

Perioperative Stroke: Anesthetic Considerations

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ABSTRACT

Background: Stroke is a devastating perioperative complication impacting the final surgical outcome. Maintenance of adequate cerebral perfusion pressure with normovolemia has become a standard anesthetic goal across specialties.

Methods: We describe two cases of perioperative ischemic stroke to highlight risk factors which increase vulnerability amidst patients undergoing major surgical interventions.

Conclusion: High index of suspicion and detailed clinical examination postoperatively are vital for early diagnosis to mitigate morbidity and mortality related to stroke.

Keywords: Anemia, Anesthesia challenges, Anticipated difficult airway, Anesthetic management in stroke, Blood loss, Hemodynamic, Hypotension, Ischemia, Perioperative management, Perioperative stroke.

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INTRODUCTION

Perioperative stroke is reported in 0.1–1.9% of patients undergoing noncardiac procedures.¹ A significantly higher incidence is reported following neurological (1.25%), vascular (1.07%), and cardiac interventions (0.98%).² With various modifiable and unmodifiable risk factors,³ surgery per se triggers an acute inflammatory response, which may initiate and exacerbate ischemic cerebral injury characterized by thrombosis, embolism, a watershed in fractions, and small vessel obstructions.⁴ The cerebral tissue hypoxia resulting secondary to the combination of anemia and β -blockade compounded by hypotension and perioperative hypercoagulable state contributing to ischemic insult leads to cerebral events occurring within 7 postoperative days. The myocardial infarction (MI) or cardiac arrest (MICA) (Table 1) calculator and the American College of Surgeons (ACS) surgical risk calculator (Table 2) are widely used to predict perioperative complications.⁵ Early diagnosis and intervention are challenging in patients undergoing prolonged, complex surgery under general anesthesia, especially if combined with elective postoperative ventilation.

CASE DESCRIPTION

Case 1

A 35-year-old male patient diagnosed with squamous cell carcinoma of the left buccal alveolar ridge is planned for a composite buccal mucosal resection with pectoralis major myocutaneous flap under general anesthesia. The patient had received three cycles of neoadjuvant chemotherapy over the preceding 3 months. Systemic examination and preoperative investigations were noted to be normal. To limit the blood loss during tumor resection,

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controlled hypotension was initiated with intravenous (IV) nitroglycerine infusion at 5 mcg/minute titrated to maintain mean arterial pressure (MAP) of 65–70 mm Hg. The surgical loss was estimated to be 1.5–2 L, replaced by 3.5 L of balanced salt solutions, 500 mL of colloid, and 350 mL of packed red blood cell (PRBC) transfusion. IV

Table 1: The MI or cardiac arrest calculator⁵

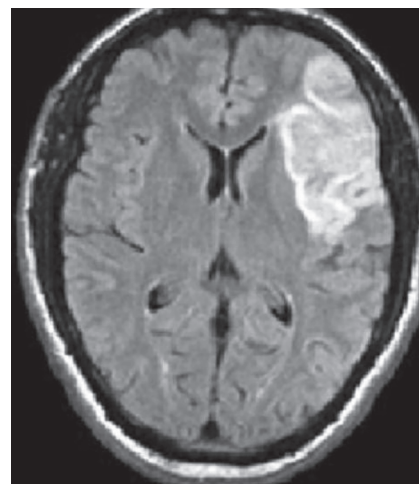
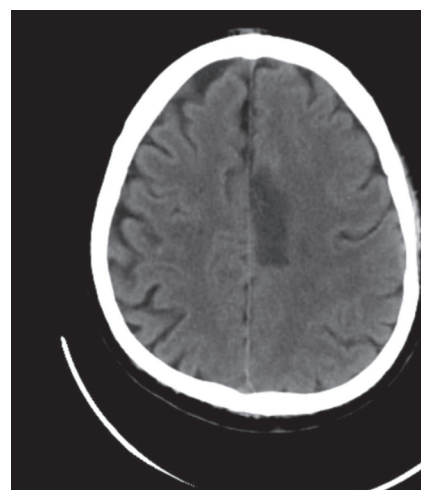
MICA
Type of surgery
Dependent functional status
Abnormal creatinine
American Society of Anesthesiologists class
Increased age

Table 2: ACS surgical risk calculator⁵

Variable	Categories*
Age group, y	<65, 65–74, 75–84, ≥85
Sex	Male, female
Functional status	Independent, partially dependent, totally dependent
Emergency case	Yes, no
ASA class	1 or 2, 3, 4, or 5
Steroid use for a chronic condition	Yes, no
Ascites within 30 days preoperatively	Yes, no
System sepsis within 48 hours preoperatively	None, SIRS, sepsis, septic shock
Ventilator dependent	Yes, no
Disseminated cancer	Yes, no
Diabetes	No, oral insulin
Hypertension requiring medication	Yes, no
Previous cardiac event	Yes, no
Congestive heart failure in 30 days preoperatively	Yes, no
Dyspnea	Yes, no
Current smoker within 1 year	Yes, no
History of COPD	Yes, no
Dialysis	Yes, no
Acute renal failure	Yes, no
BMI class	Underweight, normal, overweight, obese 1, obese 2, obese 3

y, years

nitroglycerine was discontinued in the latter part of the surgery. Hemodynamic stability with MAP between 65 and 75 mm Hg and normothermia was ensured. Arterial blood gas (ABG) was consistent with mild hyperventilation, and hematocrit was 27% at the end of the 6 hours long surgery. The patient was shifted to a recovery unit with a nasal endotracheal tube *in situ*, receiving 6 L of 100% oxygen *via* T-piece. The patient was extubated 2 hours later; he was asked to move all four limbs when a paucity of movements in his right upper and lower limb was noticed. Emergency computed tomography (CT) brain (Fig. 1) revealed patchy hypodensities in the left frontal lobe and left insular cortex suggestive of acute cerebral infarct. Carotid artery doppler and two-dimensional echocardiography showed normal study with left ventricle ejection fraction being 60%. A neurophysician consult and diagnosis consistent with ischemic stroke was made, following which a subcutaneous injection of enoxaparin sodium 40 mg was started on day 0 and continued for 5 days. Subsequently, a tablet of aspirin 75 mg was started along with physiotherapy and rehabilitation.

**Fig. 1:** CT brain, which revealed patchy hypodensities in the left frontal lobe and left insular cortex suggestive of acute cerebral infarct**Fig. 2:** Lacunar infarct in corona radiata

Case 2

A 51-year-old male diagnosed with advanced colon carcinoma was scheduled for an extended hemicolectomy. At admission, he reported good effort tolerance, and all relevant investigations were within normal limits. The surgery lasted for 6 hours with an estimated blood loss exceeding 3 L. Aggressive volume replacement consisted of 2.5 L of crystalloid, 1 L colloid, and 2 units of PRBC. There were two episodes of intraoperative hypotension with invasive pressure dropping to MAP of 50 mm Hg for approximately 10 minutes, which was stabilized with fluid bolus and intermittent doses of mephentermine (6 mg). An acceptable ABG, normothermia, and stable hemodynamic parameters lead to reversal and extubation within the operation theater. On arrival at postanesthesia care unit, the patient was noted to have slurred speech prompting an emergency CT brain (Fig. 2), revealing lacunar infarct (corona radiata) of the left temporal lobe. Neurophysician consultation confirmed a diagnosis of ischemic stroke. A subcutaneous injection of

Table 3: Recommended perioperative anticoagulation management strategies¹¹

Category	High-bleeding-risk procedure	Low-bleeding-risk procedure
High thromboembolic risk		
Warfarin	Give the last dose 6 days before the operation, a bridge with LMWH or UFH, and resume 24 hours postoperatively	Give the last dose 6 days before the operation, a bridge with LMWH or UFH, and resume 24 hours postoperatively
DOAC	Give the last dose 3 days before the operation, and resume 2–3 days postoperatively*	Give the last dose 2 days before the operation, and resume 24 hours postoperatively*
Intermediate thromboembolic risk		
Warfarin	Give the last dose 6 days before the operation, determine the need for bridging by clinician judgment and current evidence, and resume 24 hours postoperatively	Give the last dose 6 days before the operation, determine the need for bridging by clinician judgment and current evidence, and resume 24 hours postoperatively
DOAC	Give the last dose 3 days before the operation, and resume 2–3 days postoperatively*	Give the last dose 2 days before the operation, and resume 24 hours postoperatively*
Low thromboembolic risk		
Warfarin	Give the last dose 6 days before the operation; bridging is not recommended; resume 24 hours postoperatively	Give the last dose 6 days before the operation; bridging is not recommended; resume 24 hours postoperatively
DOAC	Give the last dose 3 days before the operation, and resume 2–3 days postoperatively*	Give the last dose 2 days before the operation, and resume 24 hours postoperatively*

DOAC indicates direct oral anticoagulant; LMWH, low-molecular-weight heparin; and UFH, unfractionated heparin; *in patients with creatinine clearance <50 mL/minute on dabigatran, the last dose should be given 3 days before the procedure for low-bleeding-risk surgery and 4–5 days before the procedure for high-bleeding-risk operation

enoxaparin sodium 40 mg for a week, followed by a tablet of aspirin 75 mg, was started along with physiotherapy.

DISCUSSION

Ischemic cerebral injury is characterized by thrombosis, embolism, small vessel occlusion, and watershed infarction, which are multifactorial. Underlying hypercoagulable state exacerbated by surgical stress embolic phenomenon, tissue hypoxia secondary to anemia as well as hypotension may contribute to hypoperfusion-related stroke.³ According to the American Heart Association (AHA) and American Stroke Association (ASA), hemorrhagic stroke is intra or extraparenchyma pooling of blood.⁶ Impact of tumor-related factors for stroke like embolism, neurovascular compression, and chemotherapy add to the etiology of stroke.⁷ Mechanisms like carcinoma mucins interacting with cellular selectins lead to microangiopathy and microthrombi, causing coagulation, supporting a significant increase in D-dimer levels in cancer patients.⁷ Moreover, patients receiving neoadjuvant chemotherapy have decreased cardiac function and hemodynamic instability during the perioperative; hence are more likely to develop perioperative cardiovascular events.⁸ In surgical patients, intraoperative bleeding can increase the risk of ischemic stroke and MI, which can be minimized by using antiplatelet agents perioperatively. But using antiplatelet drugs may cause bleeding, increasing the risk of thrombotic events, which outweigh its beneficial

effects. However, stopping them has been linked to a higher risk of MI and stroke. Hence, the latest guidelines and clinical judgment should be factored in when deciding to hold off on these drugs preoperatively.⁹ Recent guidelines from the ACS include recommendations for perioperative use of anticoagulants (Table 3) and antithrombotic agents (Table 4).^{7,10,11} Silent cerebral infarction, also known as “covert stroke” is an acute ischemic event that may be subclinical, hence diagnosed with a clinical decline in cognitive function, supported by radiological imaging. Following noncardiac surgery, the prevalence of ischemic stroke may reach 10%.¹² The fundamental basis of anesthetic management is to maintain adequate end-organ perfusion to all essential organs throughout the intraoperative period. Bijker et al. suggested a relation between hypotension and stroke when intraoperative MAP drops by 30% (per minute) compared to baseline.^{11,13} Levels of hemoglobin in the blood, arterial saturation, and cerebral blood flow contribute to cerebral oxygen saturation. Hence in anemia, a compensatory increase in cardiac output due to an increase in sympathetic outflow, venous return, contractility, and heart rate, together maintain cerebral blood flow and oxygen saturation.⁶ After isovolumic blood hemoglobin concentration drops to 6 gm/dL, healthy volunteers will show reversible cognitive impairment, although they will still have adequate global perfusion at blood hemoglobin concentrations as low as 5 gm/dL. However, people who have recently had a stroke or who have cerebrovascular illness do not have

Table 4: Summary of guidelines for perioperative management of antithrombotic medications¹¹

<i>Clinical area</i>	<i>Guideline</i>
Preoperative thromboembolic risk stratification	
Nonvalvular atrial fibrillation thromboembolic risk	Stratify thromboembolic risk with the congestive heart failure, hypertension, age > 75 years, Diabetes Mellitus, prior history of stroke or TIA, vascular disease, Age 65-74 years, sex category (CHA2DS2VASC) score
Prosthetic heart valve thromboembolic risk	Stratify risk according to valve type, location, and individual thromboembolic risk factors (atrial fibrillation, history of thromboembolism)
VTE thromboembolic risk	Stratify according to the time elapsed since VTE diagnosis and individual risk factors (cancer, thrombophilia); the elective operation should be deferred for ≥3 months after VTE diagnosis
Coronary artery disease coronary thromboembolism risk	The elective operation should be deferred for ≥14 days for balloon angioplasty, 30 days for bare metal stent placement, and 1 year for drug-eluting stent placement
Stroke thromboembolic risk	The elective operation should be deferred for ≥9 months after an ischemic stroke
Peripheral arterial disease thromboembolic risk	Patients presenting for surgical evaluation who receive antithrombotic medication for the symptomatic peripheral arterial disease should be managed in close consultation with a vascular specialist or vascular surgeon.
Procedural bleeding risk stratification	
The bleeding risk inherent to patient characteristic	Stratify risk with the HAS-BLED score
The bleeding risk inherent to the procedure	Largely a subjective decision on behalf of the operating surgeon; most operations under the purview of the general surgeon will be classified as at least low risk
Perioperative bridging therapy	
Antiplatelet therapy	Currently, there is no evidence to suggest a benefit from the use of antiplatelet bridging therapy perioperatively.
DOAC therapy	Currently, there is no evidence to suggest a benefit from the use of heparin bridging in patients taking DOACs.
Warfarin therapy	Use for those classified as high VTE risk; discontinue warfarin 5 days before an elective procedure, and when the INR falls below the patient's therapeutic range, begin LMWH at a therapeutic dose until 24 hours before the procedure; reinstitute warfarin 12–24 hours after operation; reinstitute LMWH 48–72 h after the operation
Perioperative antithrombotic medication management strategy	
Unfractionated heparin	
IV	Hold 4–6 hours before an elective operation
Subcutaneous	Hold 12–24 hours before an elective operation
LMWH	Hold 24 hours before operation; resume 48–72 hours after the operation
Warfarin	Hold for 5 days before an elective operation; resume at previous dosing levels 12–24 hours after the operation
Dabigatran	
Normal renal function	Hold for 2 days before high-bleeding-risk operation and 1 day before low-bleeding-risk operation; resume 2–3 days after high-bleeding-risk operation and 1 day after low-bleeding-risk operation
Impaired renal function	Hold for 4 days before high-bleeding-risk operation and 2 days before low-bleeding-risk operation
Rivaroxaban, apixaban, edoxaban	Hold for 2 days before high-bleeding-risk operation and 1 day before low-bleeding-risk operation; resume 2–3 days after high-bleeding-risk operation and 1 day after low-bleeding-risk operation

Contd...

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<i>Clinical area</i>	<i>Guideline</i>
Aspirin	Hold aspirin for 7–10 days before high-bleeding-risk operation in patients who have not had a PCI; resume when bleeding risk has diminished; in patients with recent PCI, consult with a cardiologist
Clopidogrel, prasugrel, ticagrelor	Hold 5–7 days before low- and high-bleeding-risk operation; resume when bleeding risk has diminished
Consideration in the nonelective setting	
Vitamin K antagonist	Administer vitamin K and 4-factor PCC to patients with an elevated INR secondary to warfarin who are actively bleeding or require urgent operation
Dabigatran	Administer idarucizumab to patients with evidence of significant dabigatran levels (by a history of ingestion or laboratory parameter) who are bleeding or require an emergency operation
Other DOAC	Administer 4-factor PCC transfusion (50 U/kg) for partial reversal In patients with evidence of active factor Xa inhibitor as needed in an emergency situation
Antiplatelet agent	Transfuse 1 pooled unit of platelets immediately before the operation and redose as needed for ongoing bleeding

DOAC, direct oral anticoagulant; INR, International normalized ratio; LMWH, low-molecular-weight heparin; PCC, prothrombin complex concentrate; PCI, percutaneous coronary intervention; and VTE, venous thromboembolism

the same cerebrovascular reserve as healthy volunteers, and they could experience brain hypoxia at hemoglobin thresholds higher than 6 gm/dL. The rapid development of nonfocal neurological impairments, such as agitated delirium, autonomic instability, or delayed awakening from anesthesia, is the defining feature of an acute stroke.⁶ For successful postoperative stroke management, continuous surveillance for clinical symptoms, activation of the rapid response team, emergent neurological imaging, and consultation are essential. Practice should be governed by formal protocols, which should include immediate evaluation of clinical parameters such as blood pressure, glucose management, and metabolic status.⁴ Though treatment of perioperative is open for discussion, in patients suspected of having a large vessel occlusion (LVO), additional CT angiography and perfusion studies should be performed along with a noncontrast head CT scan to rule out intracranial hemorrhage right away. As supported by recent studies, in individuals with LVO, mechanical thrombectomy can reduce impairment up to 24 hours after the onset of stroke symptoms. According to the AHA/ASA guidelines, patients following recent major surgery may be candidates for IV fibrinolysis, albeit a thorough risk-benefit analysis should be carried out first. Patients reported with symptoms of stroke following major surgery may be considered for treatment with IV alteplase within 4.5 hours from the time of last known well-being.¹¹

CONCLUSION

Anesthesiologists, as perioperative physicians, need to adopt a multidisciplinary approach to decreasing stroke-related complications in the perioperative period. Preemptive steps taken as part of patient optimization and maintenance of

perioperative hemodynamic stability being the cornerstone of anesthetic management, early diagnosis, and prompt intervention are crucial.

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