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Review

Physiology-First Strategies in Intracranial Aneurysm Surgery: Integrating Cerebrovascular Dynamics into Neurosurgical Management

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Abstract

Background: Contemporary aneurysm surgery increasingly requires the management of complex lesions with limited physiological reserve. A growing "physiology-first" paradigm emphasizes that optimizing cerebrovascular dynamics during aneurysm treatment is essential for favorable neurological outcomes. Methods: This narrative review synthesizes current evidence and expert perspectives on cerebrovascular physiology relevant to aneurysm surgery, including cerebral perfusion, autoregulation, ischemia tolerance, neuroprotection, and intraoperative monitoring. Results: Key themes include individualized blood pressure management, recognition of impaired autoregulation—particularly after subarachnoid hemorrhage—safe application of temporary arterial occlusion, and the use of multimodal neuromonitoring to detect ischemia in real time. The strengths and limitations of neuroprotective adjuncts are critically discussed in the context of available clinical evidence. Conclusions: Integrating cerebrovascular physiology into aneurysm surgery supports informed intraoperative decision-making, minimizes ischemic injury, and enhances patient outcomes. A physiology-first approach complements technical expertise and represents a cornerstone of modern neurovascular practice.

Keywords: intracranial aneurysm; cerebral blood flow; autoregulation; cerebral perfusion; neuromonitoring; subarachnoid hemorrhage; neuroanesthesia

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1. Introduction

Intracranial aneurysms represent a critical cerebrovascular pathology that neurosurgeons manage with either microsurgical clipping or endovascular techniques. The primary objective of any treatment is to exclude the aneurysm from cerebral circulation to prevent rupture or rebleeding. However, securing the aneurysm is only one piece of the puzzle. Equally important is the preservation of cerebral physiology during the perioperative period. Neurosurgeons increasingly recognize that factors such as cerebral blood flow (CBF), intracranial pressure, and cerebrovascular autoregulation can significantly influence outcomes after aneurysm repair [1].

Aneurysmal subarachnoid hemorrhage (SAH), in particular, sets off complex physiological disturbances. Acute SAH raises intracranial pressure (ICP) and often disrupts

normal autoregulation of CBF. In the days following hemorrhage, patients face the threat of cerebral vasospasm and delayed cerebral ischemia (DCI), both of which are intimately linked to microvascular dysfunction and impaired perfusion. Even in elective unruptured aneurysm surgery, periods of arterial occlusion or brain retraction can jeopardize regional blood flow. Thus, a "physiology-first" approach entails proactively managing these variables—maintaining adequate perfusion, avoiding ischemic insults, and monitoring the brain's well-being in real time—as an integral part of aneurysm surgery [2].

This review adopts a narrative format to emphasize the integration of cerebrovascular physiology into surgical management of intracranial aneurysms. We first outline key physiological principles (cerebral perfusion, autoregulation, and metabolic vulnerability of brain tissue) and the tools available to measure or protect these functions. We then discuss how these principles are applied in practice, highlighting strategies such as blood pressure optimization, controlled temporary vessel occlusion, and intraoperative neuromonitoring. The discussion addresses the clinical implications, including how a physiology-guided strategy can mitigate complications like intraoperative ischemia, and it identifies current challenges and future directions. Ultimately, this physiology-centric perspective is aimed at neurosurgeons and perioperative teams, underscoring that successful aneurysm surgery relies not only on technical clipping or coiling but also on safeguarding the brain's delicate physiological balance throughout the treatment process [3–5].

2. Materials and Methods

This review was developed as a narrative, physiology-centered synthesis of contemporary concepts relevant to intracranial aneurysm surgery. Instead of a conventional systematic methodology, the approach was deliberately thematic to reflect how neurosurgeons and neuroanesthesiologists apply physiological principles in real-time clinical practice.

Scope and Conceptual Framework.

The review integrates three core domains:

1. Cerebrovascular physiology
   - Cerebral blood flow regulation, autoregulation dynamics, CO_2 reactivity, ischemia tolerance, collateral circulation, and metabolic vulnerability.
2. Neuroprotective strategies
   - Temporary arterial occlusion principles, ischemia time management, metabolic suppression, temperature modulation, and reperfusion strategies.
3. Intraoperative physiological monitoring
   - Functional (SSEP, MEP, EEG/BIS), vascular (ICG angiography, micro-Doppler), oxygenation/metabolism ($PbtO_2$, NIRS), and anatomical (intraoperative DSA) modalities.

These domains were selected because they represent the mechanisms most strongly influencing neurological outcomes during aneurysm clipping.

Literature Identification and Integration.

Relevant literature on cerebrovascular physiology and neuromonitoring was reviewed through PubMed and Scopus, focusing on concepts applicable to aneurysm surgery. Priority was given to:

- Contemporary physiological models of cerebral blood flow and autoregulation.
- Intraoperative monitoring tools with direct implications for ischemia detection.
- Evidence regarding ischemic thresholds, metabolic suppression, and neuroprotection.
- Observational series and expert consensus from high-volume neurovascular centers.

The information was consolidated into physiological themes rather than chronological or device-oriented subsections to emphasize direct clinical applicability.

Analytical Approach.

Each physiological concept was examined with respect to:

- Mechanistic relevance (i.e., how the variable affects cerebral perfusion, metabolic demand, or ischemic vulnerability).
- Surgical translation (how neurosurgeons can actively modify or respond to the parameter).
- Monitoring feasibility (which modalities provide real-time data and how it influences decision-making).
- Impact on intraoperative decision-making (temporary clipping strategy, MAP/CPP goals, ventilation targets, and clip revision triggers).

This allowed the integration of physiology into a cohesive framework for aneurysm surgery rather than a descriptive list of techniques.

Literature search transparency.

Although this review was intentionally designed as a narrative synthesis rather than a systematic review, we sought to ensure methodological transparency and reduce selection bias. The literature was identified through targeted searches of PubMed and Scopus, covering publications from approximately 2000 to January 2025. Search terms included combinations of "intracranial aneurysm", "cerebral autoregulation", "cerebral perfusion pressure", "temporary clipping", "neuroprotection", "neuromonitoring", and "subarachnoid hemorrhage". Priority was given to peer-reviewed original studies, randomized controlled trials, guideline statements, and high-quality narrative or systematic reviews relevant to intraoperative cerebrovascular physiology. Reference lists of key articles were manually screened to identify additional relevant publications.

3. Results

3.1. Cerebral Blood Flow and Autoregulation

Cerebral blood flow (CBF) is tightly regulated under normal conditions to meet the brain's metabolic demands. An average adult CBF is about 50 mL per 100 g of brain tissue per minute, and the brain autoregulates this flow across a range of blood pressures. Through autoregulatory mechanisms, cerebral arterioles dilate or constrict to maintain near-constant perfusion when mean arterial pressure (MAP) fluctuates roughly between ~50 mmHg and ~150 mmHg. This relationship is classically depicted as a plateau in the CBF versus CPP (cerebral perfusion pressure) curve, bordered by lower and upper autoregulatory limits (Figure 1). Cerebral blood flow (CBF) remains relatively constant across a physiological range of cerebral perfusion pressure (CPP) due to autoregulatory vasodilation and vasoconstriction. Below the lower limit, CBF becomes pressure-dependent, increasing ischemic risk; above the upper limit, hyperemia and edema may occur [6].

Autoregulation in Aneurysm Patients: It is important to recognize that autoregulatory capacity may be altered in patients with aneurysm, especially those presenting with SAH. After aneurysmal rupture, blood in the subarachnoid space and the ensuing inflammatory cascade often impair the cerebral vessels' ability to autoregulate. In practical terms, this means that the CBF in some SAH patients becomes pressure-dependent—falling directly with any drop in systemic blood pressure. Consequently, even modest hypotension can precipitate cerebral ischemia in the post-SAH setting. Anesthesiologists and neurosurgeons must account for this by maintaining blood pressure in a higher-than-normal range to drive adequate perfusion when autoregulation is compromised [7].

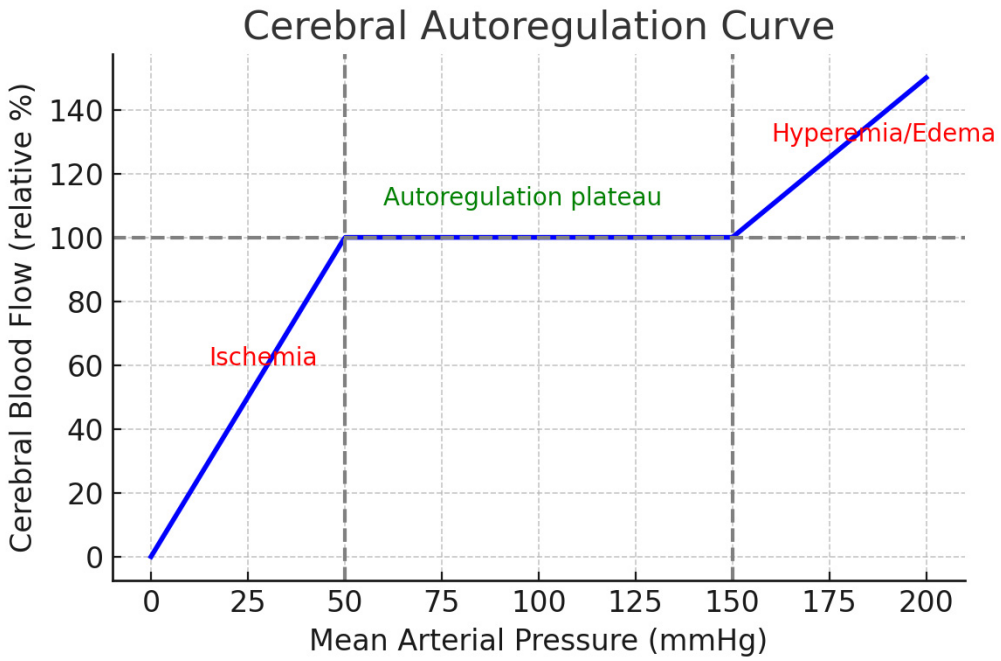


Figure 1. Cerebral autoregulation curve (CBF remains constant at ~50 mL/100 g/min across a normal CPP range (gray zone). Below the lower limit (~50 mmHg CPP), the vessels are maximally dilated, and CBF drops, risking ischemia. Above the upper limit (~150 mmHg), the vessels are maximally constricted, and CBF rises with pressure, risking hyperemia or edema.

Chronic hypertension can also shift autoregulation. Patients with long-standing hypertension (which is a risk factor for aneurysm formation and rupture) may have a rightward-shifted autoregulatory curve. Their lower limit of autoregulation might be higher than the textbook 50 mmHg CPP, meaning that they require a higher perfusion pressure to sustain normal CBF. During anesthesia, these patients may not tolerate "normal" blood pressures as well—blood pressure that seems adequate in a young healthy person could be relatively low for their cerebral needs. This underpins the principle of individualized blood pressure targets during aneurysm surgery: one must consider the patient's baseline physiology and adjust intraoperative MAP goals to ensure that cerebral perfusion remains optimal [8].

Beyond traditional macro-hemodynamic concepts, recent advances in cerebrovascular modeling have highlighted the importance of blood rheology in aneurysm physiology. Emerging thixotropic elasto-visco-plastic (TEVP) models account for the non-Newtonian behavior of blood, incorporating viscosity changes, yield stress, elasticity, and time-dependent shear thinning. These properties are particularly relevant within aneurysm sacs, where low shear regions, flow stagnation, and complex vortex formation influence wall shear stress distribution and thrombosis risk. While TEVP modeling remains largely computational and investigational, acknowledging these frameworks underscores that cerebrovascular dynamics extend beyond pressure and flow alone, reinforcing the need for comprehensive physiological understanding in aneurysm management. Furthermore, CO_2 reactivity is an important component of cerebral blood flow regulation. Normally, elevated arterial CO_2 (hypercapnia) causes vasodilation and increases CBF, whereas low CO_2 (hypocapnia) causes vasoconstriction and reduces CBF. In the operating room, intentional mild hyperventilation is often used to reduce intracranial pressure by causing cerebral vasoconstriction. However, this must be done judiciously. Excessive hyperventilation (leading to profound hypocapnia) can critically diminish CBF and should be avoided—especially if there is already risk of ischemia from surgical manipulation. Balancing ventilation to maintain near-normocarbia (or only mild hypocapnia when needed for brain relaxation) is thus a

key physiological consideration. Autoregulatory impairment can also alter CO_2 reactivity; SAH patients sometimes exhibit "vasoparalysis" where vessels no longer respond normally to CO_2 changes, again highlighting that standard rules may not fully apply in injured brains [9,10].

3.2. Ischemia Tolerance and Metabolic Vulnerability

Neurosurgeons frequently face moments in aneurysm surgery where blood flow must be intentionally reduced or stopped—for example, when placing a temporary clip on an artery to soften a tense aneurysm sac. Ischemia tolerance refers to how long brain tissue can survive such an interruption of blood supply without sustaining irreversible damage. The brain has very limited energy stores and a high metabolic rate, making it one of the least ischemia-tolerant organs. Within seconds of circulatory arrest, neurons cease firing; within minutes, energy failure triggers irreversible injury in the most vulnerable cells [11].

Experimental and clinical evidence suggest that at normal body temperature, 3–5 min of complete cerebral ischemia can lead to neuronal death in especially sensitive regions. Certain areas (e.g., hippocampal CA1 neurons and cerebral cortex neurons) are more metabolically vulnerable and succumb earlier, whereas others (white matter or brainstem structures) might endure slightly longer. This disparity is referred to as metabolic vulnerability of specific anatomical sites—it means that some parts of the brain have a higher baseline demand or a lower collateral blood supply and are thus at higher risk during an ischemic episode. Watershed zones between major arteries are another example of vulnerability due to their precarious perfusion [11,12].

Understanding these limits is crucial when employing temporary arterial occlusion during clipping. In practice, many neurosurgeons adhere to a guideline of keeping temporary clips in place for no more than roughly 5 min at a time, if possible. If longer occlusion is required for complex clipping, surgeons may opt to intermittently re-perfuse the vessel (remove the temporary clip briefly to allow blood flow before re-applying it), thereby providing short reperfusion intervals. As a rule of thumb, shorter and fewer occlusions are safer; prolonged occlusion times beyond 10–15 min dramatically raise the risk of stroke unless extraordinary protective measures are in place [13,14].

The concept of brain preconditioning is sometimes invoked: brief sub-lethal ischemic episodes can paradoxically increase tissue tolerance to a subsequent longer ischemic insult. Some surgical teams will intentionally perform a short test occlusion while observing for any neuromonitoring changes as a way of gauging tolerance (and potentially triggering a protective adaptive response in the tissue). However, this is not routine for all cases and carries its own risk, so it must be weighed carefully [15,16].

Neuroprotective strategies can extend ischemia tolerance by reducing the brain's metabolic rate or protecting neurons at a cellular level. Two main approaches have been explored: lowering brain temperature and inducing pharmacologic burst suppression. Mild hypothermia (e.g., cooling the patient to ~33 °C) can reduce cerebral metabolic rate by about 5% per degree Celsius, thereby slowing the rate of ATP depletion during ischemia. In theory, hypothermia should prolong the time neurons can survive without oxygen. This rationale led to trials of intraoperative hypothermia in aneurysm surgery. Interestingly, a large multicenter trial found that mild hypothermia did not significantly improve neurological outcomes in elective aneurysm clipping patients compared to normothermia. As a result, routine cooling for aneurysm surgery has fallen out of favor, but some centers still employ moderate hypothermia in select high-risk scenarios (such as giant aneurysm repair requiring circulatory arrest). In contrast, deep hypothermic circulatory arrest—cooling patients to ~15–18 °C with cardiopulmonary bypass—remains an extreme measure reserved for very complex aneurysms (e.g., certain giant or posterior circulation aneurysms) where

blood flow must be stopped for extended periods. Under those conditions, the brain can tolerate up to 30–40 min of no flow, but this is a highly specialized technique [17,18].

Pharmacologic metabolic suppression involves using anesthetic agents to drastically reduce neuronal activity. High-dose barbiturates (e.g., thiopental) have historically been used to induce an EEG burst suppression coma, cutting cerebral metabolic requirements and potentially protecting against ischemia. Today, intravenous anesthetics like propofol are often used similarly to achieve burst suppression. Burst suppression on EEG indicates a state of greatly lowered metabolic demand, and many neurosurgical anesthetic protocols aim for this state during temporary clipping. While it intuitively makes sense, conclusive evidence for improved outcomes with burst suppression is mixed—some studies suggest reduced intraoperative ischemic changes, while others did not show a clear benefit in cognitive outcomes. Nonetheless, in practice, when a lengthy temporary occlusion is anticipated, anesthesiologists will frequently deepen anesthesia (e.g., with propofol infusion) to achieve burst suppression just before and during the occlusion. This is a low-risk intervention that may add a margin of safety. In addition, ensuring that the patient's blood pressure is on the higher side of normal before occlusion (to maximize collateral perfusion) is a simple but vital step [19,20].

Other pharmacological adjuncts have been considered for neuroprotection (e.g., calcium channel blockers and NMDA antagonists), but none have shown definitive benefit intraoperatively. The mainstay remains metabolic suppression and meticulous perfusion management. It is worth highlighting that brain tissue can also be injured by reperfusion—when blood flow returns after an ischemic interval, a cascade of oxidative and inflammatory damage can occur (reperfusion injury). Surgeons sometimes mitigate this by restoring flow gradually (for instance, by "stuttering" the release of a temporary clip to allow a slow reperfusion instead of a sudden rush). Short, repeated occlusions rather than one long occlusion may also help because they provide partial reperfusion in between, potentially reducing the reperfusion injury in any single burst [21,22].

In summary, the brain's narrow window of ischemia tolerance demands that neurosurgeons plan every maneuver that risks compromising CBF with great care. Knowledge of how long the brain can safely go without blood (under given conditions) and how to extend that limit with cooling or metabolic suppression can directly inform surgical strategy during aneurysm clipping.

3.3. Intraoperative Monitoring of Cerebral Physiology

Modern aneurysm surgery is greatly aided by intraoperative monitoring tools that give real-time feedback on the patient's neurological status and cerebral perfusion. These tools serve as the surgical team's "eyes and ears" on the brain's physiological well-being, beyond what can be directly visualized.

Neurophysiological monitoring: somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) are widely used to monitor the functional integrity of neural pathways during aneurysm surgery. SSEPs, usually obtained by stimulating a peripheral nerve (e.g., median nerve at the wrist) and recording the cortical response, primarily reflect the dorsal column-medial lemniscal sensory pathways and their blood supply (often the anterior cerebral artery for lower extremity SSEPs and middle cerebral artery for upper extremity SSEPs). A significant drop or loss of SSEP signal warns that a part of the brain (perhaps the territory of a clamped vessel or a perforating artery) is becoming ischemic. In aneurysm surgery, this could happen if a clip inadvertently occludes or narrows a parent artery or important branch—the SSEP changes might precede a permanent deficit if not addressed promptly. MEPs involve transcranial electrical stimulation of the motor cortex and recording muscle responses; they are extremely sensitive to any interruption

of blood flow in the motor pathways (which are mainly supplied by the middle cerebral artery and anterior choroidal artery). Because MEPs can change within 1–2 min of severe ischemia, they serve as an immediate alert. If MEP amplitudes drop significantly or disappear, the surgeon can respond by removing or adjusting a clip, raising blood pressure, or re-establishing flow before ischemia becomes irreversible [23].

It is important to note that while neuromonitoring is a valuable safety net, it is not infallible. False negatives (no change detected despite an ischemic event) and false positives (transient changes that do not lead to any injury) can occur. Aneurysm surgeries that do not involve vessels supplying eloquent areas might not be well covered by standard SSEPs/MEPs (for example, a small perforating artery spasm might not show an immediate change unless it supplies an area monitored by those modalities). Therefore, neuromonitoring is combined with other strategies, but its overall impact has been positive—multiple series report that the use of SSEPs/MEPs reduces the rate of postoperative deficits by allowing early intervention [24].

Cerebral Blood Flow Monitoring: The direct measurement of CBF during surgery is challenging, but there are proxies. One simple tool is a micro-Doppler ultrasound probe, a tiny sterile Doppler that a surgeon can briefly place on an artery after clipping to check for flow. If the Doppler does not detect a normal pulsatile flow signal in a major artery that should be patent, it alerts the surgeon that the clip or surgical manipulation might be compromising that vessel. Micro-Doppler is quick and can be repeated for multiple vessels (e.g., parent artery and branches). It essentially serves as an immediate patency check. A more quantitative but less commonly used tool is an intraoperative flow probe (transit-time ultrasonic flowmetry), which is placed around a vessel to directly measure blood flow in mL/min before and after clipping. This can confirm that flow has been preserved or identify a significant reduction. However, it requires additional steps and is not routine in all centers [25].

Brain Oxygenation and Metabolism Monitoring: In some cases, especially research settings or complex cases, invasive monitors such as brain tissue oxygen tension probes ($PbtO_2$) or microdialysis catheters are used. A $PbtO_2$ probe measures the partial pressure of oxygen in brain tissue at a specific location. If placed in a region at risk (for instance, the territory of an artery that might be temporarily occluded), a drop in $PbtO_2$ could indicate developing ischemia before irreversible damage occurs. Microdialysis catheters sample extracellular fluid chemistry; rising lactate or glutamate levels can signal ischemic metabolism. These monitors are more common in the neurocritical care unit after surgery (to watch for DCI), but the concept in the OR is similar: to catch physiological signs of trouble in real time [26].

Intraoperative Angiography: Verifying vessel patency and aneurysm obliteration is so important that many aneurysm surgeries now include an on-table angiographic assessment. The simplest form is indocyanine green (ICG) videoangiography, where a fluorescent dye is injected intravenously, and the operating microscope, equipped with near-infrared filters, visualizes blood flow. Within seconds, the surgeon sees all vessels lighting up; this reveals whether the aneurysm is successfully clipped (dye should not fill the sac) and confirms that major arteries and perforators are still flowing. ICG angiography is quick and does not require moving the patient. More definitive but time-consuming is formal intraoperative digital subtraction angiography (DSA), usually done in a hybrid OR or by bringing in a portable angiography unit. DSA can find subtle issues like a small residual aneurysm neck or a tiny, occluded branch that might be missed by ICG. Any detected issue can be immediately corrected by repositioning clips. Thus, while not a "physiology monitor" per se, intraoperative angiographic evaluation is a crucial adjunct for ensuring the

physiological goal of adequate perfusion is met and that no inadvertent vessel compromises have occurred [27].

Intracranial Pressure (ICP) Management: During open aneurysm surgery, ICP is generally controlled by the fact that the skull is open (craniotomy), and CSF is often drained to relax the brain. However, preoperatively, in a ruptured aneurysm scenario, ICP might be elevated due to hydrocephalus or acute hematoma. External ventricular drains (EVDs) are commonly placed in poor-grade SAH patients to relieve hydrocephalus and allow ICP monitoring. The surgical and anesthesia team must coordinate CSF drainage carefully: if ICP is lowered drastically before securing the aneurysm, the transmural pressure across the aneurysm wall spikes (since arterial pressure is suddenly much higher than intracranial pressure), which can precipitate intraoperative aneurysm rupture. Therefore, ICP is managed in a nuanced way—enough to optimize CPP and brain relaxation but not so much as to endanger aneurysm integrity before clipping. After the aneurysm is secured, maintaining low–normal ICP is beneficial, as it improves CPP and reduces the risk of brain swelling [28].

Table 1 below summarizes key monitoring modalities and physiological parameters relevant to aneurysm surgery:

Table 1. Intraoperative monitoring modalities in aneurysm surgery.

Modality	What It Monitors	Key Utility in Aneurysm Surgery
ICG angiography	Real-time vessel patency and perfusion	Confirms complete occlusion and verifies parent/branch vessel flow immediately after clipping.
Micro-Doppler	Arterial blood flow (audible signal)	Rapid check of parent and branch vessel patency; detects inadvertent clip-induced stenosis/occlusion.
SSEP	Sensory pathway integrity	Amplitude drop signals cortical or perforator ischemia (ACA/MCA territories), prompting immediate correction. Primarily reflects cortical and dorsal column pathways; less sensitive for deep perforator ischemia.
MEP	Motor pathway integrity	Most sensitive early warning for motor pathway ischemia (MCA/perforators). Loss/decline often reversible if caught early. Highly sensitive to ischemia involving perforating arteries supplying the internal capsule and corticospinal tract.
EEG/BIS	Global cortical activity	Detects global ischemia or inadequate anesthesia; burst suppression used intentionally for protection during temporary clipping.
$PbtO_2$ probe	Local brain oxygen tension	Direct measure of regional perfusion; drop indicates compromised flow in monitored territory. Used selectively.
NIRS	Regional cortical oxygen saturation	Noninvasive trend monitor of superficial cortical oxygenation; useful gross indicator during temporary clipping.
Intraoperative DSA	Definitive vessel anatomy	Gold-standard confirmation of clip placement, vessel patency, and aneurysm obliteration in hybrid ORs.
ICP monitoring	Intracranial pressure	Guides CPP optimization (CPP = MAP − ICP) important in SAH. Helps detect postop edema/hydrocephalus.

Note: Not every modality is used in every case. Modality selection is tailored to the case complexity and available resources, with patient safety and outcome optimization as the guiding principles.

The presented results translate the physiological principles outlined above into practical surgical management themes (Figure 2). The focus here is on how adopting a physiology-first mindset influences intraoperative decisions, techniques, and patient care to improve outcomes in intracranial aneurysm treatment. Major results of this integrated approach include reduced intraoperative rupture rates, lower incidence of ischemic strokes related to the procedure, and potentially better overall neurological recovery due to fewer secondary insults.

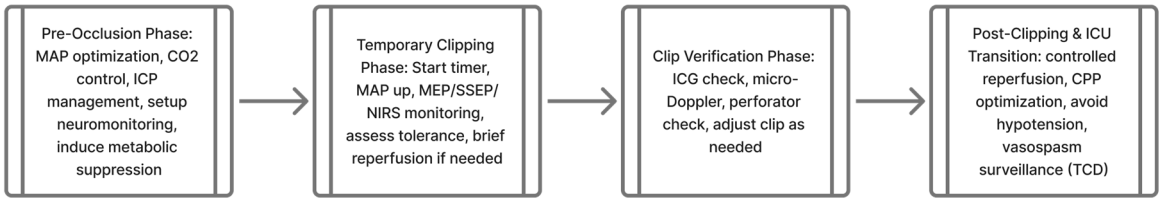


Figure 2. Workflow schematic for brain aneurysm treatment.

3.4. Optimizing Cerebral Perfusion During Aneurysm Clipping

One of the clearest applications of cerebrovascular physiology is the meticulous management of cerebral perfusion pressure (CPP) throughout the surgical procedure. By maintaining adequate MAP and controlling ICP, the surgical team works to keep CPP in an optimal range for the patient's condition. For example, at the induction of anesthesia, it is paramount to avoid hypotension. Induction agents can cause blood pressure drops; in a patient with a ruptured aneurysm and poor-grade SAH, even a transient MAP drop could critically reduce CBF if autoregulation is impaired. Therefore, anesthesiologists often use vasopressors preemptively during induction and intubation to sustain MAP. A-line (intra-arterial blood pressure) monitoring is standard, providing beat-to-beat blood pressure readings that allow immediate correction of deviations [29].

Continuous invasive arterial blood pressure monitoring via an intra-arterial line is mandatory in intracranial aneurysm surgery and should be established prior to the induction of anesthesia. Beat-to-beat monitoring allows immediate detection and correction of hypotensive or hypertensive episodes during critical phases such as induction, dural opening, brain relaxation, temporary arterial occlusion, and clip application. Anesthetic induction should be performed in a controlled and hemodynamically stable manner, avoiding abrupt reductions in mean arterial pressure (MAP), which may critically compromise cerebral perfusion pressure (CPP), particularly in patients with impaired autoregulation following subarachnoid hemorrhage. During the maintenance of anesthesia, MAP targets should be individualized based on aneurysm rupture status, baseline blood pressure, cerebrovascular reactivity, and collateral circulation. In patients with suspected or documented autoregulatory impairment, MAP is often maintained 10–20% above baseline to preserve adequate cerebral blood flow. Close coordination between the neurosurgeon and anesthesiologist is essential to anticipate periods of increased ischemic risk and proactively optimize cerebral perfusion [30,31].

Preventing Intraoperative Aneurysm Rupture: While ensuring brain perfusion, one must also prevent excessive transmural pressure on the aneurysm itself to avoid rupture. This is another balancing act. Hypertension is maintained only within reason. If blood pressure spikes too high (for example during intubation or during a painful stimulus if anesthesia is too light), the stress on the aneurysm wall could cause it to burst before clipping. Thus, adequate anesthesia depth and short-acting beta blockers or vasodilators are used as needed to blunt blood pressure surges at critical moments. The goal is a stable, high normal blood pressure—not labile extremes. Many neurosurgeons request a

relatively "tight" blood pressure band (for instance, MAP 80–100 mmHg) to be maintained continuously. This reduces the chance of both hypo- and hypertensive excursions [7,32].

Intravenous vs. Inhalational Anesthesia: From a physiological standpoint, total intravenous anesthesia (TIVA) with agents like propofol is often preferred in aneurysm cases, because it reduces cerebral blood volume and intracranial pressure compared to inhalational agents. Inhalational anesthetics (e.g., sevoflurane and isoflurane) tend to cause vasodilation and can increase CBF, potentially raising ICP (though at high concentrations they also suppress metabolism—the net effect depends on the concentration). Propofol, on the other hand, lowers cerebral metabolic rate and CBF in parallel, generally providing a drier surgical field and lower ICP. Moreover, propofol facilitates easy induction of burst suppression for neuroprotection. Therefore, many centers use a TIVA approach, when feasible, for aneurysm clipping, as part of optimizing physiology. That said, balanced anesthesia techniques are also employed—what matters is that the chosen regimen supports hemodynamic stability and neuroprotection [25,33].

Temporary Clipping Strategies: The results of a careful temporary clipping strategy are seen in reduced incidence of stroke on postoperative imaging. Studies have shown that liberal or prolonged use of temporary clips correlates with higher rates of ischemic lesions. Conversely, when surgeons are judicious—applying temporary clips only when absolutely necessary, for as short a duration as possible, and often under protective adjuncts—the incidence of both clinically apparent and "silent" (MRI-detected) infarcts is minimized. Some high-volume aneurysm centers have reported their stroke rates with clipping to be as low as a few percent, even in complex cases, attributing this success partly to rigorous physiological management. For example, diffusion-weighted MRI studies performed post-clipping have found fewer ischemic spots in patients where meticulous perfusion management and monitoring were used compared to historical controls. These positive results reinforce the importance of our physiology-first approach [25,34–36].

3.5. Neuroprotective Measures and Surgical Outcomes

It is important to distinguish between physiological management strategies with established benefit and pharmacological or temperature-based neuroprotection strategies whose clinical efficacy remains unproven. While maintaining adequate CPP and avoiding hypotension are strongly supported by physiological principles and clinical outcome data, randomized controlled trials evaluating pharmacologic neuroprotection and intraoperative hypothermia have largely failed to demonstrate consistent benefit. Notably, the Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST) showed no improvement in neurological outcomes with mild hypothermia in elective aneurysm clipping, tempering enthusiasm for its routine use. As such, neuroprotective adjuncts should be viewed as supportive measures rather than evidence-based guarantees of improved outcome. Direct evidence for the benefit of specific neuroprotective measures in aneurysm surgery has been somewhat mixed, but the consensus among experienced surgeons is that a combination of measures provides the best safeguard. Individually, mild hypothermia or barbiturate coma alone did not revolutionize outcomes in trials. But, in practice, using modest hypothermia (even just allowing the patient's temperature to drift to, say, 35 °C in a long case), combined with burst suppression and timely temporary clip management, is thought to synergistically reduce risk. Importantly, none of these protective measures should create significant downsides; for example, deep hypothermia or prolonged anesthesia might have risks, but short periods of burst suppression or mild cooling are generally well-tolerated. Thus, the attitude is "every little bit helps" when it comes to protecting the brain [37,38].

Intraoperative neuromonitoring has impacted surgical strategy and outcomes as well. A noteworthy "result" of neuromonitoring use is the change in surgeon behavior when

an alert is received. If an SSEP amplitude drops by 50% or MEPs start fading, the surgeon might loosen a temporary clip earlier than planned, reposition a permanent clip that might be causing stenosis of a branching artery, or flush the field with papaverine (a vasodilator) to relieve arterial spasm. These interventions can often restore the signals. In many documented cases, patients who had intraoperative neuromonitoring changes that were corrected woke up without deficits—whereas without monitoring, the issue might only have been discovered on wake-up (by which time the deficit could become permanent). However, the false negative rate of neuromonitoring reminds us that a lack of an alert is not 100% assurance. Therefore, physiologic vigilance is maintained even if monitors are stable—the surgeon still uses good clipping techniques (e.g., inspecting vessel patency under high magnification, using ICG angiography, etc.) [39,40].

Preventing Delayed Deficits: The influence of physiology extends beyond the operating room and into the ICU. Aneurysm surgery does not end when the clip is applied; preventing DCI in the days after is critical to a good outcome. Surgical results show that if a patient's intraoperative course was smooth physiologically—no hypotension and no major artery compromise—their risk of early brain injury is low, leaving mainly the delayed vasospasm risk. Here, again, understanding cerebral blood flow and autoregulation informs postoperative care. Patients are kept euvolemic, well-hydrated, and mildly hypertensive (as per classic "triple-H therapy" principles for vasospasm, though without inducing hypervolemia these days) to counteract any developing spasm. Transcranial Doppler ultrasounds might be performed daily to screen for vasospasm by measuring flow velocities in basal arteries. If velocities rise significantly, indicating vessel narrowing and reduced cross-sectional area, the team may intervene with medical measures (e.g., increasing blood pressure, initiating an infusion of vasospasm treatments) or endovascular therapies (angioplasty or vasodilator injections) [41].

Clinical Outcome Data: Large series and registry data indicate that the rate of permanent neurological complications from aneurysm clipping has declined over the past decades. This is partly due to better patient selection (simpler aneurysms often go to endovascular therapy now), but surgical technique refinement and physiological management also play a role. In centers that rigorously integrate intraoperative monitoring and physiological optimization, outcomes for even complex aneurysms approach those of the less complex ones. For example, one center reported that in 100 consecutive aneurysm clippings where SSEPs/MEPs and routine ICG were used, there were no unexpected postoperative deficits; any deficits that did occur were anticipated due to vessel sacrifice that was deemed necessary (and in those cases, often a bypass was done to mitigate it). Another study found that temporary clipping time was an independent predictor of DCI in SAH patients—longer occlusions during surgery were associated with higher rates of vasospasm and infarcts later. This suggests that avoiding prolonged interruptions of flow not only prevents immediate stroke but might also reduce the cascade of events leading to delayed ischemia (perhaps by reducing reperfusion injury and inflammation that contribute to vasospasm) [42,43].

Giant and Complex Aneurysms: In the realm of giant aneurysm surgery, a physiology-first approach is absolutely essential because these cases push the limits of what the brain can tolerate. Techniques such as bypass surgery are often employed in tandem: a high-flow extracranial–intracranial bypass might be created so that a giant aneurysm's parent artery can be permanently occluded (trapped) without causing infarct. The decision to do this is guided by physiological testing—for instance, balloon test occlusion of the carotid artery under awake neurological assessment or with brain blood flow measurements to see if the patient can tolerate a permanent closure. If not, the surgical plan is altered to include a bypass. Here, the integration of physiology (collateral flow assessment, cerebral perfusion

imaging) into surgical planning prevents major strokes by ensuring that adequate blood supply is maintained [44].

Endovascular vs. Surgical Physiology Considerations: It is worth noting, for completeness, that endovascular aneurysm treatment has different physiological considerations—typically less immediate risk of global perfusion issues because the arteries are not temporarily occluded (except briefly during certain adjuncts like balloon-assisted coiling). However, even in endovascular therapy, blood pressure is managed carefully (to prevent catheter-induced rupture or to augment flow if a vessel closes). Some of the lessons from surgical physiology are now informing endovascular practice too, such as maintaining blood pressure after coiling a ruptured aneurysm to prevent DCI. The synergy of surgical and critical care physiology management means that regardless of aneurysm treatment modality, the patient benefits from a comprehensive approach to cerebral protection. Importantly, many physiological principles traditionally emphasized in microsurgical aneurysm treatment are increasingly relevant to endovascular therapy. Blood pressure management, antiplatelet status, and cerebral perfusion optimization play a critical role during flow diversion, balloon-assisted coiling, and vasospasm treatment. Flow diverters, in particular, alter parent vessel hemodynamics and may affect distal perfusion, necessitating careful peri-procedural blood pressure control. Furthermore, endovascular management of vasospasm through intra-arterial vasodilators or angioplasty requires precise physiological monitoring to balance perfusion augmentation against hemorrhagic risk. Recognizing these shared principles broadens the applicability of a physiology-first paradigm across treatment modalities [45].

In summary, the results of integrating cerebrovascular physiology into aneurysm surgery are seen as: fewer intraoperative aneurysm ruptures, minimized ischemic time during necessary vessel occlusions, early detection and correction of flow impairments, and, ultimately, improved patient neurological outcomes. The process demands constant communication in the operating room and a culture of vigilance, but it pays dividends in patient safety.

3.6. Clinical Implications: A Paradigm Shift

Adopting a physiology-first approach in aneurysm surgery encourages neurosurgeons to think beyond the technical act of clipping and view themselves as acute neurointensivists in the operating room. It blurs the traditional silos between surgeon, anesthesiologist, and intensivist—requiring them to collaborate as a single unit focused on maintaining the brain's health. For neurosurgeons, it means learning to interpret neuromonitoring data and understanding hemodynamic management, while for anesthesiologists, it means an intimate awareness of neurovascular nuances. Many neurosurgery training programs now emphasize these aspects, teaching residents not just how to place a clip but when to request burst suppression or how to balance fluids and pressures for optimal CBF [46].

From a patient's perspective, these physiological considerations can be the difference between a good outcome and a devastating stroke despite technically "successful" aneurysm occlusion. Two patients with identical aneurysm clippings on angiography might have very different outcomes if one had uncontrolled hypotension and unrecognized branch occlusion during surgery and the other had carefully managed perfusion and immediate detection of an occlusion that was corrected. In this way, physiology management is an invisible but critical component of quality in aneurysm surgery [14].

Hospitals and surgical teams aiming to improve aneurysm outcomes should invest in the necessary monitoring equipment and protocols. This includes having neuromonitoring specialists available, maintaining protocols for blood pressure management (for instance, some centers have a dedicated neuroanesthesia team that automatically follows

agreed MAP targets for SAH cases), and ensuring that tools like micro-Doppler and ICG angiography are routinely at hand. It is also important to have contingency plans: if a neuromonitoring alert occurs, everyone should know their role (surgeon re-evaluate the clip, anesthesiologist optimize hemodynamics, etc., in parallel) [5].

3.7. Bullet Summary of Key Physiology-Guided Practices

- Maintain Adequate CPP: Avoid intraoperative hypotension, particularly in SAH patients with impaired autoregulation. Titrate vasopressors to keep MAP in high normal range and ensure CPP > 60–70 mmHg (or individualized to patient's baseline).
- Limit Ischemic Durations: Use temporary arterial occlusion sparingly. When necessary, keep occlusion times as short as possible (ideally <5 min at a stretch), and provide intermittent reperfusion if longer occlusion is required. Monitor the time actively and respond to nearing limits by re-establishing flow or employing protective measures.
- Employ Metabolic Suppression: During high-risk periods (e.g., temporary clipping or circulatory arrest), reduce the brain's metabolic demand. Achieve EEG burst suppression with anesthetics like propofol or barbiturate. Ensure that the patient is normothermic or mildly hypothermic, as appropriate. These measures may provide a physiological safety margin during high-risk periods, but they should complement—not replace—meticulous perfusion management and ischemia avoidance.
- Use Multimodal Monitoring: Integrate SSEP/MEP neuromonitoring to catch perfusion issues early. Utilize ICG angiography and micro-Doppler to verify vessel patency after clipping. If any monitor indicates potential ischemia, act immediately (adjust clip, raise blood pressure, etc.)—do not wait for a clinical deficit.
- Optimize CO_2 and O_2: Keep $PaCO_2$ in a range that avoids hypercapnia-induced high ICP or hypocapnia-induced vasoconstriction. Typically aim for mild hypocapnia (~35 mmHg) only if needed for brain relaxation. Ensure that the patient is well-oxygenated; avoid even transient hypoxemia, as it causes cerebral vasodilation and can steal blood from ischemic regions (inverse steal phenomenon).
- Plan for Collaterals and Bypass: Preoperatively assess the circle of Willis and collateral circulation (e.g., via angiography). If an aneurysm's treatment may require sacrificing an artery (planned or in case of rupture), be prepared with bypass options. Perform test occlusion studies for giant aneurysms when applicable. Intraoperatively, if a major branch is accidentally compromised and cannot be preserved, consider immediate bypass to prevent infarction.

These practices underscore a proactive rather than reactive approach. They shift the focus from "fixing the aneurysm" alone to "protecting the brain while fixing the aneurysm". Table 2 gives detailed coverage of all surgical decision thresholds.

Table 2. Practical physiological decision thresholds during aneurysm surgery.

Parameter	Threshold/Principle	Rationale
CPP (MAP–ICP)	Maintain $\geq$ 60–70 mmHg (higher for SAH or HTN-shifted autoregulation)	Sustains CBF when autoregulation is impaired.
Temporary clip duration	Prefer < 5 min single interval, intermittent reperfusion if >5–7 min	Limits ischemia; aligns with known metabolic vulnerability.
MEP/SSEP drop	>50% reduction = intervene immediately	Early surrogate marker of regional ischemia.

Table 2. *Cont.*

Parameter	Threshold/Principle	Rationale
$PaCO_2$	Maintain 35–40 mmHg (avoid profound hypocapnia)	Prevents CBF reduction from vasoconstriction.
Reperfusion strategy	Slow release of temporary clip	Reduces reperfusion injury.
Temperature	Mild permissive hypothermia 35–36 °C or normothermia	Minimizes metabolic demand without hypothermia complications.
ICG angiography	Mandatory confirmation after each permanent clip	Ensures no branch/perforator compromise.
MAP during temporary clipping	+10–20% above baseline	Enhances collateral flow through the circle of Willis.

4. Discussion

The integration of cerebrovascular physiology into aneurysm surgery represents a maturation of the field—recognizing that successful aneurysm obliteration is not truly a success unless the patient's brain function is preserved. In this discussion, we contextualize our narrative findings within the broader landscape of neurosurgery, examine remaining challenges, and propose future directions for research and practice.

Balancing Safety and Efficacy: Aneurysm clipping, especially in the post-endovascular era, is often reserved for cases that are complex (wide-neck aneurysms, arterial bifurcation aneurysms, those with incorporated branches, etc.). These are precisely the cases where a physiology-first approach is most needed, as the margin for error is thin. The discussion highlights that by leveraging physiologic knowledge, surgeons can push the boundaries of what's safely treatable. For instance, a giant aneurysm near the brainstem might historically have been deemed "inoperable" due to anticipated prolonged arterial occlusion time; but with deep hypothermic circulatory arrest and perfusion support, it becomes surgically treatable. However, these advanced measures come with their own risks (coagulopathy, longer ICU stays). So, the decision must always weigh the physiological cost. Ideally, improved monitoring and imaging techniques will allow us to tailor the most minimally impactful approach for each aneurysm—whether that is endovascular or microsurgical or a combination [47].

Neuromonitoring Nuances: One ongoing debate in the field revolves around neuromonitoring's reliability. The discussion notes that, despite high specificity, neuromonitoring can miss certain ischemic events or give false alarms. This underscores the need for multimodal monitoring and clinical judgment. For example, one could imagine an ideal future setup where regional cerebral blood flow could be continuously monitored in key brain areas (perhaps via novel imaging or sensors), supplementing SSEP/MEP information. Research into noninvasive CBF monitoring (like diffuse correlation spectroscopy or advanced EEG analysis to detect ischemic patterns) is underway and might eventually enhance intraoperative detection of ischemia beyond the major pathways that SSEPs/MEPs cover [48].

Autoregulation Monitoring: A cutting-edge concept in neurocritical care is the real-time monitoring of autoregulation (e.g., using indices like PRx—pressure reactivity index—derived from ICP and blood pressure). Some centers have begun experimenting with such calculations intraoperatively in an attempt to find each patient's optimal blood pressure (the CPP at which the brain vessels are the most reactive). In an OR setting, this is still experimental, but it reflects the sophistication that physiology-based management is reaching. The discussion acknowledges that at present, guidelines for intraoperative blood pressure in aneurysm surgery rely on population data and individual risk factors, but in the future,

we might have patient-specific autoregulatory thresholds measured on the fly to guide us [7].

Delayed Cerebral Ischemia (DCI): The discussion also bridges into the postoperative phase because the integration of physiology shouldn't abruptly stop once the clip is on. DCI after SAH remains a major cause of morbidity. Despite securing the aneurysm, about 30% of SAH patients can develop delayed strokes from vasospasm or microcirculatory dysfunction. The review emphasizes that the groundwork for preventing DCI is partly laid intraoperatively: avoiding additional surgical brain insults means the patient enters the critical vasospasm-prone period with as healthy a brain as possible (no compounding ischemic injuries, intact autoregulation to whatever degree possible). Intraoperative manipulation can trigger early vasospasm as well—for instance, aggressively handling arteries might cause vasospasm that becomes symptomatic later. Thus, gentle technique and occasional topical vasodilators during surgery are recommended when handling arteries in SAH cases. In the ICU, continued vigilance with modalities like TCD and maybe microdialysis or $PbtO_2$ in high-risk cases helps catch DCI early. New therapies for DCI (such as intra-arterial spasmolytics or even hypothermia) are being studied; their success will likely depend on patient selection, which circles back to understanding individual physiology [49].

Training and Teamwork: Another point of discussion is the culture and training required for a physiology-first approach. Surgeons historically were sometimes viewed as focused on the mechanical aspect ("clip it and ship it"), but modern neurosurgeons are expected to be well-versed in critical care. Likewise, neuroanesthesiology has become a distinct subspecialty that focuses on these details. The best outcomes are achieved in centers where there is seamless teamwork—for example, the anesthesiologist anticipates the surgeon's needs for temporary clipping without being prompted, and the surgeon trusts the anesthesiologist to manage blood pressure and not constantly worry about it, leaving the surgeon free to focus on the technical maneuvers. This trust and coordination are built through shared knowledge of physiology. Multi-disciplinary simulations and team training focusing on aneurysm rupture scenarios or monitoring alarm scenarios could be beneficial. When everyone in the OR is "fluent" in the language of cerebral physiology, responses to crises (like an intraoperative rupture or sudden loss of evoked potentials) are faster and more effective, mitigating harm [50].

Limitations of Current Knowledge: While we have considerable knowledge of cerebrovascular physiology, there are areas where data is limited, especially specific to aneurysm surgery. For example, exactly how long can a human brain tolerate MCA occlusion at normothermia? We extrapolate from studies and animal models, but individual variability is large. Some patients have astonishing collateral circulation and suffer no deficit after 30 min of occlusion; others have poor collaterals and show EEG changes at 3 min. Better preoperative assessment of collateral flow (via imaging techniques like CT angiography with perfusion or angiographic blood flow analysis) may in the future allow stratifying patients–those with weak collaterals might prompt a more cautious plan (like staging the surgery or doing a bypass first). More research is also needed on pharmacologic neuroprotection: is there a drug that can be given before clipping that truly reduces infarct risk? Trials of agents like magnesium, statins, or NMDA antagonists in SAH have been largely negative, but newer approaches (e.g., targeting inflammation or free radical injury specifically during reperfusion) might yield a protective adjunct that could be administered in the OR.

The discussion also touches on technology innovations, such as automated infusion systems that adjust blood pressure based on real-time feedback loops (closed-loop anesthesia systems). We can imagine an advanced monitor that integrates blood pressure, ICP, and perhaps near-infrared spectroscopy data and automatically keeps CPP within target

by adjusting vasoactive medications. These are not far-fetched, given progress in artificial intelligence applied to medicine. However, careful trials would be needed to trust such systems in something as delicate as aneurysm surgery.

Endovascular–Surgical Hybrid Approach: A nuanced point is that the lines between surgery and endovascular approaches are blurring in complex cases. Sometimes a combined approach is used, e.g., temporary balloon occlusion by an endovascular team during surgical clipping to reduce bleeding risk. This requires coordinated physiology management because the balloon occlusion creates an ischemic risk similar to a temporary clip. In such hybrid procedures, the principles discussed remain relevant and indeed more complex, since two teams (surgical and endovascular) must coordinate their actions in real time, with the anesthesiologist orchestrating the patient's physiological responses to both. Discussing these scenarios highlights the adaptability of the physiology-first approach: it is a mindset that can be applied regardless of the technique, focusing on the patient's cerebrovascular integrity as the priority [51].

Limitations of the Narrative Review: It is worth acknowledging that our review is narrative and not a formal meta-analysis. Thus, while we integrated evidence and expert opinion, there may be bias in emphasizing certain strategies. For example, one could argue that not all centers have the resources for full multimodal monitoring; yet they may still achieve good outcomes with solid basic principles. Our stance is that the core physiological principles hold universally (keep the brain perfused, avoid extremes, monitor what you can), and each center can implement these to the extent possible.

Future Directions: The physiology-first approach invites some important research questions. For instance:

- Can we develop a real-time "ischemia index" combining multiple monitor inputs to warn of impending stroke with high sensitivity?
- What is the role of novel metabolic monitoring (e.g., real-time cerebral microdialysis) in guiding intraoperative therapy—could we titrate anesthetic depth based on lactate levels from the brain?
- Could personalized autoregulation-guided blood pressure management improve outcomes compared to standard practice in a randomized trial?
- How do we best protect the brain during unavoidable prolonged occlusions (is there a place for things like remote ischemic preconditioning or novel pharmacologic agents given just before occlusion)?

These questions indicate a rich interface between basic cerebrovascular physiology research and practical neurosurgery. The discussion ultimately reinforces that intracranial aneurysm surgery, at its best, is a meticulous blend of art and science—the art of microsurgery performed within the scientific constraints of cerebral physiology. By respecting those constraints and even turning them to our advantage (e.g., using physiology to strategize), we elevate the level of care.

5. Conclusions

Intracranial aneurysm surgery has evolved from a purely mechanical endeavor into a finely tuned physiological intervention. A physiology-first approach places the patient's cerebrovascular well-being at the forefront of surgical planning and execution. By maintaining stable and adequate cerebral perfusion, respecting the limits of autoregulation, minimizing ischemic intervals, and utilizing intraoperative monitoring, neurosurgeons can significantly reduce the risk of ischemic injury and other complications during aneurysm repair. This integrative strategy demands teamwork and vigilance, but it rewards us with improved patient outcomes—patients who not only have their aneurysms secured but also wake up with their neurological functions intact.

In conclusion, the successful surgical management of intracranial aneurysms extends beyond the clip applier: it is equally about managing cerebral blood flow, metabolism, and pressure in tandem with the technical feat of aneurysm occlusion. Embracing this physiology-first paradigm is a hallmark of modern neurovascular surgery and a key to unlocking safer, more effective treatments for our patients. The operating room, in essence, becomes an ICU for the brain, and the neurosurgeon, a custodian of the brain's physiology as much as its anatomy. Through continued refinement of these principles and technologies to support them, we move closer to the ideal of treating the aneurysm while leaving the patient's brain unharmed and functionally whole.

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Abbreviations

The following abbreviations are used in this manuscript:

ACA	anterior cerebral artery
CBF	cerebral blood flow
CPP	cerebral perfusion pressure
DCI	delayed cerebral ischemia
ICP	intracranial pressure
MEP	motor evoked potential
NIRS	near-infrared spectroscopy
SAH	subarachnoid hemorrhage
SSEP	somatosensory evoked potential
TCD	transcranial Doppler ultrasound

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