Dear Member,

In our winter newsletter from the section of vascular neurosurgery, we would like to share some interesting news and aspects with you, such as re-organizing our next section meeting in Nice, an interview with Dr. Christoph Kellner about minimal invasive surgery for intracerebral hematomas, rapid ventricular pacing during aneurysm surgery and more.

Already at the beginning of the new year we would like to announce the upcoming vascular section meeting, taking place September 7\textsuperscript{th}-9\textsuperscript{th} in Nice. For the first time, the EANS section meeting will precede the ESMINT endovascular meeting with an overlapping scientific session on Tuesday, September 8\textsuperscript{th}. Admission fee will also cover the Wednesday ESMINT joint session with the EANS section. Neurosurgeons, interested in cerebrovascular diseases, should attend and present their interesting work or simply join the discussions. It is the definite goal of the organizers to accept not only the opinion leaders, but also the next generation at the level of young faculty and residence. Moreover, neurosurgeons interested in endovascular therapy can learn at the case-oriented ESMINT meeting which continues until Friday, September 11\textsuperscript{th}.

We hope you enjoy this newsletter and find interesting information. Please feel free to write to the Editorial team, if you have any suggestions for future editions. Otherwise we wish you a happy, healthy and successful year 2020!

Sincerely,

Nils Hecht, Newsletter editorial office
Technological Developments and Featured Cases

Rapid ventricular pacing (RVP) during microsurgery of complex intracranial aneurysms
Juergen Konczalla, MD; Sepide Kashefiolasl, MD; Nina Brawanski, MD; Volker Seifert, MD.
Goethe University Hospital, Frankfurt am Main, Germany

Introduction
Microsurgical clipping and clip reconstruction of aneurysms is highly developed and well-established procedures. However, neurosurgeons see more and more complex aneurysms. Depending on aneurysm size and complexity (wide neck, calcifications, incorporation of branching vessels), the risk of procedure-related morbidity and mortality increases.\textsuperscript{1,2} However, the number of complex and/or wide neck unruptured intracranial aneurysms (UIAs) is rising and treatment remains challenging to date. Different tools and techniques have been developed over the years by neurosurgeons and can be used in complex aneurysms. One of the most effective procedure during aneurysm surgery is the intraoperative manipulation of the CBF with techniques as such as temporary clipping, rapid ventricular pacing (RVP), adenosine-induced flow arrest, suction decompression, or deep hypothermia with cardiac standstill to help microsurgical treatment. All of these tools and techniques have advantages and disadvantages. RVP for flow reduction appears to be a reasonable and safe tool for complex cases.\textsuperscript{3} An additional benefit of RVP in contrast to adenosine seems to be the control of the starting time, length and intensity of pacing and continuous brain parenchyma perfusion during pacing.\textsuperscript{3,4}

As described in detail in our previous published work\textsuperscript{5}, we present our experience using RVP in complex aneurysm surgery.
Preoperative Workup
After interdisciplinary consensus on aneurysm treatment, patients selected to undergo microsurgical clipping are screened to determine whether the use of RVP would be considered to be helpful during surgery due to aneurysm complexity, size, and/or location (e.g. wide neck or small daughter sac, calcifications etc.). All patients considered for RVP during surgery are extensively evaluated by a cardiologist prior to the procedure, including a TTE to detect abnormal wall movements, valvular heart disease, or intraventricular thrombi; especially excluding left ventricular hypertrophy and aortic stenosis. Before surgery the neuro-anesthesiologists consults with the patient and evaluates the periprocedural risk based on the cardiology workup and the general condition of the patient.

Anesthesia Procedure, Probe Placement, and RVP Testing
Patients receive preoperative oral premedication (7.5 mg of midazolam). Before anesthesia induction a peripheral intravenous access line and a radial artery catheter for continuously monitoring arterial blood pressure are placed. Additionally, to a central venous catheter (9.5-Fr diameter, 5 lumens, 20 cm long), a vascular introducer sheath with a large infusion port (Arrow Flex FEP Sheath, 6-Fr diameter, 10-cm length) is placed into the subclavian vein. Standard monitoring includes pulse oximetry, ECG, invasive blood pressure monitoring, capnography, and esophageal and bladder temperature. External defibrillation pads are placed on the chest wall. A 5-Fr balloon temporary pacing catheter (Arrow, Vascostim) is introduced through the vascular introducer in the subclavian vein into the right ventricle. Correct positioning of the pacing electrode is confirmed via continuous ECG monitoring under pacer stimulation with a low pacing threshold. Prior to pacing the patients is pre-oxygenated.

Surgical Procedure
Clip placement as well as complex clip reconstruction techniques is performed by the senior authors (JK and VS) in a standardized microsurgical procedure, opening the sylvian fissure and basal cisterns after pterional craniotomy. All procedures are conducted using intraoperative monitoring (IOM). The patients are kept normovolemic with a mean arterial pressure (MAP) of 70–100 mm Hg. Additionally, mild hypothermia (35°C) and burst suppression induced induced before aneurysm clipping. Intraoperatively, indocyanine green (ICG) video angiography is routinely used to verify aneurysm occlusion as well as parent vessel perfusion after each clip placement.35 Initially, RVP is started at a rate of 150 bpm and gradually increased to approximately 200 bpm until the effect
on blood pressure is registered. The primary goal is to “titrate” the MAP to or below 50 mm Hg, depending on the surgeon’s preference (e.g., intraaneurysmal pressure reduction). A pulsatile flow in the arterial wave form is demanded, to maintain a minimum cardiac output during the procedure.

**Pearls and Pitfalls**

RVP is a very efficient technique that facilitates clip reconstruction with a low risk for the patient. RVP works mainly by softening of the aneurysm sac, even in very large or complex aneurysms as well as in calcified aneurysms, which then significantly improves the aneurysm mobilization and allows better visualization of the aneurysm’s neck and branching vessels. Postoperative work-up up to now shows no myocardial infarction or effect on cardiac enzymes (trend to lower high-sensitive troponin t and CK-MB in the RVP cohort).

However, cardiovascular events were noted in relation to RVP only in 3 to 5% of the patients: 1 patient suffered from ventricular fibrillation while two developed atrial fibrillation, which resolved after adequate intraoperative or postoperative measures without sequelae. We suspect that some degree of hypovolemia leading to a reduction of myocardial perfusion during RVP might have contributed to the development of ventricular fibrillation in the affected patient. Second, the heart rate used for RVP might have been too high and too long in this patient. After changing our guidelines with a focus on avoidance of hypovolemia and a stepwise increase of the pacing velocity until a sufficient effect was noted, we did not observe a similar event. Furthermore, we limited the RVP duration to 60 sec, which can be repeated after a short pause for heart revascularization.

**Featured Case No.1: Large 15mm paraclinoid ICA aneurysm.**

For this large paraclinoid aneurysm after pterional craniotomy and basal opening the aneurysm can clearly be identified. We performed an exclusively intradural exposure with optic nerve unroofing and tailored clinoidectomy using a drill as previously described. Before RVP the optic nerve was leaf-thin and the aneurysm was hardly compressible. During RVP the optic nerve expands immediately and the aneurysm sac was soft. Therefore, the first clip was put on the aneurysm and a residual neck was clipped out using a second clip.

As shown in the picture-in-picture (PIP) only a small wave (resulting in a MAP of 44mmHg) can be detected. Immediately after terminating RVP (108) a
'classic' arterial pulse wave can be detected. Only one episode of RVP was required (70 seconds; heart rate 190 bpm, MAP about 40-50 mm Hg) to treat the aneurysm successfully.

Featured Case No.2: Re-perfusion of a ruptured carotid bifurcation aneurysm after endovascular coil embolization.
The aneurysm was diagnosed following SAH and first treated endovascularly.
In the further course, a significant coil compaction and re-perfusion was noted and an interdisciplinary decision for microsurgical treatment was made. The first attempt at direct clipping without RVP showed, that the pressure inside the aneurysm was too high and the branches of the clip did not open wide enough to close around the neck. Here, RVP effectively reduced the pressure and volume within the aneurysm and residual neck for successful clip application.

References

**Vascular Section Journal Club**

**Long-term antithrombotic therapy and risk of intracranial haemorrhage from cerebral cavernous malformations: a population-based cohort study, systematic review, and meta-analysis**

Susanna M Zuurbier, Charlotte R Hickman, Christos S Tolias, Leon A Rinkel, Rebecca Leyerer, Kelly D Flemming, David Bervini, Giuseppe Lanzino, Robert J Wityk, Hans-Martin Schneble, Ulrich Sure, Rustam Al-Shahi Salman, for the Scottish Audit of Intracranial Vascular
Aim of this study was to clarify the uncertainty about withholding antithrombotic therapy (antiplatelets or anticoagulants) in patients with cavernous malformations (CM). A meta-analysis of current and previous prospective studies was planned.

**Summary of study**

**Methods:**

This is a Scottish population-based cohort study, using data from the Scottish Audit of Intracranial Vascular Malformations. Patients 16 years or older with first diagnosis of CM during 1999-2003 or 2006-10 were included. The authors compared the association between long term use of antithrombotic therapy (defined as at least 90 days after inclusion in the study, but before first outcome event or end of follow-up) and occurrence of a primary endpoint (intracranial hemorrhage (ICH) or focal neurological deficits attributable to CM) during up to 15 years of follow-up. Follow-up data was censored at surgical or radiosurgical CM treatment or at death not due to an outcome event. Multivariate cox regression analysis was used. The meta-analysis included comparative studies that reported data on ICH and person-years follow-up according to the use of antithrombotic therapy.

**Results:**

In this study, 306 patients with newly diagnosed CM were identified, of which 6 were diagnosed at autopsy and excluded. Sixty-one patients used antithrombotic therapy (10/61 [16%] used anticoagulation with or without antiplatelets) for a mean duration of 7.4±5.4 years during follow-up. The antithrombotic therapy group had significantly older patients (mean age 57 vs. 39 years), a significant higher prevalence of vascular comorbidities (hypertension, stroke or TIA, ischemic heart disease and atrial fibrillation) and significantly more frequent co-incidental diagnosis with no difference in ICH, epilepsy or neurological deficits upon presentation. There was no difference in sex, brainstem location or multiplicity of CM in both groups. The patients were followed up for a mean duration of 11.6±5 years with a total of 3634 person-years. Post-hoc sensitivity analyses revealed similar, but non-significant associations
between antithrombotic therapy and the primary outcome when antithrombotic therapy was a time-dependent co-variate, when cohort restricted to brainstem location or to ICH presentation. Sensitivity analysis according to type of antithrombotic therapy was not possible due to lack of primary outcome events in patients using anticoagulants. In a meta-analysis of 5 hospital-based cohort studies (1342 patients in total), the use of antithrombotic agents was associated with a lower risk of intracranial hemorrhage (8/253 [3%] vs. 152/1089 [14%]; incidence rate ratio 0.25, 95% CI 0.13–0.51; p<0.0001).

**Author’s conclusion**

Antithrombotic therapy is associated with a lower risk of intracranial hemorrhage or focal neurological deficit from cerebral cavernous malformations than absence of antithrombotic therapy. These findings provide reassurance about safety for clinical practice. The possibility that antithrombotic therapy might be beneficial for the prevention of intracranial hemorrhage from CMs should be investigated in a randomized controlled trial.

**Journal Club Comments**

In this paper, Zuurbier and colleagues investigated the association between antithrombotic therapy (AT) and intracranial hemorrhage and/or focal neurological deficits in adults with cerebral cavernous malformations (CCMs) in a large prospective, population-based cohort study, whose results were also reinforced by a precise meta-analysis. They did not find any evidence of a harmful association between the use of AT and intracranial hemorrhage. We also observed some cases under long-term AT therapy and never recorded bleedings or neurological worsening, in accordance with the data presented. The idea that AT may have a role in preventing rather than promoting CCMs bleeding is not totally original, but has never before been demonstrated as clearly as in these findings. Thrombus formation in dilated caverns of CCMs is supposed to trigger the inflammation cascade that leads to their growth or bleeding and also creates a link between DVA and CCM. Looking at pathogenesis, genetic alterations in three genes involved in endothelial cell-junction physiology, response to oxidative stress and apoptosis, namely CCM1, 2 and 3 respectively, have been found in familiar cases, but we are still far from completely understanding the origin and behavior of such lesions. The authors must be complimented for providing high quality statistical data that supposedly will not only change the clinical practice of many, but
also promote and justify further investigations to increase evidence that AT may positively influence the natural history of brain cavernomas through adequate randomized trials.

Mohammed Basamh, Hamburg, Germany, and Menno Germans, Zürich, Switzerland (Journal Club), and Paolo Ferroli, Milan, Italy (Comments)

Journal clubs are open to volunteer suggestions to feature the latest interesting articles in the field of neurovascular surgery and dedicated to critical discussion and short review.

Get in touch to volunteer your assistance!

Interviews

Dr. Christopher Kellner, MD, is an Assistant Professor in Neurosurgery specializing in the endovascular and minimally invasive treatment of ischemic and hemorrhagic stroke. He is Director of the Intracerebral Hemorrhage Program and Principal Investigator of the Cerebrovascular Translational Laboratory. Dr. Kellner received his undergraduate degree from Harvard University and earned his medical degree from the College of Physicians & Surgeons at Columbia University. He also completed his neurosurgery residency training at NewYork-Presbyterian/Columbia University Medical Center. He then performed his endovascular fellowship at Mount Sinai. Dr. Kellner has authored over 60 peer-reviewed publications and his research focuses on improving outcomes in endoscopic minimally invasive intracerebral hemorrhage evacuation, decreasing brain inflammation after stroke, early diagnosis of stroke, and early diagnosis of cerebral aneurysms.
1. **What are the advantages of MIS for ICH compared to standard ICH evacuation?**

   The results of STICH and STICH II showed that surgery did not improve outcomes in patients with supratentorial spontaneous intracerebral hemorrhage. However, numerous randomized clinical trials evaluating the effect of minimally invasive surgical evacuation have suggested a benefit. Advantages of minimally invasive evacuation include decreased brain disruption and improved intracavitary visibility that may result in improved evacuation percentages and improved ability to recognize and address intraoperative bleeding and therefore decrease the incidence of intraoperative and post-operative hemorrhage.

2. **What different MIS techniques exist and which one is your preferred technique? What are the main challenges compared to an open microsurgical approach?**

   There are more or less 6 MIS techniques. In order of most to least minimally invasive, they are: stereotactic catheter placement with aspiration and thrombolysis (MISTIE technique), endoscopic, surgiscopic, endoscope-assisted, and endoport-mediated. The information we have suggests that the ideal approach is one that permits early evacuation on a wide range of intracerebral hemorrhage patients. This approach therefore should be active rather than passive, as minimally invasive as possible, and able to safely address intraoperative hemorrhage. In my experience, endoscopic and surgiscopic techniques satisfy these criteria but ultimately, the safest and most effective procedure is going to be different in the hands of each operator.

3. **Did you change your practice based on the MISTIE III results and do you aim for an evacuation of less than 15cc ICH residual?**

   Yes, MISTIE III provided surgeons with a procedural target of 15cc. Most importantly, the study let us know that surgical performance is critical to outcome.
4. Are there ongoing randomized controlled trials for ICH and which important questions still need to be addressed?

To my knowledge there are four ongoing clinical trials evaluating minimally invasive strategies for ICH with others in planning or pilot stages. Active trials include the Minimally Invasive Endoscopic Surgery with Apollo or Artemis in Patients with Brain Hemorrhage (INVEST) single arm feasibility study to evaluate the safety and feasibility of minimally invasive endoscopic evacuation funded by Penumbra and run by the Neurosurgery Research Group at Mount Sinai, Minimally Invasive Neuro Evacuation Device in the Removal of Intracerebral Hemorrhage (MIND) trial funded and run by Penumbra evaluating endoscopic evacuation using the Artemis device as an adjunctive aspirator through the working channel of the endoscope, the Early Minimally Invasive Removal of Intracerebral Hemorrhage (ENRICH) trial evaluating early (within 24 hours) endoport-mediated evacuation funded by NICO using the Brainpath port and the Myriad evacuator, and the Dutch Intracerebral Hemorrhage Surgery Trial (DIST) evaluating early endoscopic evacuation using the Artemis device performed within 8 hours. The major question that remains of course is whether any or all of these minimally invasive techniques can improve long term functional outcome. Most importantly, we need level one evidence that these procedures are safe and can achieve their stated surgical goals. Additional major questions include what is the impact of clot location (thalamic, subcortical, and cortical), age, clot size, and time to evacuation on the effect of minimally invasive surgery. There is a lot of work to be done. MISTIE III was a major step forward to answering some of the important questions.

5. Do you think MIS for ICH should be also performed by interventionalists not residency trained in neurosurgery (e.g. interventional neurologists or radiologists)?

Some of the procedures falling under the umbrella of minimally invasive surgery are well-suited for the angiography suite and similar to procedures already performed by non-neurosurgeons, such as the MISTIE technique. The active evacuation procedures ranging from endoscopic evacuation to endoport-mediated procedures require skills that are learned during neurosurgical residency and therefore should
always have a neurosurgeon involved. I believe that is a universal requirement already.

6. How important do you consider intraoperative imaging in combination with MIS?

Given that we now have a surgical end of treatment volume goal and we do not yet have a tool that provides imaging for us, I feel strongly that intraoperative imaging is necessary to confirm and sometimes achieve the surgical goal. I perform these procedures in the angiography suite because of the accessibility of the suite for me at all hours and the ease of performing a conebeam CT to assess my work prior to closing.

7. How does the future of ICH treatment look like for you?

There is a lot of work to do to figure out the patient population that benefits from minimally invasive surgical evacuation and the technique that works best in different circumstances. There is strong preclinical and clinical evidence to suggest that time to evacuation is a major predictor of functional outcome and therefore I think that ultimately intracerebral hemorrhage will be treated emergently like large vessel occlusion now is. There may be different techniques for different patients. For example, we may discover that the MISTIE technique works best for thalamic hemorrhages where the tolerable brain disruption is small while endoscopic evacuation may work best for basal ganglia hemorrhages and endoport-mediated evacuation may work for lobar clots. In summary, this is a challenging, common, and neurologically devastating disease. Fortunately, we have learned a lot about what might work from past studies and now need to carry through the rigorous studies to prove it.

Jan-Karl Burkhardt conducted the interview with Christopher Kellner by email.

Don't forget to join our EANS Vascular Section Discussion Group and share your cases!
Case discussions are a great opportunity to debate and obtain second opinions for your cases in a secure and helpful group comprised of your fellow Vascular Section members. We’re currently running this facility on Medshr.

Join now!

Comments
Please do let us know if you have something for comment, or would like to comment yourself.

Upcoming Events from the Vascular Section

**EANS Microneurosurgery Hands-On Course**
A complete microvascular experience

4-8 November 2020
Cluj, Romania

Further information will be available soon [here](#)

**EANS Annual Vascular Section Meeting**
An interdisciplinary platform for those interested in the treatment of cerebrovascular diseases

7-8 September 2020
Nice, France

Further information will be available soon [here](#)

For more subspecialty events from the EANS' complete listing, please click [here](#)
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