Guidance for Cerebral Aneurysm Craniotomy and Clipping

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Overview:

Anesthetic management of cerebral aneurysms involves several facets which may not be familiar to anesthesia personnel who are not routinely managing these procedures. This guidance seeks to inform personnel regarding some of the unique aspects frequently encountered in these cases, and is specifically focused on cases at Baylor Scott and White Memorial Hospital in Temple Texas with Neurosurgeon Ethan Benardete, M.D., who has made specific requests concerning some aspects of anesthetic management. This is intended as a general advice and should not be construed as establishing a rigid protocol. This guidance is not meant to be an exhaustive review of the general management of cerebral aneurysms.

Dr. Benardete usually requests neuromonitoring to include EEG and Somatosensory Evoked Potential (SSEP), and sometimes requests Motor Evoked Potential (MEP) monitoring, depending on the location of the aneurysm and the area of the brain at risk for circulatory compromise. While this may be unfamiliar to many local practitioners, this request is consistent with modern neurosurgical management at many advanced centers, and it is incumbent on anesthesia staff to manage the anesthetic in a manner consistent with this monitoring if possible, unless there are specific patient co-morbidities or factors that make it unsafe in the judgement of the staff involved. Optimal anesthetic conditions usually involves some combination of propofol, narcotic, and limited (less than 0.5 -.7 "MAC") volatile anesthetic without neuromuscular blockade (if MEP is requested), which can introduce a hazard in patients secured in a Mayfield cranial pinning device. Note that neuromuscular blockade can be employed if only EEG and SSEP are requested.

Prior to actual clipping of the aneurysm, Dr Benardete will request induction of "burst suppression" using propofol as a cerebral protection strategy. The details of this will be described below.

Another technique that may be unfamiliar to many staff is the use of adenosine to induce temporary cardiac pause lasting 30-45 seconds. This is a technique that is not commonly used, but could be requested in situations requiring temporary circulatory pause to facilitate clipping or for emergent management of aneurysm rupture. The technique is well described in neurosurgical anesthesia literature and has been used successfully in several series of cases, and will be described in detail in following sections.

Additionally, Dr Benardete will usually be prepared to do Angiographic studies intra-operatively with access from the femoral artery, and this presents some positional challenges for the anesthesia team because he will create a sterile field at the groin which limits access to the patient for routing of

intravenous lines and monitors. He may also utilize Indocyanine Green dye intravenously for initial angiographic studies.

Pre operative Evaluation and preparation:

Patients can be broadly grouped in two major categories:

1) Those who have not suffered an acute aneurysmal rupture or bleeding episode and present for elective surgery. These elective cases will likely have no pre-operative neurologic compromise and may be admitted from home on the day of surgery.

2) Those who have had a recent aneurysmal rupture or bleeding episode. These patients may have widely variable neurologic impairment, and have a higher risk of post-operative neurological compromise and delayed cerebral ischemia, and are often in the ICU pre-operatively.

The pre-operative evaluation in either case should include a brief neurologic history and notation of immediate pre-operative neurologic status (awake/comatose/responsive/notation of focal deficits).

Due to the high prevalence of ECG abnormalities, ALL PATIENTS SHOULD HAVE A RECENT ECG! For recent Bleed, Troponin level is advised. Other cardiac workup, such as Echocardiography, might be considered if it can be done without delay, but is not routinely indicated in the absence of known cardiac disease.

ASA Classification. In general, any patient with a cerebral aneurysm would be considered to be at least ASA 3. A recent intracranial bleed would be considered an ASA 4, and a comatose patient with acute intracerebral hemorrhage and significant neurological impairment might be considered an ASA 5, depending on comorbidities and severity of hemorrhage.

IF the patient is intubated, it should be noted, and an airway evaluation should be noted, including whether the intubation was difficult. The patient and family should be counselled regarding expectations for post-op ventilation. Elective cases without prior bleeding have a high likelihood of being extubated at completion of surgery if there are no intra-operative complications. If the patient has had a recent intracranial hemorrhage, the expectation of immediate extubation is more guarded, but if the patient presented to the operating room arousable and without the need for ventilatory support, extubation may be considered. Other considerations such as obesity, obstructive sleep apnea, and difficulty of airway management and length of surgery will often determine the expectations. If the patient presents to the operating room with significant neurologic compromise and the need for airway protection, it is unlikely that immediate extubation would be prudent due to the risk of neurologic decline in the post-operative period, but there may be some cases where extubation could be considered (example – patient anesthetized for angiography preceeding day and remained intubated as a precaution and because of impending surgery, but is responsive and has normal airway and surgery was uneventful might be considered for extubation). Specific discussions between neurosurgeon and anesthesia senior staff is encouraged regarding expectations so that the patient and family can be prepared.

For inpatients, vascular access lines should be noted (i.e. "patient has two functioning PIV, #18, #20, and an arterial line left radial, etc.).

Patients should be consented for central line in the event it becomes needed.

Blood availability should be confirmed. Note that type and screen or crossmatch results must be within the time frame determined by blood bank (72 hours). If the patient had recent negativeT&S, but it has expired with no transfusion, a repeat sample should be sent to blood bank, but the case does not necessarily need to be delayed for results due to the low likelihood of needing blood before results would be available.

Placement of arterial line is optimally accomplished prior to entry into OR, but in elective patients presenting through the anesthesia pre-op area, there are many situations that might preclude that. IF the patient is very anxious, consideration of the risk of hypertension should be considered. Often, sedation should not be given due to waiting for the surgeon to do interim H&P and answer patient questions, or nursing tasks have not been completed. If conditions are unfavorable for pre-op placement, the arterial line can be deferred until the patient is in the OR, but is usually done pre-induction to facilitate timely control of blood pressure during induction. If radial arterial access cannot be obtained, Dr Benardete may be willing to place a femoral arterial access.

At least 2 reliable peripheral IV lines are recommended. A central line is not mandatory, but may be desired at the discretion of the staff, particularly if the patient will likely need intensive care post-op, or If PIVs cannot be placed. Discuss with Dr Benardete about the preferred route for a central line – an internal jugular line may be undesirable. A subclavian may be considered, or Dr Benardete may prefer to place a femoral venous line (this should be discussed with him before anesthesia places a femoral line as it may impact his planned femoral access).

Pre-induction and Induction:

It is likely that during surgery the bed will be turned with head 180 degrees away from anesthesia machine, so this should be considered when routing lines and monitors. Some anesthesia staff may elect to induce anesthesia with the bed already turned away to simplify the process, but many will prefer not to do this, particularly if there is any concern for airway difficulty.

Induction is performed with caution to maintain stable hemodynamics, particularly avoiding acute hypertension. There are no requirements specific to Dr Benardete, other than possibly avoidance of non-depolarizing neuromuscular blocking agents if MEP monitoring is anticipated (if MEP will not be done in the first hour, a judicious dose of rocuronium might be permissible).

Positioning/Pre-incision

Dr Benardete may elect to place a lumbar drain post induction. He is willing to place it himself or with his resident. It is done in the lateral position. Care should be taken to be sure it is well secured and

accessible during the case, and all involved should clearly understand how he wants drainage to be managed.

Most cases will be supine or slightly turned with a bolster under the upper body and head turned. Posterior circulation aneurysms could be done in full lateral, park bench, or prone position – be sure to discuss with surgeon or OR staff. Dr Benardete has not mentioned plans for doing cases in the sitting position, but there could be situations where this could be considered (example very obese patient that presents problems with lateral or prone position).

The head will usually be secured in the Mayfield frame. Depth of anesthesia should be considered immediately prior to pin placement and anesthesia should be prepared to treat promptly if stimulation causes hypertension. Options include bolus propofol
(most common), remifentanil, fentanyl or Sufenta, or esmolol or clevidipine (Cleviprex).

Surgeon will most likely request Keppra 500 mg. This must be ordered via EPIC, so early confirmation and ordering will facilitate.

Surgeon will likely request Decadron, Mannitol, and Lasix – the timing and dose of these can be important, so clarify doses and when he wants each given. Regarding Mannitol, either the bottled 25% solution or the 20% solution which comes in an IV bag can be used. For doses over 25 gr I prefer the 20% solution infused with an infusion pump (20 grams per 100 cc, so for example, 50 gr would be 250 ml). It should be administered through the appropriate filter into an infusing IV or central line.

A Tapscope is recommended in the event Adenosine is requested. It can also be helpful if bradycardia develops for other reasons. (Use of Adenosine is very unlikely).

IF the prep area/surgical field leaves access to the forehead for a BIS (or SEDLINE), it can be helpful as an extra monitor of anesthetic depth, but most often the forehead is prepped and/or the pin placement precludes placement of the BIS. The Neuromonitoring technician can provide some idea of EEG activity. In some cases, an appropriately deep anesthetic may result in EEG suppression with some degree of "burst suppression" (before it is requested) – this may simply reflect the anesthetic depth required, or may indicate indication to lighten anesthesia (possibly reduce Desflurane).

Anesthetic Maintenance:

There are numerous anesthetic plans that could be used, as long as they facilitate neuromonitoring. The following regimen has worked well over multiple recent cases and can serve as a general recommendation. Since Burst Suppression with Propofol will be requested, and Propofol facilitates neuromonitoring, moderate dose propofol in combination with a potent narcotic is reasonable. Volatile anesthetic (I prefer Desflurane due to rapid emergence) may be used in combination with propofol, up to about .7 "MAC" (or ~.5 MAC if MEP is monitored) as long as the combination does not result in excessively deep anesthesia which suppresses the EEG/SSEP/MEP too much. The rationale for the combination is that Desflurane reduces the total propofol administered, which can be significant over a 12 hour case, and may be more effective at preventing movement. Propofol can be increased to

provide "burst suppression" when requested. At the end of the case, the propofol can be discontinued during the last hour as Desflurane is increased as needed, and then Desflurane provides a very rapid emergence. Sevoflurane could be used instead of Desflurane, but would likely result in a slower emergence. In patients that are not expected to be extubated, Sevoflurane may provide some advantages.

The following dose ranges seem to be effective:

Propofol 50-100 ug/kg/min

Desflurane .4-.7 MAC

Sufenta .2-.4 ug/kg/<u>HOUR</u> or Remifentanil 0.1-0.5 ug/kg/<u>MINUTE</u>

Choice of narcotic is staff dependant. I prefer Sufenta for these longer cases for stability and a predictable analgesic effect at emergence, and due to my familiarity with it. Other staff prefer Remifentanil for rapid titration and complete elimination at emergence. Note that cost of Sufenta is ~ $10 for 250ug, which typically lasts for 8 hours, whereas Remifentanil is ~$50 per mg, which generally last about 1 hour, so $400 for an 8 hour case would not be unusual. Despite the cost, Remifentanil is very popular among Neuroanesthesiologists. Fentanyl could be used, but its duration becomes less predictable when used at equivalently high doses for several hours. If managed appropriately, any of these narcotic choices is reasonable.

Dr Benardete will request moderate hyperventilation to an ET CO_2 of 25 as an adjunct for ICP reduction and/or "cerebral relaxation". An ABG can be drawn at some point to check $PaCO_2$, which will likely be in the 30's (allowing for difference between ET and arterial CO_2). At the end of the case, wait until after dural closure/skull patch replacement before allowing CO_2 to gradually rise for return of spontaneous ventilation. Elevation of CO_2 before closure may result in some degree of cerebral blood volume increase, possibly making closure more difficult.

Propofol Burst Suppression:

Dr Benardete will request burst suppression as he nears the time for clipping. This is usually easily accomplished with modest doses of propofol (30-50 mg increments) and a slight increase in propofol infusion rate (Example – baseline anesthetic 70ug/kg/min propofol with .5 MAC Des, give 30 mg bolus and increase rate to 100). The Neuromonitoring Tech will report the degree of burst suppression. The target level is less than 4-6 bursts per minute, which is about one short burst per screen sweep. If activity increases, give additional propofol. If EEG is flat with very little burst activity, decrease or pause propofol until target rate of activity returns. Surgeon will want to maintain burst suppression until he has confirmed clipping and possibly angiographic evaluation. Once he no longer wants burst suppression, propofol can be decreased substantially or even turned off (unless further MEP readings are anticipated).

Adenosine Cardiac Pause:

In some situations, temporary profound bradycardia can facilitate aneurysm clipping by lowering pressure on the sac and reducing movement. The use of Adenosine to cause 30-60 seconds of profound bradycardia has been described in papers dating back to 1999. References are included at the end of this paper. It is not a commonly used strategy, but it is well known among neurosurgeons and the capability of using it is desired in select situations. It may be used during the clipping of an unruptured aneurysm to avoid placement of temporary clips on the feeding vessel, and it has also been used as an emergency technique in the event of aneurysm rupture. (see articles).

The dosage usually required to induce 30-60 seconds of bradycardia averages 0.34mg/kg/IV, or about 30 mg as a rapid bolus. Smaller dosages beginning with 3-6 mg can be used to gauge sensitivity and adjust dose (see articles attached). Placement of external pacing pads or a TAPSCOPE is recommended for rescue if spontaneous rhythm is delayed. I routinely place a TAPSCOPE after induction, confirm that it captures, and have at least 30 mg of Adenosine available in the room (but I do not open the vials). Note that if surgeon decides to use it non-emergently, I would recommend having at least 60 mg immediately available due to the likelihood of using it more than once.

Usual Clipping routine:

The "usual" case progression is as follows:

- Prep/drape both head and groin.
- Craniotomy/exposure/initial dissection toward aneurysm location under direct vision
- Introduction of Microscope, further exposure under microscope to expose aneurysm
- Request for burst suppression as time for temporary clipping nears
- Temporary clipping of feeding vessels – it is good practice to use timer and document temporary clips on/off. There may be several cycles of temporary clipping in preparation for permanent clipping
- Lowering of blood pressure may be requested. Alert Anesthesiology staff and discuss if MAP below 65 is desired.
- This may be the time period for Adenosine request. Anesthesia Sr Staff should be present if Adenosine is contemplated.
- Placement of permanent clip (or clips), followed by removal of temporary clips (flow restored).
- Blood pressure manipulation may be requested. Increased BP to evaluate flow or bleeding at higher pressure might be requested.
- Request for Indocyanine Green dye ("ICG") IV injection and evaluation of clip placement. Normal dose is 25 mg – it comes as a powder with 25 mg in vial. Reconstitute with 10cc sterile water.
- After this, he may (or may not) choose to do detailed Angiography through femoral arterial catheter. If he decides to do angiography, expect at least an hour before closure.
- When satisfied with clip placement he will request no more burst suppression. Propofol may be reduced or turned off, depending on whether more MEPs need to be done.

- If using Sufenta, it should probably be discontinued at this time. Remifentanil is continued until shortly before emergence. Desflurane is increased to maintain adequate anesthetic depth.
- After dural placement and skull flap replacement, ventilator adjustment to facilitate return of spontaneous ventilation can be initiated.

Emergency Procedures for bleeding or Aneurysmal Rupture:

Complete discussion of this topic is beyond the scope of this paper. A recent review article is available in the NeuroAnethesia Binder in Operating Room 1 and on the Anesthesia Sharepoint. The citation is:

**Controversies in the Anesthetic Management of
Intraoperative Rupture of Intracranial Aneurysm, Tomul Chowdhury et.al.,**
Anesthesiology Research and Practice
Volume 2014, Article ID 595837, 10 pages
http://dx.doi.org/10.1155/2014/595837

If rupture occurs while surgeon has gained exposure of the aneurysm and involved vessels, control is usually accomplished by temporary occlusion of involved vessels and blood loss may be minimal to moderate. If rupture/hemorrhage occurs at a point where local control by the surgeon is not possible, blood loss can be rapid, and volume resuscitation and control of hemodynamics is priority. Moderate hypotension (MAP 50-70) may be considered for brief periods. Adenosine cardiac pause may be considered.

Emergence:

Smooth emergence with minimal coughing and control of blood pressure to avoid hypertension is very important. Studies show that even brief episodes of hypertension increase risk of post-operative intracerebral bleeding. There are multiple strategies to accomplish a smooth emergence that will be chosen by Sr Staff Anesthesiologist depending on patient factors and staff preference.

- Extubation awake – advantages – less risk of airway incident such as laryngospasm or obstruction. Confirmation that patient has regained some degree of neurologic recovery prior to extubation. Disadvantage – a sudden rise in BP at the time of return of airway reflexes and responsiveness is common, and can easily get out of control resulting in hypertension. Adequate level of narcotic (titrated to pre-emergence respiratory rate of 8-12) can blunt this response.
- An antihypertensive strategy should be discussed and prepared. Options include any combination of incremental labetalol, nicardipine, esmolol, and cleviprex (if unfamiliar with Cleviprex, see note below). (Nitroglycerin can be used for rapid control for a brief period, but there are some concerns with cerebral vasodilation – Cleviprex is emerging as the preferred choice) Treatment must be pro-active, prompt and aggressive! If agitation occurs, small doses of propofol may be appropriate.
- Extubation Deep, with natural airway or oral/nasal airway. Advantages – smooth emergence with minimal coughing/hypertension. Rise in Blood pressure is usually more gradual and easier

to manage. Disadvantage – after extubation, an anesthesia provider usually must devote attention and hands to managing mask ventilation for 5-10 minutes. Less effective ventilatory assistance. More difficult to manage all the tasks associated with patient transfer while holding mask.

- Extubation Deep with LMA Exchange. This technique has gained favor among Neuroanesthesia specialists. The described technique ("Bailey maneuver" Google it if curious) is to place the LMA behind the ETT tube and then extubate. This can be cumbersome with modern LMA's (compared to the LMA Classic with smaller cuff and flexible tube) but is feasible and has the advantage that any response to airway manipulation will likely occur before the ETT is withdrawn; another option is to simply remove the ETT tube (after confirming that the patient is truly DEEPLY Anesthetized and thoroughly suctioned) and then place the LMA. After confirming a good seal and easy ventilation with the LMA, discontinue volatile anesthesia and turn up gas flow. If using Desflurane, patients are usually arousable in 5-10 minutes with a minimum of coughing and hypertension. The LMA provides a stable airway while dressings are completed and the patient is prepared for transfer off the OR table, thus there is no significant delay.

- Some words of caution for Deep Extubation – any patient feature that increases risk of airway problems, such as morbid obesity, difficult intubation, or swelling from surgical manipulation should be considered. Also consider the possibility that the patient may have suffered neurologic injury during the procedure and may not wake up, so a plan for airway support including re-intubation should be considered. If non-depolarizing neuromuscular blocking drugs were used and neostigmine was given, the use of succinylcholine in the event of airway difficulty will result in prolonged weakness (this problem can be avoided by discontinuing neuromuscular blockers at least two hours before the end of the case and verifying return of full train-of-four response so that neostigmine use is not required). BE sure the patient is truly deeply enough anesthetized so that airway reflexes are not triggered. Vigorous suctioning of the pharynx and movement of ETT should not elicit any response. If there is any indication that the patient is responsive, deepen anesthetic with lidocaine, propofol, or increased volatile anesthesia, or change strategy to awake extubation. Finally, experience with deep extubation is highly variable. If staff present are not experienced and comfortable with deep extubation, consider awake extubation instead.

- As soon as patient awakens, the surgical team will want to perform neurological checks such as having patient move extremities, follow commands etc. Rarely, a patient will fail to waken or will exhibit a neurological sign of concern that prompts surgeon to intervene. Usually an urgent CAT scan is done, but if the patient does not maintain airway, reintubation may be required.

- If emergence and awakening are uncomplicated, transfer to SICU. Blood Pressure should be controlled. Ask surgical team for BP parameters, but in general, systolic less than 130 is advised. Nicardipine and Clevidipine are probably the preferred agents.

- **Clevidipine** is an rapid acting calcium channel blocker that is rapidly metabolized by ester hydrolysis (similar to remifentanil). Its onset and duration are comparable to nitroglycerin and nitroprusside. It is rapidly becoming the preferred agent in Cerebrovascular cases because, like nicardipine, it does not adversely affect cerebrovascular volume. It is usually used as an infusion,

with a concentration of .5mg/ml, starting at 1-2 mg/hr (which would be 2-4 cc/hr). If rapid control is desired, start the infusion at higher range, and double every 90 seconds until BP begins to decline. Alternatively, it can be given in bolus doses of 0.25 mg (0.5 ml) increments every minute. Due to its potency and concentration, it is very important that doses get flushed through the IV to avoid multiple doses accumulating in the IV tubing! If BP drops too low, stop giving it and recovery occurs rapidly within a few minutes. SICU has protocols for Cleviprex use, so it can be used during transfer and recovery in SICU.

I hope this guidance is helpful. It will be revised periodically, so please provide feedback, additions, deletions, changes or comments.

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<div align="center">**QUICK NOTES**</div>

<div align="center">**CEREBRAL ANEURYSM**</div>

Room set-up:

Infusions: Propofol, Narcotic (Sufenta or Remifentanil), phenylephrine. Have a plan for where infusions will plug in – will probably need extensions on infusion lines (microbore extensions recommended)

Have available: Mannitol, Adenosine, Keppra (order from pharmacy), Anti-hypertensives (Nicardipine or Cleviprex). TAPSCOPE. Arterial line set-up (cable etc.).

Pre op:

Confirm ECG, blood availability, other critical info. Place a-line if appropriate.

Induction: Control BP carefully

Be prepared for turning bed 180 degrees, pinning, lumbar drain, routing of lines/cables, vascular access

Anesthetic:

.5 MAC Desflurane, Propofol 50-150 ug/kg/minute, Sufenta .2-.4 ug.kg/<u>hour</u>, or Remifentanil .1-.5 ug/kg/<u>minute</u>

<u>Control BP carefully</u> – usually 100-130 systolic during exposure, slightly lower as approach aneurysm – coordinate with surgeon request.

Burst Suppression:

Propofol 30-60 mg bolus and increase infusion as needed to maintain no more than 4-6 bursts per minute. Coordinate with Neuromonitoring tech.

Adenosine: (Rare, but be prepared)

Will need 6-12 vials at least! Have available, but do not draw up unless usage imminent.

"test dose" 6-12 mg to gauge response. Average effective dose for 30-60 seconds profound bradycardia is .34 mg/kg, commonly ~ 30 mg. Confirm TAPSCOPE capture before use if possible, then turn off before dosing. Expect profound bradycardia and associated hypotension. Heart rate should recover in about 30-45 seconds. If not, turn on TAPSCOPE. BP recovery may take a couple minutes and may require vasopressor (be careful).

Clipping:

Record timing of temporary clips on/off and permanent clip placement, control BP per surgeon request.

Post-clip – if requested, mix and give Indocyanine Green dye in coordination with surgeon.

Post Clipping:

Prepare for angiography if needed. Stop burst suppression when requested. Be prepared to discontinue propofol and Sufenta, and increase Desflurane during closure. Keep CO2 ET below 30 until skull closed.

Emergence:

Decide on Emergence strategy (Awake extubation, deep extubation, or LMA exchange) – set yourself up for success by creating conditions for smooth emergence (narcotic titration, spontaneous ventilation at skin closure, discontinuation of neuromuscular blockers etc.)

Have a plan for hypertension and prepare and plug in infusions such as nicardipine of Cleviprex if use is anticipated.

APPENDIX:

Adenosine-Induced Transient Asystole

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Abstract

Cerebral aneurysms are an important health issue in the United States, and the mortality rate following aneurysm rupture, or SAH, remains high. The treatment of these aneurysms uses endovascular options which include coil placement, stent assistant coiling and, recently, flow diversion. However, microsurgical clipping remains an option in those aneurysms not suited for endovascular therapy. These are often the more complicated aneurysms such as in large, giant aneurysms or deep-seated aneurysms. Circumferential visualization of the aneurysm, parent vessels, branches, perforators, and other neurovascular structures is important to prevent residual aneurysms or strokes from vessel or perforator occlusion. Decompression of the aneurysm sac is

often required and we believe that adenosine-induced transient asystole should be an important option for clipping of complex cerebral aneurysms.

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Go to:

Introduction

Cerebral aneurysms are an important health issue in the United States, and it is estimated that approximately 5% to 15% of all stroke cases are due to ruptured saccular aneurysms.1 Although cerebral aneurysms can present with other symptoms related to their mass effect, such as cranial nerve palsies, the most significant sequelae are related to subarachnoid (SAH) secondary to aneurysm rupture. The mortality rate following aneurysm rupture, or SAH, remains at 20% to 40%, and up to 50% of those who survive are left disabled.2–4 Poor outcome is largely related to the effects of the hemorrhage; therefore, preventing rehemorrhage in ruptured aneurysms and initial hemorrhage in unruptured aneurysms is the primary strategy for lowering mortality. This can only be achieved by successfully excluding the aneurysm from the circulation, which can be accomplished with either open microsurgical or endovascular treatment strategies.

This review explores the benefits and risks of endovascular versus surgical treatment of aneurysms, with a specific focus on microsurgical clipping using adenosine-induced flow arrest as a viable option for patients who are not candidates for endovascular therapy.

Go to:

Comparison of Endovascular Occlusion and Microsurgical Exclusion

Endovascular occlusion of cerebral aneurysms is appealing for its lower approach-associated morbidity; it also has shown to be safer than clipping. However, the primary goal of treatment is to exclude the aneurysm from the circulation and prevent hemorrhage or rehemorrhage in unruptured and ruptured aneurysms, respectively. When comparing endovascular treatment with

surgical occlusion for complete obliteration of aneurysms, the efficacy of endovascular aneurysm occlusion appears less optimal.

Aneurysm treatment using endovascular occlusion compared to microsurgical exclusion is quite different, and this difference may have significant implications for residual aneurysms after treatment. In the clipped aneurysm residua, the walls are closely apposed and the remaining aneurysm is completely excluded from the circulation. With endovascular techniques, however, coils keep the remnant's walls apart. Moreover, although experimental models of coiled aneurysms demonstrate that the aneurysm neck becomes entirely occluded by organized thrombus and that the free luminal surface is covered by endothelium, endothelialization is not observed in coiled aneurysms immediately after treatment and has been absent in some cases obtained at autopsy or when viewed later at the time of surgery.[5] These factors mean that any intra-aneurysmal thrombus or coil is exposed to circulating blood, which may allow compaction of the coils or flow around the coil's periphery into the aneurysm sac. This "efficacy" has been an important factor in favor of microsurgical clipping, since clipping results in more durable outcomes in both the short- and long-term.

Most series report a 92% to 96% exclusion rate of the aneurysm from the circulation with microsurgical clipping, as confirmed by postoperative angiography.[6–8] This efficacy is preserved with a 0.5% rate of recurrence per year in completely clipped aneurysms.[6] Most importantly, microsurgical clipping significantly changes the natural history of the disease. Over a 4.4-year follow-up period of patients with ruptured aneurysms, David and colleagues reported a 0% incidence of rebleeding in 147 aneurysms that had been completely clipped.[6] Twelve (8.2%) of the 147 aneurysms had a residual neck, and these were divided into two groups: *dog ear* residua and *broad-based* residua. Patients with the dog-ear type had a 1.9% annual risk of recurrent hemorrhage, and patients with the broad-based type had no recurrent hemorrhage although they had significant regrowth. Combined, these residuals had a recurrent bleeding rate of 1.5% per year in the 8.2% of aneurysms with residual necks after clipping.[6] The impact of microsurgical clipping in altering the natural history has also been found in unruptured intracranial aneurysms (UIAs).

With respect to endovascular coiling, most series report 40% to 55% complete exclusion, 35.4% to 52% near-complete exclusion, and 3.5% to 8% incomplete exclusion of the aneurysms from the circulation.[9,10] The Cerebral Aneurysm Re-rupture After Treatment (CARAT) study found a rate of rupture after treatment to be 1.8%, which is comparable to the 1.7% rerupture rate reported earlier in the International Subarachnoid Aneurysm Treatment study.[11] Recently, their subtotal occlusion cohort study of 1,010 patients treated with coil embolization or surgical clipping found that degree of occlusion was associated with a lower risk of rerupture. Cumulative risk over a 9-year period was 1.1% for complete occlusion, 2.9% for 91% to 99% occlusion, 59% for 70% to 90% occlusion, and 17.6% for < 70% occlusion, with a higher rate of subtotal occlusion occurring in coiled aneurysms. Risk of rerupture was greater in those aneurysms that were coiled versus clipped in univariate analysis (cumulative hazard 3.4% versus 1.3%; $P < 0.09$). However, the difference did not persist after adjusting for degree of aneurysm occlusion and other potential confounders (HR 1.09; 95% CI, 0.32 to 3.69; $P < 0.89$). The only characteristic that independently predicted rerupture was peripheral vascular disease ($P < 0.034$).

The long-term durability of endovascular coiling is concerning, with rates of recanalization reported to range from 0.6% to 28%.[10–12] This recanalization, however, was found to be associated with larger aneurysms and those with a poor dome-to-neck ratio.[10] Despite the fact that microsurgical clipping provides a far superior anatomic cure compared to endovascular coiling, coiling has been shown to be effective in changing the natural history of unruptured and ruptured aneurysms as well. Therefore, complete anatomic cure is not required to change the natural history of cerebral aneurysms. In the report by Kuether et al. on 74 patients with 77 aneurysms, including both ruptured and unruptured aneurysms, the authors had no reported hemorrhage over a follow-up period of 1.9 years in those aneurysms that demonstrated complete exclusion.[9] In those with near-complete occlusion, a hemorrhage rate of 1.4% per year was found in the same follow-up period.[9] In a meta-analyses on the treatment of UIAs in 1,379 patients, Lanterna et al. found a total of 13 nonprocedural bleeding events occurring in 703 eligible patients during an average follow-up time of 0.5 to 3.8 years.[13] The overall annual bleeding rate was 0.9% per year, and, importantly, only partially occluded UIAs of 10 mm or more hemorrhaged. Specifically, the bleeding rate of the UIAs larger than 10 mm was 3.5% per year.[13] Therefore, although endovascular treatment does change the natural history of a cerebral aneurysm, it can be considered inferior to clipping with regard to complete occlusion.

Therefore, despite the fact that intracranial aneurysm treatment has evolved over the last 10 years and despite advances in endovascular techniques, microsurgical clipping remains an important treatment option for those patients who are not ideal candidates for endovascular therapy. This is particularly true for wide-necked, blister-like, large and giant, and complex cerebral aneurysms.

Go to:

Challenges of Microsurgical Clipping

Microsurgery and clip ligation can be challenging in large, giant aneurysms or deep-seated aneurysms as circumferential visualization of the aneurysm, parent vessels, branches, perforators, and other neurovascular structures is important to prevent residual aneurysms or strokes from vessel or perforator occlusion. Decompression of the aneurysm sac is often required for large aneurysms and can be accomplished with several techniques, including temporary parent vessel occlusion, intraoperative adenosine-induced transient asystole,[14,15] deep hypothermia with circulatory arrest,[16–18] and rapid ventricular pacing for flow arrest.[19] Temporary parent vessel occlusion can potentially injure the vessel and cause dissection or stroke from ischemia. Furthermore, it is not feasible in deep areas or areas in close proximity to the skull base, where paraclinoid, basilar apex, and certain anterior and posterior communicating aneurysms would cause additional space limitations. Deep hypothermia with circulatory arrest, which is ideal for providing cerebral protection during surgery, is associated with significant complications such as coagulopathy, and overall complication rates are in the range of 40% to 80%.[18] Rapid ventricular pacing for flow arrest is another good option, albeit more complicated, and perforation of the atrium has been reported. We believe that adenosine-induced transient asystole should be the first option for clipping of complex cerebral aneurysms.

Go to:

Adenosine-Induced Transient Asystole

Adenosine-induced asystole for cerebral aneurysms surgery was first described by Groff et al.[14] in 1999 in posterior circulation aneurysms. Adenosine is an endogenous nucleoside analog that alters electrical conduction at the atrioventricular (AV) node and has a negative chronotropic effect on the sinoatrial node. Adenosine acts on cardiac A1 receptors to reduce cyclic adenosine monophosphate activity, which decreases inward calcium conductance and diminishes pacemaker current, resulting in bradycardia, AV nodal blockade, and sinus pauses. It has a very short half-life time (less than 10 seconds) and is rapidly taken up by the vascular endothelium and erythrocytes. The effect on heart rate is seen within 10 to 20 seconds after administration, with the duration of asystole reaching a plateau between 40 to 60 seconds at 1 mg/kg. There is a relative hypotension period of 1 minute after asystole.

Multiple doses are usually required for very large and complex aneurysms to obtain repeated episodes of asystole; however, there is limited data to assist in the selection of an appropriate initial dose. Hashimoto et al. presented dose-response data for patients undergoing embolization of arteriovenous malformations.[20] They recommended establishing an individual dose-response relationship for each patient by injecting escalating doses of adenosine separated by an interval of 3 to 10 minutes. Bebawy et al. recommended an initial dose of between 0.3 and 0.4 mg/kg ideal body weight (IBW) as the starting dose to achieve approximately 45 seconds of profound systemic hypotension.[21] Powers et al. gave between 2 and 5 escalating doses during aneurysm clipping, repeating the dose as often as every 1 to 2 minutes.[22] The standard initial dose of 6 mg was used on all patients and escalated to 6 mg more than the previous dose (e.g., 6 mg, 12 mg, 18 mg, 24 mg) until 30 to 40 seconds of asystole was reached.

Very few case series have described the use of adenosine in intracranial aneurysm surgery. Luostarien et al. reported the first series of 16 patients demonstrating its safety and efficacy during surgery for ruptured intracranial aneurysm.[23] Of these 16 patients, 12 received a single adenosine bolus and 4 received repeated boluses. The median dose for a single bolus was 12 (6–18) mg, whereas the median total dose for multiple boluses was 27 (18–89) mg. Ten minutes after adenosine administration, all patients were hemodynamically stable, and 13 patients required vasoactive drugs during the procedure. Bebawy et al. reported the second series of 24 patients using adenosine to facilitate surgery for intracranial aneurysms, a large number of which were internal carotid artery aneurysms with difficult anatomy for temporary clip.[21] Only two patients developed transient but hemodynamically stable atrial fibrillation on recovery from adenosine; one converted to sinus rhythm spontaneously and the other required treatment with amiodarone. No patient had any pulmonary side effects. The third case series, reported by Guinn et al.,[15] included 27 patients whose aneurysms were primarily in the anterior circulation and whose surgeries where primarily elective. The individual adenosine dose range was 3 to 60 mg, and the total dose range was 3 to 285 mg. They demonstrated adenosine's effectiveness in decompressing intracranial aneurysms, thereby facilitating exposure and clip ligation in cases when temporary clipping is not feasible. Of the 27 patients, one had prolonged extreme hypotension after rapid redosing due to intraoperative aneurysm rupture, requiring closed chest compression and pressors; spontaneous restoration of circulation occurred after 3 minutes.

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Advantages of Adenosine-induced Transient Asystole

Adenosine-induced flow arrest briefly reduces cerebral perfusion pressure and reduces the turgor of the aneurysm, thereby facilitating the clip ligation (Figure 1). Periods of flow arrest have to be carefully coordinated with the surgeon such that necessary working time is available for aneurysm dissection and clip placement. Adenosine-induced transient asystole is safe and efficacious when administered at an average of 0.3 to 0.4 mg/kg IBW in combination with remifentanil/low-dose volatile anesthetic with propofol. The adenosine dose will achieve approximately 45 seconds of controlled systemic hypotension and a bloodless surgical field. Adenosine offers the advantage of easy applicability in different situations without advanced preparation or complex logistical coordination with anesthesiology and cardiovascular surgery. This technique also allows the surgeon to have the maximum amount of space available to manipulate the aneurysm and place the clips, as no temporary clips are in the field of view. Also, temporary clips only decrease flow from the clipped inflow, whereas adenosine produces a more global hypotension and therefore often a better collapse of the aneurysm.
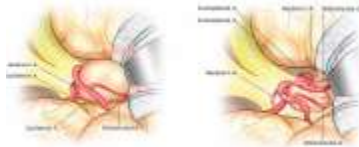
Figure 1.
Schematic representation of an anterior communicating artery aneurysm. On the left (pre-adenosine), the large mass does not allow circumferential visualization of the aneurysm, branches, and perforators. On the right (post-adenosine), the aneurysm is **...**
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Disadvantages, Complications, and Contraindications of Adenosine-Induced Transient Asystole

Adenosine vasodilates healthy coronary arteries but not atherosclerotic vessels, therefore patients with coronary artery disease may have a relative contraindication to adenosine therapy. Post-adenosine arrhythmias and troponin 1 elevation have been reported with an incidence of less than 1%. Adenosine is also a potent systematic vasodilator, and the major complications encountered have been persistent hypotension, sometimes requiring chest compression and vasopressor boluses. External defibrillator pads are recommended for all patients who receive adenosine to provide external pacing if prolonged bradycardia or asystole were to develop or cardioversion in case of hemodynamically unstable atrial fibrillation. In addition, adenosine can cause bronchoconstriction and therefore may be contraindicated for patients with asthma or chronic obstructive pulmonary disease.[14,15,20–23]

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Conclusion

Despite the fact that an open craniotomy and clipping of a cerebral aneurysm is now the second line of therapy, clipping remains a viable option in certain aneurysms. Adenosine-induced flow arrest reduces cerebral perfusion pressure briefly and reduces the turgor of the aneurysm, which facilitates circumferential exposure of the aneurysm and therefore a safer and more effective clip ligation. This technique therefore should be part of the armamentarium of the microvascular neurosurgeon.

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Adenosine-induced flow arrest to facilitate intracranial aneurysm clip ligation: dose-response data and safety profile.

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Abstract

BACKGROUND:

Adenosine-induced transient flow arrest has been used to facilitate clip ligation of intracranial aneurysms. However, the starting dose that is most likely to produce an adequate duration of profound hypotension remains unclear. We reviewed our experience to determine the dose-response relationship and apparent perioperative safety profile of adenosine in intracranial aneurysm patients.

METHODS:

This case series describes 24 aneurysm clip ligation procedures performed under an anesthetic consisting of remifentanil, low-dose volatile anesthetic, and propofol in which adenosine was used. The report focuses on the doses administered; duration of systolic blood pressure <60 mm Hg (SBP(<60 mm Hg)); and any cardiovascular, neurologic, or pulmonary complications observed in the perioperative period.

RESULTS:

A median dose of 0.34 mg/kg ideal body weight (range: 0.29-0.44 mg/kg) resulted in a SBP(<60 mm Hg) for a median of 57 seconds (range: 26-105 seconds). There was a linear relationship between the log-transformed dose of adenosine and the duration of a SBP(<60 mm Hg) ($R(2) = 0.38$). Two patients developed transient, hemodynamically stable atrial fibrillation, 2 had postoperative troponin levels > 0.03 ng/mL without any evidence of cardiac dysfunction, and 3 had postoperative neurologic changes.

CONCLUSIONS:

For intracranial aneurysms in which temporary occlusion is impractical or difficult, adenosine is capable of providing brief periods of profound systemic hypotension with low perioperative morbidity. On the basis of these data, a dose of 0.3 to 0.4 mg/kg ideal body weight may be the recommended starting dose to

achieve approximately 45 seconds of profound systemic hypotension during a remifentanil/low-dose volatile anesthetic with propofol induced burst suppression.

Adenosine-induced transient asystole for intracranial aneurysm surgery: a retrospective review.

Guinn NR[1], McDonagh DL, Borel CO, Wright DR, Zomorodi AR, Powers CJ, Warner DS, Lam AM, Britz GW.

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Abstract

BRIEF SUMMARY: We describe the use of adenosine-induced cardiac arrest to facilitate intracranial aneurysm clip ligation.

BACKGROUND:

Cerebral aneurysms are highly variable which may result in difficult surgical exposure for clip ligation in select cases. Secure clip placement is often not feasible without temporarily decompressing the aneurysm. This can be accomplished with temporary clip ligation of proximal vessels, or with deep hypothermic circulatory arrest on cardiopulmonary bypass, although these methods have their own inherent risks. Here we describe an alternate method of decompressing the aneurysm via adenosine-induced transient asystole.

METHODS:

We examined the records of 27 patients who underwent craniotomy for cerebral aneurysm clipping in which adenosine was used to induce transient asystole to facilitate clip ligation. Duration of adenosine-induced bradycardia (heart rate <40) and hypotension (SBP < 60) recorded on the electronic anesthesia record and outcome data including incidence of successful clipping, intraoperative and postoperative complications, and mortality were recorded.

RESULTS:

Satisfactory aneurysm decompression was achieved in all cases, and all aneurysms were clipped successfully. The median dose of intravenous adenosine resulting in bradycardia greater than 30 seconds was 30 mg. The median dose of adenosine resulting in hypotension greater than 30 seconds was 15 mg, and greater than 60 seconds was 30 mg. One case of prolonged hypotension after rapid redosing of adenosine required brief closed chest compressions before circulation was spontaneously restored. No other adverse events were observed.

CONCLUSIONS:

Adenosine cardiac arrest is a relatively novel method for decompression of intracranial aneurysms to facilitate clip application. With appropriate safety precautions, it is a reasonable alternative method when temporary clipping of proximal vessels is not desirable or not possible.