent Graftmaster (Abbott) or multiple overlapping intracranial stents such as the Neuroform (Stryker) or Enterprise (Cordis) stent [4, 12, 21, 22]. More recent reports have explored the utility of the Pipeline Embolization Device (Covidien/ev3) and the SILK flow diverter (Balt Extrusion) in the treatment of blister aneurysms [23-26]. Although good clinical results can be achieved utilizing flow diversion techniques, the durability of this strategy has yet to be determined in long-term studies. The need for dual antiplatelet therapy has also led some to utilize flow diversion mainly in the subacute setting [25] or only in select cases where platelet inhibition is thought less problematic [23]. It is also notable that the rates of initial complete aneurysm occlusion after endovascular flow diversion are low and angiographic follow-up is mandatory [21, 23].

**Conclusion**

Ruptured blister aneurysms are difficult lesions to treat and are associated with high rates of morbidity and mortality. A number of microsurgical and endovascular strategies have been developed to obliterate these lesions. While there is no consensus on the optimal therapeutic approach for managing blister aneurysms, a tailored approach taking into account the specific clinical scenario as well as the expertise of the treating team seems prudent.
Figure Captions

Figure 1. **Internal carotid artery (ICA) blister aneurysm.** A broad-based aneurysm (arrow) arising from the supraclinoid segment of the ICA is demonstrated on this lateral projection angiogram (**A**). A three-dimensional rendering after rotational angiography further delineates the aneurysm morphology (**B**). Intraoperative photograph shows the thin-walled, blister-like nature of the aneurysm (**C**).

Figure 2. **Parallel clipping of ICA blister aneurysm.** This 55 year-old man presented with a Hunt-Hess grade IV subarachnoid hemorrhage (**A**). A broad-based aneurysm arising from the anterior (dorsal) wall of the supraclinoid ICA is seen on CTA (**B**). After external ventricular drain placement and pterional craniotomy, the aneurysm was directly clipped incorporating a small portion of the parent vessel wall between the clip blades (**C**).
Figure 3. Stent-assisted coiling of posterior cerebral artery (PCA) blister aneurysm. This 36 year-old man presented with a Hunt-Hess grade IV subarachnoid hemorrhage (A). A small blister aneurysm (arrow) of the P1 segment of the right PCA is demonstrated after left vertebral injection angiogram (B). Three-dimensional reconstruction shows that the aneurysm is associated with a fusiform dilatation of the P1 and proximal P2 segments suggestive of arterial dissection (C). The diseased PCA segment was stent-coiled (D) and adequate distal flow was initially seen (E). Subsequent angiographic runs demonstrated progressive thrombosis of the stent-coiled PCA segment despite systemic anti-coagulation and administration of both local and systemic ReoPro (E).

References
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