ADVANCES in both neurosurgical and anesthetic techniques have considerably improved the surgical treatment of cerebral aneurysms. In parallel, endovascular treatment has gained progressively greater acceptance in the last 10 yr. However, there remains a small subset of patients in whom conventional neurosurgical approaches still carry an exceptionally high morbidity and mortality. The use of deep hypothermic circulatory arrest (DHCA) in well-selected patients offers a reasonable risk-to-benefit profile when compared with the natural history of the untreated disease.

The DHCA approach is not new. Renewed enthusiasm for this technique as a modality of treatment for complex cerebral aneurysms that are not amenable to traditional surgical or endovascular techniques has been fostered by recent advances in cardiopulmonary bypass technology. 

This article will briefly review the rationale for DHCA in the setting of cerebral aneurysm treatment. We will then use the main aspects of the protocol practiced by the senior author (WLY), as a point of departure to review the issues regarding anesthetic and perioperative management.

Rationale

The ability to temporarily eliminate or reduce blood flow into an aneurysm gives the surgeon an important advantage—without flow, an aneurysm is converted from a hard, pulsating mass into a soft, collapsed sac, allowing more aggressive manipulation of the aneurysm to complete its dissection. With most aneurysms, temporary occlusion of the proximal parent artery or arteries will effectively control blood flow into the lesion. With large or complex aneurysms, the aneurysm mass may prevent optimal visualization and clip application to the neck. Collapse of the aneurysm mass creates more working space for dissection and precise clip application.

Deep hypothermic circulatory arrest is used for aneurysms that cannot be adequately controlled by conventional surgical or endovascular techniques. Aneurysms in the anterior circulation are, in general, accessible to operative exposure. When proximal and distal arteries are inaccessible with these complex aneurysms, DHCA may provide the only safe and effective means of vascular control. Deep hypothermic circulatory arrest should be considered an option of last resort for these unusual aneurysms, when all conventional techniques have failed or have been carefully considered. Rarely, DHCA has also been proposed or described for other central nervous system lesions, such as tumors or arteriovenous malformations, but this discussion is not within the scope of this article.

**Perioperative Management Protocol**

The logistics for neurosurgical DHCA require careful planning and excellent communication. There may be multiple healthcare personnel involved in the perioperative care, including but not limited to anesthesiologists, neurosurgeons, cardiac surgeons, neurologists, cardiologists, intensivists, nurses, and perfusionists.

Preoperative preparation includes assessing the power capabilities (including availability of both normal and emergency outlets) of all operating room electrical cir-
cuits to meet the extremely large perioperative power demands required to operate all required anesthesia equipment, (the cardiopulmonary bypass machine, the neurosurgical operating microscope, and video display monitors).

Preoperative evaluation of the patient should include evaluation of cardiovascular disease that might contraindicate femoral cannulation. If significant aortic insufficiency is present, median sternotomy and left ventricular venting may be required for safe conduct of cardiopulmonary bypass (CPB).

Before induction of general anesthesia, arterial line placement is facilitated by the judicious use of local anesthetics, anxiolytics, and narcotics. Oversedation of a patient with altered sensorium from subarachnoid hemorrhage (SAH) may increase the risk of aspiration or, by affecting oxygenation and ventilation, may increase intracranial pressure. Calcium channel blockers are frequently used in the preoperative medication of patients harboring ruptured intracranial aneurysms, and some practices use them as a prophylactic measure even for unruptured lesions.

Anesthesia is induced with an intravenous sedative-hypnotic and a relatively generous dose of narcotics (e.g., fentanyl 10–50 µg/kg). Use of benzodiazepines such as midazolam during the peri-induction period may minimize the potential for intraoperative recall. Tracheal intubation is facilitated with a nondepolarizing muscle relaxant and ventilation is adjusted to provide a Paco₂ in the 32–34 mmHg range. To minimize the risk or consequences of air embolism (either from extracorporeal circulation or neurosurgical exposure), nitrous oxide is not administered and a low-dose volatile anesthetic is titrated to maintain amnesia and hemodynamic stability. Hemodynamic management before the initiation of cardiopulmonary bypass is focused on maintaining a cerebral perfusion pressure within ± 10–15% of the preoperative range.

For intraoperative management and monitoring, large bore peripheral intravenous access is obtained, a pulmonary artery catheter is placed, external defibrillator pads are applied, and a transesophageal echocardiography (TEE) probe and a bladder catheter are inserted. The patient is temporarily turned into the lateral position to place a spinal subarachnoid drainage system. Then, the patient is positioned to allow surgical access to the head as well as both inguinal regions and, if necessary, the chest for median sternotomy. The majority of aneurysms may be accessed by approaches that are routinely performed in the supine position (e.g., orbitozygomatic or transpetrosal approach). It is possible to perform a far-lateral craniotomy for which the head and shoulders are positioned in the "3/4 prone" position and the torso is rotated so that the groin is close to supine. Using positioning other than supine, however, might make access to the chest for median sternotomy more difficult. (Should this become necessary). The head is locked in rigid pin fixation according to the neurosurgical approach. Temperature probes are placed against the tympanic membrane, nasopharynx, axilla, and rectum. Scalp electroencephalogram (EEG) is monitored using a 2-channel (bihemispheric) montage. Mannitol (0.5–1 g/kg) can be given for brain relaxation once the craniotomy is underway.

During craniotomy and dural opening, platelet-rich plasma and red blood cells can be harvested for postbypass reinfusion to aid in the return of normal coagulation status. Euvolemia is maintained by replacing the amount of blood withdrawn with an equal volume of albumin. A baseline kaolin activated coagulation time (ACT) is drawn to guide heparinization. After dural opening, a temperature probe (Mon-a-Therm, Mallinckrodt, St. Louis, MO) is placed directly into the exposed cortex (hemispheric cortex for carotid territory exposures or cerebellar cortex for posterior approaches).

During the period just before CPB, thiopental or propofol is titrated in small (50–100 mg) doses to achieve burst-suppression pattern on the raw EEG signal. A continuous infusion is established to maintain the EEG pattern during normothermia. Once cooling begins, the infusion is left constant at the normothermic rate. Alpha-stat PaCO₂ management is used. During circulatory arrest, the drug infusion used for EEG burst-suppression is interrupted and then restarted at the same rate during rewarming.

The aneurysm is dissected free as much as possible during spontaneous circulation. Dissection time varies greatly depending on the surgical approach, but typically 2 or 3 h after the craniotomy begins, CPB can be established. Before cannulation, heparin 300 U/kg is administered intravenously via a central venous line. After intravascular mixing is complete (1–2 min), an ACT is measured to ensure adequate heparinization, with the goal of an ACT ≥ 400 sec (or three times the control value). Adequacy of muscle relaxation is confirmed and additional doses of muscle relaxant, fentanyl, and midazolam are administered to counteract the dilutional effect of CPB initiation.

After the common femoral artery and vein are cannulated by percutaneous cannulation or direct surgical cutdown, and the position of the venous cannula at the level of the right atrium is confirmed with transesophageal echocardiogram, cardiopulmonary bypass is initiated. Fluid loading and a phenylephrine infusion assist in maintaining bypass flow at 2.5 L·min⁻¹·m⁻² with a mean arterial pressure of approximately 50 mmHg. Once adequate flow is achieved, systemic hypothermia is induced by cooling the oxygenated blood through the extracorporeal exchanger. Once ventricular fibrillation occurs, potassium is given through the right atrial port of the pulmonary artery catheter to achieve asystole. Usually
less than three boluses of 20 mEq are necessary. When the brain temperature reaches 15°C, the circulation is arrested and blood is drained through the venous can-
nula until the cerebral vasculature appears relaxed. Too much drainage can result in a negative pressure gradient with the consequences of air embolism and perhaps the tearing of small fragile perforating vessels emanating from the aneurysm dome or parent vessels.

After circulatory arrest, aneurysm clipping may pro-
ceed. An occasional beat occurs even during circulatory
arrest, which can be a problem if continued cardiac
ejection causes significant vascular movement in the
operative field. After the aneurysm is secured, CPB is
slowly reestablished and extracorporeal blood flows and
systemic cardiovascular pressures are monitored to test
the repair and assess hemostasis. If further periods of
circulatory arrest are deemed necessary, hypothermic
flow can be reinstituted until the systemic venous oxy-

gen saturation returns to near the prearrest level. Based
on theoretical and practical considerations, 45 min is
thought to be a safe upper limit of total arrest time, but
shorter periods are usually used. When the neurosur-
geon believes optimal clip placement has been achieved,
CPB is resumed and rewarming commences.

Nitroprusside (with or without some use of potent
volatile anesthetic agents) may be used to control arterial
vascular resistance and arterial blood pressure. Sponta-
neous cardiac rhythm usually reappears between 20 and
26°C. If present, ventricular fibrillation may be elec-
trically cardioverted. In patients without any cardiac co-
morbidity, inotropes are rarely needed to wean the pa-
tient from CPB. After separation from CPB, heparin is
reversed with protamine (0.75 mg protamine per 100 U
heparin initially administered). Initial post-CPB hemat-
crit, platelet count, and coagulation studies (e.g., PT,
apTT, fibrinogen, etc.) are obtained to guide further
therapy for disturbances of hemostasis after cardiopul-
monary bypass. Autologous blood removed before CPB
may be returned to the patient and the pump perfusate
is concentrated and administered. An additional ACT is
measured to confirm complete heparin reversal (ACT <
150 or within 10% of baseline value). Additional protamine
is administered, if necessary, to counteract remaining he-
parin effect. Based on the clinical context, blood products
are administered to correct any coagulopathies.

The patient is transported to the intensive care unit
with cardiovascular monitoring and remains intubated and
mechanically ventilated until return of adequate
sensorium, ventilatory parameters, and muscle strength
for extubation of the trachea. This might be within 3 or
4 h if propofol is used to induce and maintain EEG
burst-suppression; a longer period of ventilatory support
might be anticipated with use of thiopental or other
barbiturates.

Discussion

There are many possible permutations on the above
intraoperative protocol. If the goals of the various stages
are met, the exact choice of agents or techniques to
attain those goals is of secondary importance. There are
a limited number of small series upon which to base
recommendations.

Choice of Monitoring

In addition to pulmonary artery catheter, TEE monitor-
ing may be useful in closed chest bypass methods. Trans-
esophageal echocardiography allows (1) for assessment
of ventricular volume and contractility (short-axis view
at the papillary muscle level), (2) verification of the
proper position of bypass cannulae (longitudinal view
of the atria and cavae), and (3) monitoring of left and right
ventricular distension during bypass (short-axis view at
the papillary muscle level or four-chamber view). How-
ever, the advantages of additional information must
be weighed against the risks of TEE monitoring, which
include pressure necrosis of the tongue or soft tissues,
esophageal injury, or cervical spine injury with head
flexion. Access to the TEE probe for intraoperative ma-
nipulation should be carefully considered when position-
ing the patient. A reasonably accessible “tunnel” can
be fashioned with the drapes and various attachments to
the operating table to make for intraoperative manipu-
lation of the TEE probe possible.

Patients who have undergone recent SAH may be vol-
ume contracted, as a result of the disease process or recent
osmotic diuresis used to treat elevated intracranial
pressure or from contrast agents used during neuro-
imaging. Central venous access is desirable for both drug
and pressure monitoring, and the incremental morbidity
of placing a pulmonary artery catheter, especially with
the use of ultrasound guidance for internal jugular vein
 cannulation, should be minimal. Care should be taken to
insure that the right atrium is used as the zero reference
for central pressures, but that an appropriate correction
factor is introduced for monitoring cerebral perfusion
pressure, either because of head placement above or be-
low the level of the heart. In determining arterial
blood levels, central venous pressure should be taken
into account to most adequately indicate distal cerebral
perfusion. A detailed description of measuring cardiac
versus cerebral pressures is discussed elsewhere.

The electroencephalogram may also provide a means of
titrating anesthetic agents to some physiologic end
point such as some clinically discernible ratio of burst-
suppression. It must be kept in mind however, that burst-suppression does not necessarily correspond to
“maximally-protective” doses of agents. Evoked poten-
tials may also be of some use in monitoring, especially
with posterior fossa lesions.
CPB Methodology

There are several potential concerns with closed-chest femoro-femoral bypass. Myocardial protection relies on a reduction of myocardial oxygen consumption by affording hypothermia, empty ventricles, and asystole. Pharmacologic protection by cardioplegic solution is not available without aortic cross clamping. Assessing the adequacy of ventricular drainage is necessary, and this may be accomplished by monitoring central venous and pulmonary artery pressures or by direct visualization by TEE. Because of a lack of a left ventricular vent, overdistension of the left ventricle may require a conversion to open-chest bypass. Right ventricular overdistension often can be treated by augmenting venous drainage by increasing the height of an operative table relative to a venous reservoir. A bypass circuit with two centrifugal pumps or application of vacuum suction to the venous reservoir using a regulator may be used to increase venous drainage.19 Active venous return may facilitate reaching adequate bypass flow20 (Fig. 1).

The effects of hypothermia, CPB, heparin, and protamine on hemostasis may result in significant postoperative bleeding. There are theoretical advantages of using heparin-bonded circuits that may allow lower systemic heparin doses and decrease the inflammatory effects of CPB. For a discussion of such topics (especially as they relate to cerebral dysfunction), as well as general considerations regarding hemostasis in bypass methodology, the reader is referred elsewhere.21

Spinal Catheters

Although not universally used by all aneurysm surgeons, indwelling lumbar spinal subarachnoid drainage is frequently used to achieve improved brain relaxation. Although patients are fully heparinized, we know of no problems with placement of spinal catheters. The lack of information about this topic is doubtlessly related to the fact that such catheter-related complications rarely occur, and we are discussing them in the context of an infrequently used procedure. This is presumably related to the fact that catheters are both placed and removed in a state of normal coagulation function, i.e., the catheter is immobile during the period in which heparin is given and reversed with protamine. Nevertheless, vigilance for the rare complication of epidural or spinal hematoma is reasonable.

Conduct of Anesthesia

When setting goals for safe management of CPB and of cerebral aneurysm clipping we must consider the high incidence of cerebral injury during both of these procedures. Many patients who undergo these procedures have generally sound cardiovascular systems, making management of CPB relatively uncomplicated. The mechanisms of cerebral injury in this setting are similar to those seen when circulatory arrest is used for cardiac lesions, with some modification. The ability of deep hypothermia to afford protection from global cerebral hypoperfusion during circulatory arrest is well documented. In addition, there is also the possibility of focal cerebral ischemia from various embolic sources includ-
ting gas, blood products, and vascular wall debris. Deep hypothermia should protect against focal ischemia as well, but the time of maximal vulnerability for the occurrence of embolic focal injury may be before cooling and after rewarming— the time periods when thromboembolic cannula are being manipulated and systemic heparinization is being instituted or reversed.

In addition to the above general considerations, specific neurosurgical sources of focal brain injury may result from brain retraction and interruption of small end-arteries by dissection or clip placement. Furthermore, there may be areas of disturbed cerebral autoregulation if the patient has undergone a recent SAH, even if the patient is not overtly symptomatic. If such focal areas of cerebral ischemia exist, a particularly vulnerable period is during rewarming, for two reasons. First, inadvertent cerebral hyperthermia can happen during rewarming. Second, there seems to be an uncoupling of cerebral metabolic oxygen consumption and perfusion during the rewarming phase,22 which might adversely affect the brain already injured by SAH.

The interaction of the period of hypothermic arrest and brain regions previously damaged from a presenting SAH is unknown. Although most centers maintain relatively low mean arterial pressures during rewarming after routine CPB, it is probably reasonable to keep cerebral perfusion pressure within a patient’s normal range (\( \pm 10\% \)) in the patient having experienced a recent SAH or with any preoperative evidence of vasospasm or ischemia.

Barbiturate, propofol, or volatile anesthetic has been suggested to afford some modicum of protection for potential areas of focal cerebral ischemia, both permanent (vessel interruption), and transient (retraction, hypotension).7,16 23–25 Unfortunately, there is no compelling evidence that they protect the brain in the setting of routine cardiopulmonary bypass,26,27 and no evidence at all that they are protective during neurosurgical procedures. Nevertheless, given the high morbidity of DHCA for aneurysm clipping and the relative safety of using thiopental, propofol, or volatile anesthetic, incorporating such agents into a part of the anesthetic maintenance plan may be reasonable.

**Does Burst-Suppression Therapy Cause Adverse Cardiac Effects?**

There is a common and appropriate concern that drugs used to induce EEG burst-suppression (barbiturates and propofol) may cause cardiac depression (we emphasize again that burst-suppression may not correspond to maximal protection, should protection even exist). That barbiturates seem not to cause cardiac dysfunction in the immediate post-CPB weaning period was documented by Stone et al.24 Patients (\( n = 24 \)) without significant cardiac disease underwent DHCA for aneurysm clipping using a fentanyl, nitrous oxide, and isoflu-rame anesthetic. Thiopental was titrated to achieve EEG burst-suppression before CPB (as per the protocol cited previously), and the infusion was continued until after separation. Thiopental infusion continued for 2–3 h until after the bypass was terminated, and the overall infusion rate was \( 18 \pm 5 \text{ mg·kg}^{-1}·\text{h}^{-1} \). All patients were easily separated from bypass without inotropic support. Following bypass, there were minimal changes in vascular resistance (decreased), and heart rate, filling pressures, and cardiac index (increased); stroke volume had returned to its baseline; and ejection fraction was unchanged. Similar results have been reported by this same group in patients (\( n = 13 \)) receiving propofol, with the added benefit of earlier emergence from anesthesia.25 Nine of the 13 patients emerged from anesthesia and were able to follow commands at 3.1 ± 1.4 h. Three others had strokes and a fourth had cerebral swelling.

**Temperature Monitoring and Management**

When profound hypothermia is rapidly induced and reversed, temperature measurements made at standard monitoring sites may not reflect cerebral temperature.28 There appears to be no ideal site from which to monitor temperature in this setting of rapid temperature flux. Measurements from the nasopharynx, esophagus, and pulmonary artery tend to match brain temperature best (standard pulmonary artery catheters do not measure down to the temperature used during DHCA).29 Using an array of temperature-measuring locations may make it easier to interpret conflicting or discordant readings.

It has been suggested that Nitroprusside accelerates rewarming. There is, however, no convincing evidence to support this contention for neurosurgical DHCA in doses that will maintain adequate cerebral perfusion pressure,29 at least in comparison to volatile anesthetics such as isoflurane.30

Unrecognized hyperthermia in patients admitted to the hospital is a major unresolved management problem.31 It is exceedingly common after all types of cerebral hemorrhage. Postbypass hyperthermia is common in cardiac surgery. For example, in one study of open chest for elective coronary or valve surgery, Yared et al., found that, compared with placebo, patients receiving dexamethasone had a lower incidence of early postoperative fever (20% vs. 37%, \( P = 0.009 \)).32 Since many patients will be receiving dexamethasone for their neurosurgical management, perhaps the lower figure is more applicable. The lower number notwithstanding, given current knowledge about the deleterious effects of hyperthermia on the outcome from cerebral ischemia,33,34 it is still an alarmingly high fraction. The combination of post-CPB and post-SAH febrile states makes it highly likely that patients undergoing DHCA will have an increase in their body temperature postoperatively. In light of the evidence linking hyperthermia with adverse
neurologic outcome, considering aggressive temper-
ture control should be entertained.

Acid-base management, i.e., pH-stat versus α-stat during
CPB, remains a point of controversy. In pediatric
patients, pH-stat may hasten recovery of EEG activity. Alpha-stat management may result in favorable cognitive
function in adult patient after CPB. During moderate
hypothermic CPB, Murkin et al., found no differences in
outcome between pH-stat and α-stat strategies, except in
patients who were on bypass for more than 90 min. The
relevance of these findings to neurosurgical applica-
tion of DHCA is unclear.

On the theoretical level, relatively higher cerebral
blood flow with pH-stat might facilitate faster cooling or
warming of the brain. Conversely, higher flows and
lower cerebral resistance may increase delivery of em-
bolic material to the cerebral circulation. Relatively
greater cerebral blood flow may also interfere with brain
relaxation, or exacerbate decreased intracranial compli-
ance with the cranium closed.

Outcome

A detailed review of outcome is beyond the scope of
this review. However, one set of recently reported data
from a highly experienced group will serve to make an
important point—despite the ability of DHCA to afford
definitive therapy to some patients, it is an exceedingly
morbid procedure. Lawton et al. reported their experi-
ence with 60 patients treated with 62 DHCA procedures
over a 12-yr period. Treatment complications occurred
in 37% of patients and included postoperative intracra-
nial hematoma (15%), some type of cerebral infarction
(16%), and cranial nerve morbidity (55%, more than half of
which was transient). Major medical complications
included a fatal myocardial infarction, sepsis in 4 pa-
tients, and transfusion-related hepatitis in 1 patient. The
operative mortality in these 60 patients was 8.3%. De-
layed deaths related to treatment occurred in an addi-
tional 10%. Surgical morbidity included transient neuro-
logic deterioration in 15% and permanent neurologic
deterioration in 6.7%.

Summary and Conclusions

For the future, advances in less invasive methods of
circulatory manipulation may one day further decrease
the need to use deep hypothermic circulatory arrest. Such
methods might include temporary cardiac pause and
new developments in endovascular ap-

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