REVIEW ARTICLE

CURRENT CONCEPTS

Perioperative Stroke

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STROKE IS ONE OF THE MOST FEARED COMPLICATIONS OF SURGERY. TO PROvide adequate preventive and therapeutic measures, physicians need to be knowledgeable about the risk factors for stroke during the perioperative period. In this article, I review the pathophysiology of perioperative stroke and provide recommendations for the stratification of risk and the management of risk factors.

INCIDENCE

The incidence of perioperative stroke depends on the type and complexity of the surgical procedure. The risk of stroke after general, noncardiac procedures is very low. Cardiac and vascular surgeries — in particular, combined cardiac procedures — are associated with higher risks[1-7] (Table 1). The timing of surgery is also important. More strokes occur after urgent surgery than after elective surgery.[1]

Despite advances in surgical techniques and improvements in perioperative care, the incidence of perioperative strokes has not decreased, reflecting the aging of the population and the increased number of elderly patients with coexisting conditions who undergo surgery. Perioperative strokes result in a prolonged hospital stay and increased rates of disability, discharge to long-term care facilities, and death after surgery.[7]

PATHOPHYSIOLOGY

Radiologic and postmortem studies indicate that perioperative strokes are predominantly ischemic and embolic.[8-10] In a study of 388 patients with stroke after coronary-artery bypass grafting (CABG), hemorrhage was reported in only 1% of patients; 62% had embolic infarcts[11] (Fig. 1). The timing of embolic strokes after surgery has a bimodal distribution. Approximately 45% of perioperative strokes are identified within the first day after surgery.[1,11] The remaining 55% occur after uneventful recovery from anesthesia, from the second postoperative day onward.[1,11] Early embolism results especially from manipulations of the heart and aorta or release of particulate matter from the cardiopulmonary-bypass pump.[1,7,13] Delayed embolism is often attributed to postoperative atrial fibrillation, myocardial infarction resulting from an imbalance between myocardial oxygen supply and demand, and coagulopathy.[13] Surgical trauma and associated tissue injury result in hypercoagulability. Several studies have shown activation of the hemostatic system and reduced fibrinolysis after surgery, as evidenced by decreased tissue plasminogen activator (t-PA) and increased plasminogen activator inhibitor type 1 activity and increased levels of fibrinogen-degradation products, thrombin–antithrombin complex, thrombus precursor protein, and D-dimer immediately after surgery and up to

14 to 21 days postoperatively.[14-16] General anesthesia, dehydration, bed rest, stasis in the postoperative period, and perioperative withholding of antiplatelet or anticoagulant agents can aggravate surgery-induced hypercoagulability and increase the risk of perioperative thrombogenic events, including stroke.

There is increasing recognition that short- and long-term cognitive changes, manifested as short-term memory loss, executive dysfunction, and psychomotor slowing, occur after CABG.[7] The multifactorial causes of these changes include ischemic injury from microembolization, surgical trauma, preexisting vascular changes, and temperature during surgery.

Contrary to common belief, most strokes in patients undergoing cardiac surgery, including those with carotid stenosis, are not related to hypoperfusion. Deliberate hypotension induced by anesthesia does not seem to adversely affect cerebral perfusion, nor does it considerably increase the risk of perioperative stroke due to hypoperfusion in patients with carotid stenosis.[6,11,15] Most perioperative strokes in such patients are embolic and are either contralateral to the affected carotid artery or bilateral (Fig. 2), so they cannot be attributed to carotid stenosis alone.[6] In one study, only 9% of strokes after CABG were in watershed (hypoperfusion) areas.[11] As expected, most were identified within the first day after surgery. Delayed hypoperfusion strokes, when they occur, are often precipitated by postoperative dehydration or blood loss. Other, less common causes of perioperative stroke include air, fat, or paradoxical embolism and arterial dissection resulting from neck manipulations during induction of anesthesia and neck surgery (Table 2).

Table 1. Incidence of Stroke after Various Surgical Procedures.

Procedure	Risk of Stroke (%)
General surgery[2]	0.08–0.7
Peripheral vascular surgery[3]	0.8–3.0
Resection of head and neck tumors[4]	4.8
Carotid endarterectomy[5]	5.5–6.1
Isolated CABG[1,7]	1.4–3.8
Combined CABG and valve surgery[1,7]	7.4
Isolated valve surgery[1]	4.8–8.8
Double- or triple-valve surgery[1]	9.7
Aortic repair[7]	8.7

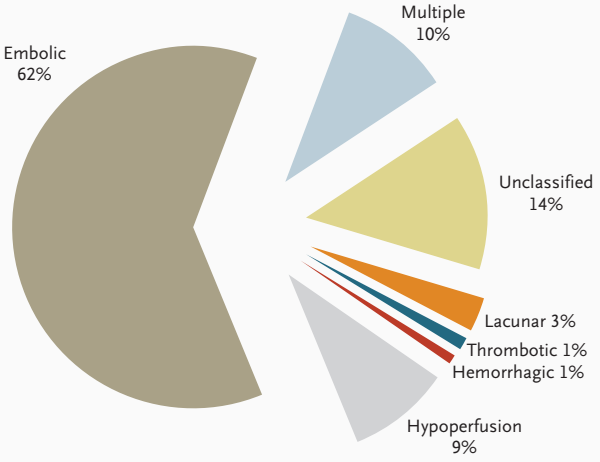

Figure 1. Mechanisms of Perioperative Stroke.
Data are from Likosky et al.[12]

RISK STRATIFICATION

Several patient- and procedure-related factors are associated with an increased risk of perioperative stroke (Table 3).[2,4,6,8,13,15,16] Evaluating the risk–benefit ratio for each patient before surgery is essential to optimize care. There are several models for stratifying the risk of perioperative stroke.[7,17] Investigators from the Northern New England Cardiovascular Disease Study Group used bootstrapping techniques to develop and validate a model predicting the risk of stroke after CABG, according to weights assigned to seven preoperative variables. These variables were identified in an observational study of 33,062 consecutive patients undergoing CABG.[17] Table 4 summarizes the major elements of this predictive model.[18]

RISK MODIFICATION

Physicians can implement diagnostic, therapeutic, and procedural measures to modify the perioperative risk in order to prevent stroke and minimize morbidity. A history of stroke or transient ischemic attack is a strong predictor of perioperative stroke.[2,4,6-8,12,13,17] Therefore, physicians must inquire specifically about such a history and fully investigate and treat the cause of a stroke or transient ischemic attack that has occurred within the previous 6 months, especially if a previous

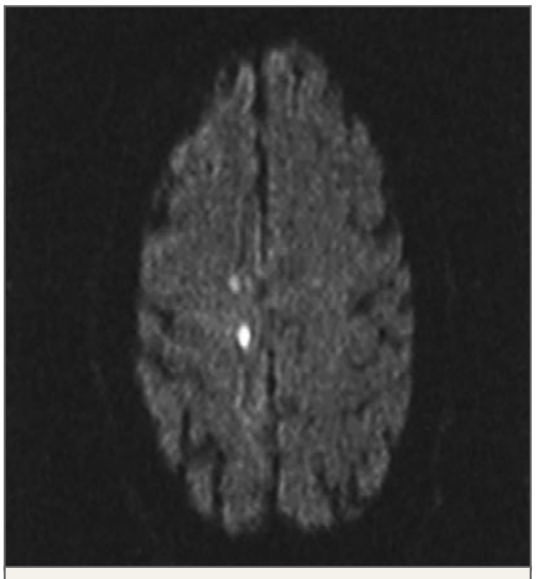

Figure 2. MRI Scan Showing Embolic Infarcts in a 74-Year-Old Man with Stroke after CABG.

The patient had left extracranial internal carotid stenosis (60 to 69% on Doppler ultrasonography), type 2 diabetes mellitus, hypertension, and hyperlipidemia. The diffusion-weighted MRI scan shows small, bright-signal abnormalities in the right hemisphere, which are consistent with embolic infarcts, with no evidence of infarcts ipsilateral to the carotid lesion.

evaluation was not done or was incomplete or if the patient's neurologic status worsened after the event. Brain vascular reserve is often tenuous in the days after a stroke, so it is important to allow sufficient time after a stroke for the patient's hemodynamic and neurologic status to stabilize before an elective surgical procedure is performed.

The risk of perioperative stroke is high among patients with symptomatic carotid stenosis.[6,19] Such patients should be evaluated by means of carotid Doppler ultrasound; patients with carotid stenosis that has been symptomatic within the previous 6 months benefit from carotid revascularization before undergoing cardiac or major vascular surgery.[20] In patients with both cardiac and carotid disease who are undergoing urgent cardiac surgery — a population in which the risks of complications and death from cardiac causes exceed the risk of stroke — a reversed-stage approach (carotid revascularization after CABG) or a combined approach (simultaneous carotid revascularization and CABG) may be undertaken. However, the combined approach may be associated with higher morbidity.[21] The safety of carotid endarterectomy as compared with carotid stenting is under investigation. Preliminary evidence suggests that carotid stenting is probably more suitable for patients with concomitant symptomatic carotid and coronary artery disease in whom preoperative carotid revascularization is being considered.[22]

The effect of asymptomatic carotid stenosis, especially when it is unilateral, on the risk of perioperative stroke is often overstated. A review of the literature from 1970 to 2000 showed an overall risk of stroke of 2% after CABG; the risk increased to 3% among patients with asymptomatic unilateral carotid stenosis of 50 to 99%, 5% among those with bilateral stenoses of 50 to 99%, and 7% among those with carotid occlusion.[6] Sixty percent of perioperative infarcts in patients with carotid stenosis were attributed to causes other than carotid disease.[6]

The discovery of asymptomatic carotid stenosis often begins with the detection of a cervical bruit during preoperative evaluation. Since the presence of an asymptomatic bruit, in itself, is not correlated with the risk of perioperative stroke or the severity of the underlying carotid stenosis,[23] routine carotid evaluation by means of Doppler ultrasound is unnecessary in these circumstances. However, carotid ultrasound may be warranted in patients with bruits who have a recent history of transient ischemic attack–like symptoms. Furthermore, few data provide support for the routine use of prophylactic revascularization before major cardiovascular surgery in patients with asymptomatic carotid stenosis.[24]

Revascularization before surgery is generally unwarranted because it exposes patients to the risks of perioperative stroke and myocardial infarction twice without significantly reducing the

Table 2. Uncommon Causes of Perioperative Stroke.

Air embolism after endoscopic procedures, intravascular interventions, and cardiopulmonary bypass
Fat embolism after orthopedic procedures
Paradoxical embolism from postoperative deep-vein thrombosis in patients with patent foramen ovale
Extracranial carotid- or vertebral-artery dissections resulting from neck manipulations and hyperextension of the neck during induction of anesthesia, neck surgery, or dental procedures
Dislodgment of arterial atherosclerotic plaques resulting from manipulations of extracranial internal carotid or vertebral arteries during neck surgeries
Spinal cord infarct after surgery to repair an abdominal aortic aneurysm

Table 3. Risk Factors for Perioperative Stroke.

Preoperative (patient-related) risk factors
Advanced age (>70 yr)*
Female sex
History of hypertension, diabetes mellitus, renal insufficiency (creatinine, >2 mg/dl [177 μmol/liter]), smoking, chronic obstructive pulmonary disease, peripheral vascular disease, cardiac disease (coronary artery disease, arrhythmias, heart failure), and systolic dysfunction (ejection fraction, <40%)†
History of stroke or transient ischemic attack
Carotid stenosis (especially if symptomatic)
Atherosclerosis of the ascending aorta (in patients undergoing cardiac surgery)
Abrupt discontinuation of antithrombotic therapy before surgery
Intraoperative (procedure-related) risk factors
Type and nature of the surgical procedure
Type of anesthesia (general or local)
Duration of surgery and, in cardiac procedures, duration of cardiopulmonary bypass and aortic cross-clamp time
Manipulations of proximal aortic atherosclerotic lesions
Arrhythmias, hyperglycemia, hypotension, or hypertension
Postoperative risk factors
Heart failure, low ejection fraction, myocardial infarction, or arrhythmias (atrial fibrillation)
Dehydration and blood loss
Hyperglycemia

* Age itself does not predict the risk of stroke, and the 70-year cutoff is arbitrary. However, advanced age is a marker of decreased cerebrovascular reserve and multiple coexisting conditions.
† The effect of systolic dysfunction on the risk of perioperative stroke is particularly pronounced among patients undergoing left-main-stem revascularization and those with atrial fibrillation.

risk of stroke.[6,19,20] However, some patients with hemodynamically significant, high-grade, asymptomatic carotid stenosis — in particular those with bilateral stenoses — may benefit from carotid revascularization before elective surgery. Therefore, the extent of the preoperative evaluation of patients with asymptomatic carotid disease should be individualized. At a minimum, the evaluation should include a detailed neurologic examination, a history taking designed to elicit unreported symptoms of transient ischemic attack, and brain computed tomographic (CT) or magnetic resonance imaging (MRI) studies to rule out "silent" ipsilateral infarcts. Additional tests such as transcranial Doppler ultrasonography and intracranial CT or magnetic resonance angiography to determine the microembolic signal load, intracranial blood flow, and hemodynamic significance of the carotid stenosis[25,26] may provide incremental information to identify patients who could benefit from carotid revascularization before surgery. However, the clinical usefulness and cost-effectiveness of hemodynamic testing before surgery are debatable, and further development and validation of these tests are required before their routine preoperative use in patients with carotid stenosis can be advocated.

Aortic atherosclerosis is an independent predictor of the risk of perioperative stroke, particularly among patients undergoing cardiac surgery and revascularization of the left main-stem artery.[1,13] Identifying the extent and location of aortic atherosclerosis before or at the time of surgery by means of transesophageal echocardiography or intraoperative epiaortic ultrasound is important to modify the surgical technique and change the site of aortic cannulation or clamping to avoid calcified plaques. The use of echocardiography-guided aortic cannulation[27] and intraaortic filtration[28] during CABG can reduce the risk of perioperative stroke.

Systolic dysfunction increases the risk of perioperative stroke, particularly among patients with atrial fibrillation.[13] Preoperative echocardiogra-

Table 4. Model for Predicting the Risk of Stroke among Patients Undergoing CABG.*

Risk Factor	Weighted Score
Advanced age	
60–69 yr	1.5
70–79 yr	2.5
≥80 yr	3.0
Nonelective surgery	
Immediate	1.5
Within hours	3.5
Female sex	1.5
Ejection fraction <40%	1.5
Vascular disease†	1.5
Diabetes mellitus	1.5
Creatinine >2 mg/dl (177 μmol/liter), or dialysis	2.0
Total Score	**Risk of Stroke (%)**
0–1	0.4
2	0.6
3	0.9
4	1.3
5	1.4
6	2.0
7	2.7
8	3.4
9	4.2
10	5.9
11	7.6
12	>10.0

* Adapted from Charlesworth et al.[18] The risk factors have an additive effect, producing an aggregate estimate of the risk of perioperative stroke among patients undergoing CABG.

† This includes a history of stroke or transient ischemic attack, vascular surgery, carotid stenosis or bruit, or leg amputation or vascular bypass surgery.

phy to assess the ejection fraction and to look for intracardiac emboli and aortic atherosclerosis may help to stratify the risk of stroke and modify the treatment strategy for patients with heart failure, atrial fibrillation, or suspected valvular disease and those undergoing revascularization of the left main stem.

Atrial fibrillation occurs in 30 to 50% of patients after cardiac surgery, with a peak incidence between the second and fourth postoperative days, and it is a major cause of many perioperative strokes.[1,8,9,13,17,18,29] Postoperative electrolyte imbalance and shifts in the intravascular volume increase atrial ectopic activity, which confers a predisposition to arrhythmia[29] (Table 5). It is therefore important to monitor patients for arrhythmias for a minimum of 3 days after cardiac procedures as well as to correct electrolytes and fluid volume during the postoperative period. The incidence of postoperative atrial fibrillation and stroke may be reduced by the prophylactic administration of amiodarone and beta-blockers, beginning 5 days before cardiac surgery.[30] Patients with preexisting atrial fibrillation may be receiving antiarrhythmic or rate-controlling agents, which should be continued throughout the perioperative period, with the use of intravenous formulations if needed. No controlled trials have specifically addressed the use of anticoagulation therapy for new-onset, postoperative atrial fibrillation, which often resolves spontaneously after 4 to 6 weeks. The American College of Chest Physicians recommends the consideration of heparin therapy particularly for high-risk patients, such as those with a history of stroke or transient ischemic attack, in whom atrial fibrillation develops after surgery and the continuation of anticoagulation therapy for 30 days after the return of a normal sinus rhythm.[31]

The discontinuation of warfarin or antiplatelet agents in anticipation of surgery exposes patients to an increased risk of perioperative stroke.[32,33] The risk is particularly high among patients with coronary artery disease.[32] A review of the perioperative outcomes of patients requiring long-term warfarin therapy showed that rates of thromboembolic events varied according to the management strategy; the rate was 0.6% for discontinuation of warfarin without the administration of intravenous heparin and 0% for discontinuation of warfarin with intravenous heparin used as bridge therapy.[34] The rate of major bleeding that occurred while the patient was receiving a therapeutic dose of warfarin was 0.2% for dental procedures and 0% for arthrocentesis, cataract surgery, and upper endoscopy or colonoscopy with or without biopsy.

A study of patients at high risk for thromboembolism who were undergoing knee or hip replacement surgery showed that continued use of moderate-dose warfarin therapy (international normalized ratio, 1.8 to 2.1) during the perioperative period was safe and effective in preventing embolic events.[35] These studies suggest that most patients can undergo dental procedures, arthrocentesis, cataract surgery, diagnostic endos-

copy, and even orthopedic surgery without interrupting their antiplatelet or oral anticoagulation regimen. When oral anticoagulation must be withheld for other invasive procedures, the time during which anticoagulation is being withheld should be minimized. Bridge therapy with heparin after discontinuation of warfarin and early postoperative resumption of anticoagulation is recommended, especially in patients at high risk for thromboembolism, such as those with a history of systemic embolism or atrial fibrillation and those with mechanical valves.[36]

Surgeons should attempt to minimize the duration of surgery whenever possible. Lengthy operations are associated with higher risks for perioperative illness and stroke. The choice of the surgical technique according to the patient's risk profile is also important. Among patients with a low ejection fraction, the risk of stroke may be lower with coronary angioplasty than with CABG,[37] and off-pump as compared with on-pump cardiopulmonary bypass may be associated with a lower risk of stroke among patients with severe atheromatous aortic disease.[38] A "no-touch" technique, avoiding manipulations of the ascending aorta, is advised whenever feasible in patients with aortic arch disease.[39]

The type of anesthesia and the anesthetic agent are additional considerations. Regional anesthesia is less likely than general anesthesia to result in perioperative complications.[40] Some data suggest that isoflurane and thiopentone may provide neuroprotection.[41]

The optimal level of blood pressure during surgery is debatable.[12,17] In one study, the incidence of cardiac and neurologic complications, including stroke, was significantly lower when the mean systemic arterial pressure was 80 to 100 mm Hg during CABG, as compared with 50 to 60 mm Hg, suggesting that a higher mean systemic arterial pressure during CABG is safe and improves outcomes.[42] Charlson et al.[43] suggested that intraoperative blood pressure should be evaluated in relation to preoperative blood pressure; they reported that prolonged changes of more than 20 mm Hg or 20% in relation to preoperative levels result in perioperative complications. Efforts to match intraoperative and early postoperative blood pressure to the patient's preoperative range can reduce the risks of perioperative stroke and death.[27]

The management of the patient's temperature during surgery also influences outcomes. A review showed a trend toward a reduction in the rate of perioperative stroke when the patient's core body temperature during cardiopulmonary bypass was 31.4 to 33.1°C, as compared with a temperature of more than 33.2°C.[44] However, this benefit is offset by a higher rate of death among patients with lower core temperatures. On balance, it is advisable to maintain mild hypothermia (approximately 34°C) during cardiopulmonary bypass and to avoid rapid rewarming and hyperthermia after surgery in order to minimize the risk of cognitive impairment after CABG.[44]

Table 5. Predictors of Postoperative Atrial Fibrillation.

Advanced age
History of preoperative atrial fibrillation or supraventricular arrhythmias
Preoperative heart failure or low ejection fraction
Perioperative withdrawal of angiotensin-converting–enzyme inhibitors or beta-blockers
Previous inferior-wall myocardial infarction
Combined CABG and valve-replacement surgery
High postoperative magnesium levels

Hyperglycemia, intraoperatively and postoperatively, is associated with increased rates of atrial fibrillation, stroke, and death.[45] Intensive monitoring and control of the patient's glucose level during the perioperative period is important. The administration of insulin and potassium during and after surgery to keep blood glucose levels below 140 mg per deciliter (7.8 mmol per liter) is associated with improved outcomes.[46]

The prevention and treatment of inflammation and infections during the preoperative and postoperative periods are always indicated. A high white-cell count correlates with an increased incidence of stroke, poor outcome, and the development of postoperative atrial fibrillation.[47,48]

Postoperative systolic dysfunction and arrhythmias are associated with an increased incidence of postoperative stroke.[1,7-9] Therefore, electrolyte levels and fluid volume should be optimized, and the patient must be closely monitored for signs of heart failure and arrhythmias during the postoperative period. It is also helpful to encourage early postoperative mobility and implement prophylactic measures to prevent deep-vein thrombosis. A paradoxical embolism leading to stroke may occur in patients with a right-to-left shunt.

Finally, there is evidence that initiation of antiplatelet therapy such as aspirin after cardiac and

carotid surgeries reduces the incidence of postoperative stroke without increasing the odds of bleeding complications.[49,50] There is also evidence that supports the preoperative use of statins, irrespective of the patient's lipid profile, to reduce the risk of perioperative stroke in patients undergoing cardiovascular surgery.[51]

MANAGEMENT

In patients who have recently undergone major surgery, treatment with intravenous t-PA is contraindicated because of an increased risk of bleeding. However, intraarterial administration of t-PA and endovascular mechanical clot disruption are alternative options. A few case series suggest that the use of intraarterial thrombolysis within 6 hours after the onset of a perioperative stroke is relatively safe.[52,53] In a study of 36 patients who received intraarterial t-PA after a perioperative stroke, partial to complete recanalization was achieved in 80% of the patients, 38% had no symptoms or only slight disability after discharge, and the mortality rate was similar to that reported in nonsurgical patients treated with intraarterial thrombolysis.[53] Bleeding at the surgical site occurred in 17% of the patients. Most of this bleeding was minor. Intracranial hemorrhage occurred in 25% of the patients; however, only 8% had worsening symptoms. Intracranial hemorrhage was most common in patients who underwent a craniotomy. There are few data on the use of mechanical thrombectomy or embolectomy in patients with perioperative stroke. However, these techniques may be useful in the postoperative setting, especially when the use of intraarterial thrombolysis is contraindicated. The limited window for implementing these interventions highlights the importance of rapid recognition of perioperative stroke and immediate neurologic consultation.

FUTURE DIRECTIONS

Preoperative prophylaxis against perioperative stroke is an appealing concept. A few randomized trials have assessed the effect of neuroprotective drugs on the risk of stroke and cognitive decline among patients undergoing CABG.[54-56] Preoperative administration of statins[51] or beta-blockers[30] does appear to reduce the incidence of stroke and cognitive decline after CABG. There is also some evidence, albeit controversial, that the antifibrinolytic agent aprotinin may have similar effects.[56] These results indicate that neuroprotection may be successful in the perioperative setting and that it merits further investigation. Randomized, controlled clinical trials are also needed to identify the best preventive and management strategies for perioperative stroke.

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