

## Section I

## Iatrogenic ischemic strokes: peri- and postoperative strokes

## Chapter

## 1

## Stroke after general surgery

Magdy Selim and Arne Lindgren

**Introduction**

Stroke during the perioperative period is a devastating complication of surgery. It offsets the potential benefits of surgery and results in dramatic increases in mortality and healthcare costs. There is a paucity of information about stroke in patients undergoing general surgery such as abdominal, thoracic, orthopedic, dental, and gynecological procedures. In this chapter, we review the incidence, predisposing risk factors, etiological mechanisms, and preventive and management strategies of stroke in patients undergoing general, non-cardiovascular, non-neurosurgical procedures.

**The prevalence and burden of stroke in general surgery patients**

The true incidence rate of stroke in patients undergoing general surgery is uncertain. The reported incidence rates vary from <1% up to 4.8% [1–10], depending on the nature of the study – retrospective vs. prospective, whether a detailed neurological examination or diagnostic brain imaging was performed, and whether advanced imaging using diffusion-weighted magnetic resonance imaging (DWI-MRI) was obtained. The vast majority of published studies have been retrospective and lacked detailed neurological and radiological assessments, in particular DWI-MRI. It is therefore likely that the actual rates of stroke after general surgical procedures are higher than reported as many patients with minor or rapidly resolving deficits due to stroke might be misdiagnosed with “post-operative confusion” or “residual effects of anesthesia.” In our own experience, approximately 13% of surgical patients seen by the neurology service for postoperative confusion were found to have a stroke.

Stroke in surgical patients is associated with high morbidity and mortality – about 26% up to 60% in patients with history of prior stroke [3,7]. It increases the cost of care as these patients tend to have longer length of hospitalization, often require an intensive level of care, and frequently require transfer to rehabilitation or long-term care facilities upon discharge.

**Risk factors for stroke in general surgery patients**

Although surgery and anesthesia themselves contribute to stroke risk, the patient’s baseline comorbidities play a dominant role. Table 1.1 summarizes the patient-related risk factors for stroke after general surgical procedures. Overall, they do not significantly differ from the risk factors predisposing to stroke in the general population. However, a case-control study of 61 patients with ischemic strokes after urogenital, gastrointestinal, orthopedic, and pulmonary surgical procedures and 122 age-, sex-, and procedure-matched controls showed that surgery substantially increases the risk of stroke (odds ratio = 2.9) [4], indicating that the risk of stroke after surgery does not simply represent the random chance of stroke occurrence in the general population.

Advanced age (usually >70 years), preoperative history of stroke or transient ischemic attack (TIA), and atrial fibrillation emerge as the most important risk factors for stroke in patients undergoing general surgery [1–5,8].

The type of surgery also influences the risk of perioperative stroke. The stroke risk is higher in head and neck resection and orthopedic procedures, in particular hip replacement, than in other general surgical procedures.

### Section I: Iatrogenic ischemic strokes: peri- and postoperative strokes

**Table 1.1** Patient-related risk factors for stroke in general surgery patients.

Risk factor	Comments
Age	Older age is a marker of increased comorbidities, and is often associated with restricted cerebral autoregulation and subclinical vascular disease, which makes older patients more susceptible and vulnerable to cerebral ischemic insult
Sex	Women appear to be at greater risk for perioperative stroke. This may be attributed to a prothrombotic state due to estrogen or use of hormone replacement therapy
Previous history of stroke or TIA	Previous stroke or TIA suggests existing pathological cerebrovascular condition(s), which may predispose to stroke recurrence during the perioperative period
Diabetes mellitus	Diabetics have macro- and microvascular disease, and impaired autoregulation, which increase their risk for stroke after surgery
Smoking and chronic obstructive pulmonary disease	Smoking and COPD are associated with increased risk of perioperative complications including stroke
Hypertension	Chronic hypertension is often associated with heart failure and impaired cerebral autoregulation. Significantly elevated blood pressure can also cause a hemorrhagic stroke
Peripheral vascular disease	This is a marker of generalized atherosclerosis, which could involve the cerebral vasculature
Renal insufficiency – preoperative serum creatinine >2 mg/dL (176 μmol/L)	Patients with renal failure are at greater risk of electrolyte derangements, perioperative atrial arrhythmias, and fluctuations in blood pressure
Atrial fibrillation (AF)	Patients with chronic AF on oral anticoagulation are at significant risk if anticoagulation is withheld before surgery. Perioperative electrolyte derangements, in particular high magnesium levels, and preoperative withdrawal of some medications, such as beta-blockers, can lead to the development of postoperative AF de novo
Heart failure	Heart failure and low cardiac output can lead to hemodynamic instability, impaired cerebral perfusion, and intracardiac clot formation in the setting of perioperative dehydration, hypovolemia, and blood loss
Carotid stenosis	Carotid stenosis is associated with increased risk for perioperative stroke in patients with preoperative symptoms of stroke or TIA, i.e., symptomatic carotid stenosis. The relationship between asymptomatic carotid stenosis and stroke risk after surgery is less certain
Perioperative discontinuation of antithrombotic therapy	Abrupt discontinuation of antithrombotic therapy has been associated with increased risk of ischemic stroke, particularly in patients with cardiovascular risk factors

Lengthy procedures may also carry a higher risk for perioperative stroke. The variables that affect cerebral blood flow and oxygen consumption during surgery, such as changes in intraoperative blood pressure, ventilation, oxygenation, fluid status, and depth of anesthesia, are more likely to occur during longer surgeries. A retrospective review of the outcome of various major elective non-cardiac surgeries in 797 patients found a strong association between operation time and the

POSSUM score (a quantitative score of preoperative risk of morbidity and mortality due to pre-morbid medical conditions) regarding negative outcome, defined as hospital stay >10 days with a morbid condition including stroke or death. The incidence of negative surgical outcome was 10.3% in operations lasting <220 minutes vs. 38.2% in those with a duration of >220 minutes [9].

Individual risk factors should not be viewed in isolation during preoperative assessment of stroke

risk. Unlike cardiac surgeries, predictive models for preoperative estimation of stroke risk in patients undergoing general surgical procedures have not been fully studied. Press *et al.* [11] compared various models that are widely used to assess the cardiac risk of patients undergoing non-cardiac surgical

procedures, and reported that a revised cardiac risk index [12] (Table 1.2) can predict non-cardiac, medical, surgical, and neurological complications including stroke. However, the use of this revised cardiac risk index in predicting stroke in general surgery patients requires validation. It has been suggested that CHADS<sub>2</sub> or CHA<sub>2</sub>DS<sub>2</sub>-VASc scores can better predict major perioperative events including mortality in patients with atrial fibrillation [13].

**Table 1.2** The revised cardiac risk index.

Six independent predictors of perioperative complications:

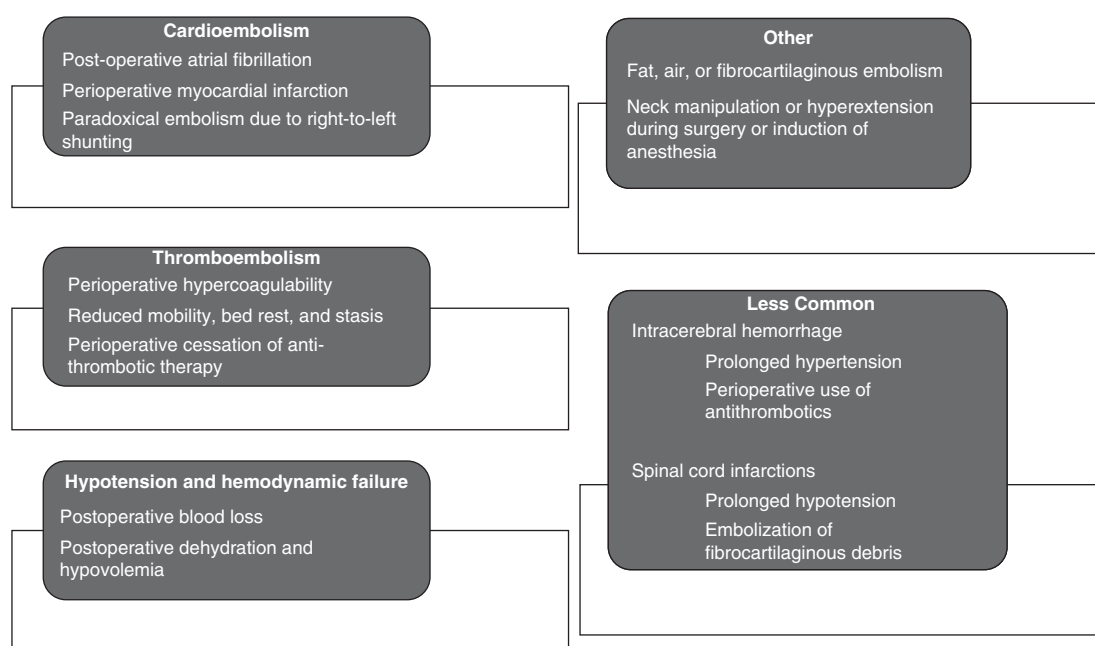
1. High-risk type of surgery
2. History of ischemic heart disease
3. History of congestive heart failure
4. History of cerebrovascular disease
5. Preoperative treatment with insulin
6. Preoperative serum creatinine >2.0 mg/dL (176 μmol/L)

The presence of two or more of these factors can aid with preoperative evaluation of patients undergoing non-urgent major non-cardiac surgery. Perioperative complication rates were reported as moderate (7%) in patients with two factors; and high (11%) in patients with more than two factors [12].

## Pathophysiology and etiological mechanisms of stroke in general surgery patients

Most strokes after general surgery are ischemic – only a few are hemorrhagic [1–3]. The mechanisms of stroke in patients undergoing general surgery are variable, and depend on the nature of the surgical procedure, patient's risk factors, and intra- and postoperative course. Figure 1.1 summarizes the potential mechanisms of perioperative stroke in general surgery patients.

Hypotension can result in low flow and subsequent borderzone infarcts. Intraoperative hypotension (IOH) is frequently misconceived as a cause for perioperative stroke. While IOH might contribute to stroke risk in cardiac surgery patients, studies in general surgery



**Figure 1.1** Potential mechanisms of stroke in general surgery patients

**Section I: Iatrogenic ischemic strokes: peri- and postoperative strokes**

patients showed little or no association between IOH and perioperative stroke risk [1,4].

Hypotension during the postoperative period might be more important than hypotension induced by anesthesia or hypotension during the highly monitored and controlled intraoperative period. A case-control study in 24,241 patients who underwent non-cardiac, non-neurological surgeries found that the duration that the mean blood pressure was decreased more than 30% from baseline was associated with the occurrence of postoperative stroke [14].

The timing and topography of stroke in general surgery patients provide clues to its pathophysiology and etiology. Several studies reported that the majority of perioperative strokes occur during the postoperative period [1–4]. In one study, only 10 out of 61 strokes in patients who had general surgery occurred during the procedure [4]. The median time interval between the procedure and stroke onset/detection was 2 days; maximum 16 days. Brain imaging (CT or MRI) was negative in 5 patients, and showed infarcts in a single arterial territory in 48 patients, infarcts in multiple territories in 6 patients, and borderzone (watershed) infarcts in only 7 patients. A review of 10 published studies found that only 5.8% of patients (14 out of 242) awoke with a stroke from a general surgical procedure [15]. These findings indicate that intraoperative mechanisms are rarely the immediate cause of perioperative stroke; that postoperative events are more important; and that most strokes after general surgery are related to thromboembolism.

The major cause of thromboembolism appears to be cardiac embolism. In one study, cardiac embolism was the cause of perioperative stroke in 42% of cases, and most were related to postoperative atrial fibrillation [1]. Another cause is perioperative myocardial infarction as a result of supply–demand mismatch due to hypertension, hypotension, or tachycardia during the perioperative period.

However, thromboembolism may be multifactorial. The perioperative period is characterized by adrenergic stimulation, increased prothrombotic activity, platelet activation, and reduced fibrinolytic activity resulting in transient hypercoagulability [16]. This is further exacerbated by reduced mobility, bed rest, stasis, dehydration, and withholding of antiplatelets or anticoagulants perioperatively. A population-based study showed that among 2,197 patients with ischemic stroke, 5.2% had withdrawal of antiplatelet

or antithrombotic medications (in nearly half of these cases stopped for procedures) during the 60 days preceding their acute stroke onset, presumably due to rebound hypercoagulability [17]. A surgery-related hypercoagulability increases the risk of thrombogenesis and perioperative vascular events including paradoxical cerebral embolism via a patent foramen ovale in patients who develop lower extremity or pelvic venous embolism during the postoperative period.

Blood loss, hypovolemia, dehydration, and prolonged hypotension can contribute to hemodynamic failure during the perioperative period. This can reduce cerebral perfusion and cause subsequent stroke especially if cerebral collateral perfusion is inadequate or autoregulation fails, or in the presence of pre-existing cerebrovascular arterial occlusive lesions. Hemodynamic failure and subsequent hypoperfusion may also increase the risk for thromboembolism by reducing the wash out of microemboli [18]. Neck manipulations and hyperextension during surgery and induction of anesthesia may also play a role, either by kinking or aggravating rupture of a pre-existing plaque in the presence of carotid or vertebral artery stenosis, or causing arterial dissection. Fat, air, or fibrocartilaginous embolism during orthopedic and spine procedures are other sources of embolization.

It is important to point out that stroke following general surgical procedures may not always be localized to the brain. Occasionally, spinal cord infarction might complicate general surgical non-aortic procedures, such as orthopedic and spinal surgery [19–20]. This is often attributed to significant and prolonged hypotension or embolization of fibrocartilaginous debris.

## Prevention of stroke in general surgery patients

### Preoperative assessment

Prevention of perioperative stroke in patients undergoing general surgery should include closer evaluation of the patient's risk profile, and a detailed neurological history for signs or symptoms of prior stroke/TIA before posing an indication to surgery. A history suggestive of prior stroke/TIA should prompt neurological consultation and detailed neurological assessment with brain and vascular imaging, particularly if these neurological events were not previously

investigated or prior workup was incomplete. Patients with previously undiagnosed symptomatic hemodynamically significant carotid stenosis might benefit from preoperative carotid revascularization, if the general surgery is elective and can be delayed.

The timing of surgery in a patient who had a recent stroke should be carefully considered based on the urgency of surgery and its risks, the cause and size of the infarct, stability of stroke symptoms, and whether anticoagulation is required. Cerebrovascular reserve can be tenuous during the days to weeks following a stroke, and may increase the risk of stroke recurrence during the perioperative period. Although there are no systematic studies or outcome data to guide this decision, it is advisable to delay elective surgery in patients who had a recent stroke/TIA for six to eight weeks after stroke symptom onset to allow the cerebral autoregulation to recover before encountering the hemodynamic stresses of surgery. A recent study indicated that the risk of adverse outcomes following surgery may be increased up to nine months after a previous acute stroke [21].

## Risk factor management

Close monitoring and optimal management of the identified risk factors in the perioperative period is essential to minimize the risk for stroke, and the stroke's sequelae if it occurs. Measures should be taken to prevent arrhythmias, thromboembolic complications, and sharp fluctuations in blood pressure, fluid volume status, and electrolytes during the perioperative period. Special considerations include the following:

**Glycemic control** Close attention should be paid to glycemic control in the perioperative period. Preoperative hyperglycemia and impaired fasting glucose levels, independent of diabetes and other comorbidities, are associated with increased risk for perioperative stroke, myocardial infarction, and death [22]. Hyperglycemia is also associated with worse outcome after stroke [23].

**Perioperative management of atrial fibrillation** Patients with chronic atrial fibrillation undergoing surgery require close monitoring during the perioperative period. Anti-arrhythmia and rate-controlling medications, such as  $\beta$ -blockers, should often be continued without interruption, and electrolytes and fluid status should be carefully monitored and corrected on an ongoing basis. Most patients with chronic atrial fibrillation on oral

anticoagulation should continue to receive anticoagulation during the perioperative period. Bridging therapy with heparin or heparinoids (as detailed below), and promptly restarting oral anticoagulation after surgery, as soon as the risk of bleeding from the surgical site is minimal and hematocrit is stable, are recommended especially in patients at intermediate or high risk for thromboembolism (Table 1.3). Clinical prediction rules, such as CHADS<sub>2</sub> or CHA<sub>2</sub>DS<sub>2</sub>-VASc scores could help to estimate stroke risk in the perioperative setting [13] and those with low scores may not necessarily need bridging therapy [24]. In some situations for patients with AF, bridging may even increase the risk of adverse events [25].

Patients who develop atrial fibrillation de novo postoperatively may have increased risk of subsequent stroke both after non-cardiac and cardiac surgery [26]. Initiation of anticoagulation may be warranted, especially in high-risk patients such as those with a history of stroke/TIA. Anticoagulation therapy should continue for 30 days after the return of normal sinus rhythm based on the recommendations of the American College of Chest Physicians [27] and the American Association for Thoracic Surgery guidelines [28].

**Perioperative management of antithrombotic agents** The perioperative management of patients taking an antithrombotic agent before undergoing an elective surgery is often challenging. The decision of whether to discontinue antithrombotic therapy before a surgical procedure should be based on careful assessment of the risk of bleeding complications vs. the benefit of preventing thromboembolic events during the perioperative period. Temporary cessation of antithrombotics in anticipation of a surgical procedure is associated with increased risk of thromboembolic events either due to the indication for treatment itself, rebound hypercoagulability due to discontinuation of the antithrombotic agent, or surgery-induced hypercoagulable state [16,17,29,30]. Given that bleeding is a treatable perioperative complication, the decision-making should place a high value on preventing thromboembolism in patients at high or moderate risk for thromboembolism, and preventing bleeding in patients at low risk for thromboembolism (Table 1.3) [31]. The time off antithrombotic therapy should be minimized in patients on antiplatelets or anticoagulants to decrease the risk of systemic thromboembolism and stroke during the perioperative period.

### Section I: Iatrogenic ischemic strokes: peri- and postoperative strokes

**Table 1.3** Thromboembolic risk categories for patients taking antithrombotic therapy.

Thromboembolism risk category	Indication for antithrombotic therapy				Perioperative bridging therapy
	Prosthetic heart valve	Atrial fibrillation	Venous embolism		
High	<ul style="list-style-type: none"> <li>History of stroke/TIA</li> <li>Any mitral valve</li> <li>Caged ball or single leaflet aortic valve</li> </ul>	<ul style="list-style-type: none"> <li>History of stroke/TIA</li> <li>Rheumatic valvular heart disease</li> <li>CHADS<sub>2</sub> score &gt;4</li> </ul>	<ul style="list-style-type: none"> <li>Recent venous embolism (within 3 months)</li> <li>Thrombophilia</li> </ul>		Strongly recommended
Moderate	<ul style="list-style-type: none"> <li>Bi-leaflet aortic valve and ≥1 stroke risk factor</li> </ul>	<ul style="list-style-type: none"> <li>≥2 stroke risk factors</li> <li>CHADS<sub>2</sub> score 3–4</li> </ul>	<ul style="list-style-type: none"> <li>Venous embolism within 3–12 months</li> <li>Active cancer</li> <li>Recurrent venous thromboembolism</li> </ul>		Strongly recommended
Low	<ul style="list-style-type: none"> <li>Bi-leaflet aortic valve and no stroke risk factors</li> </ul>	<ul style="list-style-type: none"> <li>No history of stroke/TIA</li> <li>CHADS<sub>2</sub> score &lt;3</li> </ul>	<ul style="list-style-type: none"> <li>Single venous embolic event &gt;12 months ago</li> <li>None of the above</li> </ul>		Optional – may sometimes be recommended, if feasible

Adapted from the American College of Chest Physicians Clinical Practice Guidelines [31].

There are no large randomized controlled trials to guide the optimal strategy for management of anti-thrombotic therapy, in particular anticoagulants, during the perioperative period. The decision of when to stop or continue antithrombotics during the perioperative period should be individualized, and should always involve a discussion involving the patient and the physicians involved in his/her care weighing the risks of thromboembolic events in that particular patient vs. the risks of major perioperative bleeding complications.

#### Perioperative management of antiplatelet agents

There is accumulating evidence to suggest that continuation of aspirin perioperatively outweighs the risks of its discontinuation. Interruption of aspirin preoperatively is associated with increased risk of ischemic stroke within the following days, particularly in patients with multiple cardiovascular risk factors [17,29]. In a retrospective, cross-sectional, case-control study of 648 patients, aspirin interruption yielded an odds ratio of 3.4 for ischemic stroke/TIA within a mean of 9±7 days of its interruption [29]. On the other hand, continuation of aspirin therapy during the perioperative period does not seem to

increase the risk of intraoperative bleeding during cataract surgery [32], and only prolonged the duration of self-limiting hematuria and rectal bleeding in patients undergoing transrectal prostate biopsy [33]. Kovich and Otley [34] reported increased risk of thromboembolic complications, including stroke/TIA, among patients in whom use of aspirin and warfarin was discontinued for dermatological procedures, and no increase in hemorrhagic complications when these agents were continued perioperatively. A prospective study in 213 patients undergoing tooth extractions concluded that the procedure can be performed safely in patients taking aspirin alone, warfarin alone, or aspirin and warfarin in combination. All cases of postoperative bleeding were controlled easily by using local hemostatic measures [35]. In addition, preoperative use of aspirin did not result in increased perioperative blood loss in patients who underwent unexpected urgent gynecological procedures [36]. Bridging with use of low molecular weight heparin (LMWH) for patients with coronary stents undergoing non-cardiac surgery seems to increase the risk for perioperative complications [37]. Therefore continuation of aspirin therapy seems to be acceptable



in many procedures, in particular dental, dermatological, ophthalmologic, and endoscopic procedures with or without biopsy [38].

There are insufficient data to make specific recommendations regarding the use of other antiplatelet agents, such as clopidogrel and dipyridamole. In the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial, the risk of major bleeding complications following coronary revascularization procedures was increased among patients treated with clopidogrel vs. aspirin, when the drug was discontinued less than five days before the procedure [39]. It is unclear how to manage this drug preoperatively in patients undergoing general surgery, and whether withholding it for at least five days prior to major general surgery is required as is the case with cardiac procedures. However, continuing clopidogrel and aspirin during the perioperative period has been advised in patients with a bare metal coronary stent who require surgery within six weeks of stent placement and in patients with a drug-eluting coronary stent who require surgery within 12 months of stent placement to prevent stent-related coronary thrombosis [31].

**Perioperative management of oral anticoagulation** Is surgery feasible on anticoagulation? Larson *et al.* [40] studied 100 consecutive patients at high risk for thromboembolic events who continued warfarin therapy, targeting a goal for the INR of 1.5 to 2.0, perioperatively while undergoing invasive procedures including hip replacement, gastrointestinal, vascular, and even cardiothoracic surgery. This moderate intensity of anticoagulation was considered safe and feasible. Only six patients had bleeding complications (two major; four minor) and two patients had thromboembolic events. These findings suggest that some patients can be maintained on oral anticoagulation during the perioperative period, if necessary. However, the clinical question is often whether or not to use anticoagulation bridging therapy during the preoperative period. A systematic review reported a 1.6% rate of thromboembolic events among 1,868 surgical patients receiving warfarin (0.4% for continuation of oral anticoagulation, 0.6% for discontinuation of warfarin, 0% for discontinuation of warfarin and bridging therapy with intravenous heparin, and 0.6% for discontinuation of warfarin and bridging therapy with LMWH).

The overall rate of stroke was 0.4%, and major bleeding rate while receiving therapeutic doses of warfarin was 0.2% for dental procedures and 0% for cataract extraction surgery [41].

The American College of Chest Physicians Evidence-Based Clinical Practice Guidelines [31] has made the following recommendations regarding perioperative management of anticoagulation:

1. In patients who require temporary interruption of oral anticoagulation and preoperative bridging therapy, the use of subcutaneous (SC) low molecular weight heparin (LMWH), which can be administered in an outpatient setting, is preferable to intravenous (IV) unfractionated heparin (UFH) from a cost-containment perspective.
2. Bridging warfarin with therapeutic-dose SC LMWH (for example, dalteparin 200 IU/kg qd or enoxaparin 1.5 to 2.0 mg/kg qd) or IV UFH is recommended preoperatively in patients with a mechanical heart valve, or atrial fibrillation, or venous thromboembolism, or clotting disorder at high risk for thromboembolism.
  - The last preoperative dose of SC LMWH should approximate half the total daily dose instead of 100% and should be administered 24 hours before the procedure.
  - If IV UFH is used as a bridging anticoagulation, it should be stopped approximately 4 hours before surgery.
3. In patients with a mechanical heart valve, or atrial fibrillation, or venous thromboembolism at low risk for thromboembolism, no bridging over bridging with therapeutic-dose SC LMWH or IV UFH is recommended.
4. Continuation of warfarin during the perioperative period in patients undergoing minor dental or dermatological procedures, or cataract removal.

There is also evidence to suggest that patients can be maintained on oral anticoagulation for other procedures, such as lithotripsy and low-risk endoscopic procedures such as diagnostic colonoscopy and sigmoidoscopy [38–42].

Little is known about the management of newer anticoagulants, such as direct thrombin or factor Xa inhibitors, during the perioperative period and their

**Section I: Iatrogenic ischemic strokes: peri- and postoperative strokes**

impact on perioperative bleeding risks. The duration for which these drugs need to be withheld prior to a procedure depends on baseline renal function and creatinine clearance.

**Perioperative management of blood pressure**

Patients with poorly controlled hypertension preoperatively have an exaggerated hypertensive response to the induction of anesthesia and pain. Hypertensive patients are also more likely to experience more fluctuations in blood pressure, including hypotension, intraoperatively. During the postoperative period, blood pressure and heart rate tend to increase as patients recover from anesthesia and as a result of excessive release of catecholamines due to surgical stress response and pain. In an observational study of 797 patients undergoing non-cardiac surgeries, intraoperative systolic hypertension and tachycardia were independently associated with increased risk for perioperative morbidity, including stroke [43]. In another study, the duration that the intraoperative mean blood pressure was decreased more than 30% from baseline was associated with the occurrence of postoperative stroke [9]. The optimal intraoperative target range for blood pressure is uncertain. Some recommend maintaining mean or systolic blood pressure within 20% of the preoperative baseline blood pressure [15].

Optimal control of blood pressure preoperatively, coupled with careful monitoring of blood pressure intra- and postoperatively is of critical importance to prevent hypertension or hypotensive episodes and to maintain adequate cerebral perfusion. Therefore anti-hypertensive agents should be continued up to the time of surgery to maintain a near-normal blood pressure. Special caution should be considered with: (1) abrupt preoperative discontinuation of some anti-hypertensive medications, such as clonidine, that may result in rebound hypertension; and (2) initiation of acute therapy with extended-release metoprolol (*de novo*) shortly before surgery, as this might be associated with increased risk of postoperative stroke [44].

**Intraoperative interventions**

Intraoperative factors can lead to perioperative arrhythmias, respiratory compromise, hypotension or hypertension, reduced cerebral perfusion, and thromboembolism, all of which can be associated with increased stroke risk. Taking additional precautionary measures to avoid these complications can help to reduce the risk for perioperative stroke.

These include: (1) considering local instead of general anesthesia when possible; (2) taking measures to maintain near-normal BP, heart rate, and respiratory and fluid status during surgery; and (3) attempting to minimize the duration of surgery when feasible.

The use of local anesthesia is associated with less postoperative morbidity and a shorter hospital stay, thereby decreasing postoperative thromboembolic complications and arrhythmias. Regional anesthesia also allows clinical monitoring of neurologic function by assessing level of consciousness, speech, and strength of hand grip during surgical procedures, thus allowing timely detection and the taking of necessary measures to correct inadequate cerebral perfusion. A population-based, case-control, retrospective study of 1,455 stroke patients and 1,455 age- and gender-matched controls identified risk factors associated with ischemic stroke in patients undergoing surgery involving general or local anesthesia, using a conditional logistic regression model to estimate the odds ratio of surgery and anesthesia for perioperative stroke, while adjusting for other known risk factors. After adjusting for classical stroke risk factors, the odds ratio for stroke during the perioperative period was 3.9 in an analysis that excluded matched pairs, where the case and control underwent “high risk” surgery (cardiac, vascular, or neurologic procedures), also “low-risk” surgical procedures were found to be a significant independent risk factor for stroke (odds ratio = 2.9) [45].

**Postoperative management**

Continued and close monitoring of patients for postoperative arrhythmia, development of heart failure, neurologic status, vital signs and fluid volume status, electrolytes, hemostatics, and blood sugar in the days after major surgery is essential to implement immediate corrective actions. It should be emphasized for personnel performing the monitoring that there is a risk that stroke symptoms in the postoperative phase can be undiagnosed because these symptoms are misinterpreted as “general deterioration” due to, for example, anesthesia or metabolic imbalance. Rapid identification of postoperative neurological complications including focal neurological deficits is essential and allows timely management to optimize the patient’s recovery. It is also important to identify and treat remedial causes of postoperative hypertension such as pain, agitation, bladder distension, hypoxia, etc.



Early postoperative use of prophylactic strategies to minimize the risk of systemic thromboembolism is recommended to prevent potential paradoxical embolism and stroke. A prospective study of patients undergoing gynecologic surgery showed that the incidence of thromboembolic complications, especially deep vein thrombosis (DVT), can be reduced by using elastic stockings, early postoperative mobilization, hematocrit and volume control, and heparin [46]. A randomized trial in patients undergoing major abdominal surgery has shown that combined treatment drug strategies (compression stockings and LMWH) for preventing thromboembolic complications after surgery are more effective than either strategy alone [47]. Similarly, a Cochrane database systematic review showed that the use of compression stockings is effective in diminishing the risk of thromboembolic events in hospitalized patients after various surgeries, and that using stockings with another method of DVT prophylaxis is more effective than using stockings alone [48].

## Management of acute stroke in general surgery patients

The general supportive management principles of acute stroke – *timely* resuscitation of salvageable brain tissue and prevention and management of complications to improve recovery – are the same during the perioperative period. Improved and early recognition of stroke by the surgical staff and immediate consultation of the stroke team (or a neurologist familiar with acute stroke treatment) for suspected stroke are crucial to facilitate early treatment. Brain imaging should be performed as soon as possible to rule out intracranial hemorrhage or an undiagnosed brain lesion.

Many patients with ischemic stroke following general surgery may not be candidates for intravenous thrombolysis, which is often contraindicated during the first two weeks after a major procedure. However, the use of endovascular revascularization strategies, especially thrombectomy, appears to be a reasonable and safe alternative for the management of hyperacute ischemic stroke in the perioperative setting [43].

## Summary

Stroke after general surgical procedures is not as uncommon as once thought. It usually occurs postoperatively, largely due to thromboembolism, and

intraoperative events are rarely the direct immediate cause. Increased awareness of the etiology and pathophysiology of the predisposing risk factors and mechanisms of perioperative stroke and rapid recognition of its onset are vital to prevent it and to improve outcomes.

## References

- Hart R, Hindman B. Mechanisms of perioperative cerebral infarction. *Stroke*. 1982; **13**:766–73.
- Larsen S F, Zaric D, Bosen G. Postoperative cerebrovascular accidents in general surgery. *Stroke. Acta Anaesthesiol Scand*. 1988; **32**:698–701.
- Parikh S, Cohen J R. Postoperative stroke after general surgical procedures. *NY State J Med*. 1993; **93**:162–5.
- Limburg M, Wijdicks E F, Li H. Ischemic stroke after surgical procedures: Clinical features, neuroimaging, and stroke factors. *Neurology*. 1998; **50**:895–901.
- Kikura M, Oikawa F, Yamamoto K, *et al*. Myocardial infarction and cerebrovascular accident following non-cardiac surgery: Differences in postoperative temporal distribution and risk factors. *J Thromb Haemost*. 2008; **6**:742–8.
- Nosan D K, Gomez C R, Maves M D. Perioperative stroke in patients undergoing head and neck surgery. *Ann Otol Rhinol Laryngol*. 1993; **102**:717–23.
- Bateman B T, Schumacher H C, Wang S, Shaefi S, Berman M F. Perioperative acute ischemic stroke in non-cardiac and non-vascular surgery: Incidence, risk factors, and outcomes. *Anesthesiology*. 2009; **110**:231–8.
- Polanczyk C A, Marcantonio E, Goldman L, *et al*. Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. *Ann Intern Med*. 2001; **134**(8):637–43.
- Reich D L, Bennett-Guerrero E, Bodian C A, *et al*. Intraoperative tachycardia and hypertension are independently associated with adverse outcome in noncardiac surgery of long duration. *Anesth Analg*. 2002; **95**(2):273–7.
- Brooks D C, Schindler J L. Perioperative stroke: Risk assessment, prevention and treatment. *Current Treatment Options in Cardiovascular Medicine*. 2014; **16**:282.
- Press M J, Chassin M R, Wang J, Tuhim S, Halm E A. Predicting medical and surgical complications of carotid endarterectomy: comparing the risk indexes. *Arch Intern Med*. 2006; **166**(8):914–20.
- Lee T H, Marcantonio E R, Mangione C M, *et al*. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999; **100**(10):1043–9.
- van Diepen S, Youngson E, Ezekowitz J A, McAlister F A. Which risk score best predicts

## Section I: Iatrogenic ischemic strokes: peri- and postoperative strokes

- perioperative outcomes in nonvalvular atrial fibrillation patients undergoing noncardiac surgery? *Am Heart J*. 2014; **168**(1):60–7.
14. Bijker J B, Persoon S, Peelen L M, *et al*. *Anesthesiology*. 2012; **116**(3):658–64.
  15. Ng J L, Chan M T, Gelb A W. Perioperative stroke in noncardiac, nonneurosurgical surgery. *Anesthesiology*. 2011; **115**(4):879–90.
  16. Hinterhuber G, Böhler K, Kittler H, Quehenberger P. *Dermatol Surg*. 2006; **32**(5):632–9.
  17. Broderick J P, Bonomo J B, Kissela B M, *et al*. Withdrawal of antithrombotic agents and its impact on ischemic stroke occurrence. *Stroke*. 2011; **42**(9):2509–14.
  18. Sedlacek O, Caplan L, Hennerici M. Impaired washout-embolism and ischemic stroke: further examples and proof of concept. *Cerebrovasc Dis*. 2005; **19**(6):396–401.
  19. Kim J S, Ko S B, Shin H E, Han S R, Lee K S. Perioperative stroke in the brain and spinal cord following an induced hypotension. *Yonsei Med J*. 2003; **44**(1):143–5.
  20. Langmayr J J, Ortler M, Obwegeser A, Felber S. Quadriplegia after lumbar disc surgery. A case report. *Spine*. 1996; **21**(16):1932–5.
  21. Jorgensen M E, Torp-Pedersen C, Gislason G H, *et al*. Time elapsed after ischemic stroke and risk of adverse cardiovascular events and mortality following elective noncardiac surgery. *JAMA*. 2014; **312**(3):269–277.
  22. Biteker M, Dayan A, Can M M, *et al*. Impaired fasting glucose is associated with increased perioperative cardiovascular event rates in patients undergoing major non-cardiothoracic surgery. *Cardiovasc Diabetol*. 2011; **10**:63.
  23. Gentile N T, Seftchick M W, Huynh T, Kruus L K, Gaughan J. Decreased mortality by normalizing blood glucose after acute ischemic stroke. *Acad Emerg Med*. 2006; **13**(2):174–80.
  24. Douketis J D, Spyropoulos A C, Kaatz S, *et al*. Perioperative bridging anticoagulation in patients with atrial fibrillation. *New England Journal of Medicine*. 2015; **373**(9):823–33.
  25. Steinberg B A, Peterson E D, Kim S, *et al*. Use and outcomes associated with bridging during anticoagulation interruptions in patients with atrial fibrillation: Findings from the outcomes registry for better informed treatment of atrial fibrillation (ORBIT-AF). *Circulation*. 2015; **131**(5):488–94.
  26. Gialdini G, Nearing K, Bhave P D, *et al*. Perioperative atrial fibrillation and the long-term risk of ischemic stroke. *JAMA*. 2014; **312**(6):616–22.
  27. Epstein A E, Alexander J C, Gutterman D D, Maisel W, Wharton J M, American College of Chest Physicians. Anticoagulation: American College of Chest Physicians guidelines for the prevention and management of postoperative atrial fibrillation after cardiac surgery. *Chest*. 2005; **128**(2 Suppl):24S–27S.
  28. Frendl G, Sodickson A C, Chung M K, *et al*. AATS guidelines for the prevention and management of perioperative atrial fibrillation and flutter for thoracic surgical procedures. *J Thorac Cardiovasc Surg*. 2014; **148**(3):e153–93.
  29. Maulaz A B, Bezerra D C, Michel P, Bogousslavsky J. Effect of discontinuing aspirin therapy on the risk of brain ischemic stroke. *Arch Neurol*. 2005; **62**(8):1217–20.
  30. Genewein U, Haerberli A, Straub P W, Beer J H. Rebound after cessation of oral anticoagulant therapy: the biochemical evidence. *Br J Haematol*. 1996; **92**(2):479–85.
  31. Douketis J D, Spyropoulos A C, Spencer F A, *et al*; American College of Chest Physicians. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012; Feb;**141**(2 Suppl):e326S–50S. Erratum in: *Chest*. 2012; **141**(4):1129.
  32. Assia E I, Raskin T, Kaiserman I, Rotenstreich Y, Segev F. Effect of aspirin intake on bleeding during cataract surgery. *J Cataract Refract Surg*. 1998; **24**(9):1243–6.
  33. Giannarini G, Mogorovich A, Valent F, *et al*. Continuing or discontinuing low-dose aspirin before transrectal prostate biopsy: results of a prospective randomized trial. *Urology*. 2007; **70**(3):501–5.
  34. Kovich O, Otley C C. Thrombotic complications related to discontinuation of warfarin and aspirin therapy perioperatively for cutaneous operation. *J Am Acad Dermatol*. 2003; **48**(2):233–7.
  35. Bajkin B V, Bajkin I A, Petrovic B B. The effects of combined oral anticoagulant-aspirin therapy in patients undergoing tooth extractions: a prospective study. *J Am Dent Assoc*. 2012; **143**(7):771–6.
  36. Ferraris V A, Swanson E. Aspirin usage and perioperative blood loss in patients undergoing unexpected operations. *Surg Gynecol Obstet*. 1983; **156**(4):439–42.
  37. Capodanno D, Musumeci G, Lettieri C, *et al*. Impact of bridging with perioperative low-molecular-weight heparin on cardiac and bleeding outcomes of stented patients undergoing non-cardiac surgery. *Thromb Haemost*. 2015; **114**(2):423–31.
  38. Armstrong M J, Schneck M J, Biller J. Discontinuation of perioperative antiplatelet and anticoagulant therapy in stroke patients. *Neurol Clin*. 2006; **24**(4):607–30.