Perioperative Stroke in Noncardiac, Nonneurosurgical Surgery

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ABSTRACT

Perioperative stroke after noncardiac, nonneurosurgical procedures is more common than generally acknowledged. It is reported to have an incidence of 0.05–7% of patients. Most are thrombotic in origin and are noted after discharge from the postanesthetic care unit. Common predisposing factors include age, a previous stroke, atrial fibrillation, and vascular and metabolic diseases. The mortality is more than two times greater than in strokes occurring outside the hospital. Delayed diagnosis and a synergistic interaction between the inflammatory changes normally associated with stroke, and those normally occurring after surgery, may explain this increase.

Intraoperative hypotension is an infrequent direct cause of stroke. Hypotension will augment the injury produced by embolism or other causes, and this may be especially important in the postoperative period, during which monitoring is not nearly as attentive as in the operating room. Increased awareness and management of predisposing risk factors with early detection should result in improved outcomes.

STROKE is an important cause of morbidity and mortality, particularly in patients more than 65 yr old. In cardiac, neurologic, and carotid surgery, the incidence is known to be high (2.2–5.2%). However, little is known regarding perioperative stroke following other types of surgery including general, urologic, orthopedic, thoracic, and gynecologic procedures. The aims of this article are to review the incidence, pathophysiology, risk factors, and outcomes associated with perioperative stroke following noncardiac, nonneurologic, and vascular surgery. Suggestions regarding the timing of elective surgery after stroke and ways in which one can reduce the incidence and improve outcomes are also outlined.

STROKE is an important cause of morbidity and mortality, particularly in patients more than 65 yr old. In cardiac, neurologic, and carotid surgery, the incidence is known to be high (2.2–5.2%). However, little is known regarding perioperative stroke following other types of surgery including general, urologic, orthopedic, thoracic, and gynecologic procedures. The aims of this article are to review the incidence, pathophysiology, risk factors, and outcomes associated with perioperative stroke following noncardiac, nonneurologic, and vascular surgery. Suggestions regarding the timing of elective surgery after stroke and ways in which one can reduce the incidence and improve outcomes are also outlined.

Definition

The World Health Organization definition of stroke is a “focal or global neurologic deficit of cerebrovascular cause that persists beyond 24 h or is interrupted by death within 24 h.” Transient ischemic attack is acute loss of focal cerebral or ocular function with symptoms lasting less than 24 h and is usually presumed to be embolic or thrombotic in origin. In addition, a third type of cerebrovascular event has recently attracted much attention in the nonsurgical setting. Covert stroke is an asymptomatic ischemic event usually only detected by advanced neuroimaging techniques, such as diffusion-weighted magnetic resonance imaging sequences. Although the diagnosis is often missed at the time of the event, covert stroke has been associated with an adverse effect on cognitive function and quality of life. Currently other than in cardiac and carotid artery surgery, there is no study evaluating the incidence, impact, and risk factors of covert stroke in the general surgical population. This review therefore concentrates on periopera-

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tive overt stroke that is commonly defined as one that occurs during and up to 30 days after surgery.

Incidence, Morbidity, and Mortality of Perioperative Stroke in Noncardiac and Nonneurosurgical Procedures

The reported incidence of stroke following procedures other than cardiac, neurosurgical, and carotid artery surgery ranges between 0.05 and 7.4% (table 1). Differences in patient population, changing clinical practice over 40 yr (1967–2009), study design, diagnostic tests, and duration of follow up may account for the large variance in reported preoperative stroke rates. The majority of the older and current studies are retrospective reviews of administrative databases. Although most major strokes are usually revealed in these databases, it is likely that minor strokes, covert strokes, and

Table 1. Incidence of Perioperative Stroke after Noncardiac Surgery

<table>
<thead>
<tr>
<th>First Author</th>
<th>Period of Analysis</th>
<th>Study Design</th>
<th>Patient Population</th>
<th>Strokes, n</th>
<th>Patients, n</th>
<th>Risk of Stroke (%)</th>
<th>Length of Follow-up</th>
<th>Diagnostic Criteria</th>
<th>Mechanisms of Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knapp⁴</td>
<td>1959–1962</td>
<td>Retrospective</td>
<td>Male patients older than 50 yr undergoing all types of surgery</td>
<td>34</td>
<td>8,984</td>
<td>0.4</td>
<td>Unclear, Less than 3 yr</td>
<td>Neurologic examination</td>
<td>Not reported</td>
</tr>
<tr>
<td>Cooperman⁵</td>
<td>1978</td>
<td>Retrospective</td>
<td>Vascular surgery</td>
<td>4</td>
<td>566</td>
<td>0.7</td>
<td>Hospital discharge</td>
<td>Hospital discharge</td>
<td>Unclear</td>
</tr>
<tr>
<td>Turnipseed⁶</td>
<td>1977–1979</td>
<td>Prospective</td>
<td>Peripheral vascular surgery</td>
<td>7 (2 had TIA)</td>
<td>160</td>
<td>4.4</td>
<td>Hospital discharge</td>
<td>CT</td>
<td>Thrombosis: 43% Hypoperfusion: 0% Embolism: 57% Hemorrhagic: 0%</td>
</tr>
<tr>
<td>Hart⁷</td>
<td>1975–1982</td>
<td>Retrospective</td>
<td>Adult patients undergoing noncarotid and noncardiac surgery</td>
<td>12</td>
<td>24,500</td>
<td>0.05</td>
<td>Hospital discharge</td>
<td>CT</td>
<td>Thrombosis: 8% Hypoperfusion: 17% Embolism: 50% Hemorrhagic: 0% Unclear: 25%</td>
</tr>
<tr>
<td>Larsen⁸</td>
<td>1981–1983</td>
<td>Prospective</td>
<td>Patients older than 40 yr, undergoing noncardiac, noncarotid artery surgery</td>
<td>9 (3 had TIA)</td>
<td>2,463</td>
<td>0.4</td>
<td>Hospital discharge</td>
<td>Neurologic examination</td>
<td>Thrombosis: 0% Hypoperfusion: 0% Embolism: 33% Hemorrhagic: 0% Unclear: 23%</td>
</tr>
<tr>
<td>Landercasper⁹</td>
<td>1980–1988</td>
<td>Retrospective</td>
<td>Patients with a history of cerebrovascular disease undergoing noncardiac, noncarotid artery surgery</td>
<td>5</td>
<td>173</td>
<td>2.9</td>
<td>Hospital discharge</td>
<td>CT</td>
<td>Thrombosis: 0% Hypoperfusion: 0% Embolism: 20% Hemorrhagic: 60% Unclear: 20%</td>
</tr>
<tr>
<td>Parikh¹⁰</td>
<td>1987–1992</td>
<td>Retrospective</td>
<td>Noncardiac, noncarotid artery surgery</td>
<td>19</td>
<td>24,641</td>
<td>0.08</td>
<td>Hospital discharge</td>
<td>CT</td>
<td>Thrombosis: 37% Hypoperfusion: 5% Embolism: 47% Hemorrhagic: 5% Unclear: 6%</td>
</tr>
<tr>
<td>Limburg¹¹</td>
<td>1986–1996</td>
<td>Retrospective</td>
<td>Selected patients at risk of perioperative stroke</td>
<td>70</td>
<td>2,002</td>
<td>3.5</td>
<td>Hospital discharge</td>
<td>CT/MRI</td>
<td>Hypoperfusion: 19% Embolism: 27% Hemorrhagic: 3% Include ischemic stroke only</td>
</tr>
<tr>
<td>*Kikura¹²</td>
<td>1991–2002</td>
<td>Prospective</td>
<td>Consecutive adult patients undergoing general orthopedic, vascular, and thoracic surgery</td>
<td>97</td>
<td>21,903</td>
<td>0.4</td>
<td>30 days after surgery</td>
<td>CT/MRI</td>
<td>Thrombosis: 51% Hemorrhagic: 3% Include ischemic stroke only</td>
</tr>
<tr>
<td>Parvizi¹³</td>
<td>2004–2005</td>
<td>Prospective</td>
<td>Patients undergoing hip or knee arthroplasties</td>
<td>6 (include TIA)</td>
<td>1,636</td>
<td>0.4</td>
<td>6 weeks after surgery</td>
<td>Unclear</td>
<td>Not reported</td>
</tr>
<tr>
<td>*Kikura¹⁴</td>
<td>1991–2006</td>
<td>Retrospective</td>
<td>Patients undergoing noncardiac, noncarotid artery surgery</td>
<td>126</td>
<td>36,634</td>
<td>0.34</td>
<td>30 days after surgery</td>
<td>CT/MRI</td>
<td>Not reported</td>
</tr>
<tr>
<td>Popa¹⁵</td>
<td>1998–2002</td>
<td>Retrospective</td>
<td>Patients older than 65 yr, undergoing major hip surgery</td>
<td>76</td>
<td>1,886</td>
<td>4.0</td>
<td>1 yr after surgery</td>
<td>CT/MRI</td>
<td>Thrombosis: 88% Hemorrhagic: 12%</td>
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<tr>
<td>Bateman¹⁶</td>
<td>2002–2004</td>
<td>Retrospective</td>
<td>Patients older than 18 yr undergoing: Hemicolectomy</td>
<td>939</td>
<td>131,067</td>
<td>0.7</td>
<td>Hospital discharge</td>
<td>CT/MRI</td>
<td>Include ischemic stroke only</td>
</tr>
<tr>
<td>Hip replacement</td>
<td>420</td>
<td>201,235</td>
<td>0.2</td>
<td>CT/MRI</td>
<td>Include ischemic stroke only</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Lung resection</td>
<td>242</td>
<td>39,339</td>
<td>0.6</td>
<td>CT/MRI</td>
<td>Include ischemic stroke only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huang¹⁷</td>
<td>2002–2007</td>
<td>Retrospective</td>
<td>Cesarean section undergoing regional or general anesthesia</td>
<td>151</td>
<td>303,862</td>
<td>0.05</td>
<td>Hospital discharge</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

* Patient population overlapped in these two reports.
CT = computer tomography; MRI = magnetic resonance imaging; TIA = transient ischemic attack.

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Transient ischemic attacks are missed because they are not noted by the caregivers or the clinical notes are not correctly interpreted by the coding officers.

Outcome after perioperative stroke is usually devastating. In contrast to the 12.6% mortality rate associated with strokes in the nonsurgical setting, mortality from perioperative stroke ranges from 26% after general surgery to 87% in patients who have had a previous stroke. Early mortality from major stroke may result from delayed recognition and diagnosis on surgical services, cerebral edema, and intracranial hypertension, whereas late mortality may be caused by aspiration, pneumonia, metabolic derangement, sepsis, or myocardial infarction.

Extensive evidence implicates inflammation in multiple phases of stroke pathophysiology, and there is increasing awareness that inflammatory events outside the brain have an important impact on stroke susceptibility and outcome, perhaps by amplification of those pathways activated in stroke (fig. 1). It is probable that the acute systemic inflammatory response triggered by surgery initiates or exacerbates ischemic cerebral injury. Laboratory studies using sepsis models in conjunction with neurologic injury and clinical studies demonstrate more severe neurologic deficits, especially when preceded by respiratory and urologic infections. Various cytokines have been implicated in the postoperative inflammatory response including interleukin-1, interleukin-6, and tumor necrosis factor α, and an increased C-reactive protein level. Interleukin-6 appears to be the major mediator of the stress response after surgery. Interestingly, the peak plasma concentration of interleukin-6 correlates significantly with computed tomography brain infarct volume and clinical outcome assessed by modified Rankin scale score at 3 months in patients who suffer an acute ischemic stroke. A peak plasma interleukin-6 concentration greater than 30 pg/ml was associated with increased mortality at 12 months. The association between interleukin-6 measured on admission and in-hospital mortality in patients with acute ischemic stroke has been demonstrated in another study, which found that a 1-unit increase in interleukin-6 predicted an 18% higher risk of dying during hospitalization for acute ischemic stroke.

**Pathophysiology**

Strokes are either ischemic or hemorrhagic. Ischemic stroke may be classified according to presenting symptoms and signs, using the Oxfordshire Community Stroke Project categories, or etiologically, according to the definition in the Trial of Org 10172 in Acute Stroke Treatment. The latter identifies the pathophysiologic mechanism of vessel occlusion, including large artery thrombosis, artery to artery embolism, cardioembolic, and small vessel (lacunar) occlusion. Watershed infarction is another important mechanism of ischemic stroke. Cortical and internal (white matter, centrum ovale) watershed areas occur at the junction of the distal fields of two or more nonanastomosing arterial systems and are vulnerable to ischemia because of their position, where perfusion pressure is the lowest. The pathophysiology of watershed infarcts is controversial, with substantial evidence supporting both low flow and multiple microembolic mechanisms. An embolic component is most frequent with cortical watershed infarcts, especially when associated with atheromatous stenosis of inflow vessels. Hemodynamic factors seem most important for internal watershed infarcts or in-
The role of extracranial carotid artery stenosis on perioperative stroke remains controversial. Carotid bruit does not correlate with the severity of the underlying carotid artery stenosis, per se, and has not been shown to increase the risk of perioperative stroke. Even in patients with significant carotid artery stenosis who are undergoing cardiac surgery, strokes are often contralateral to the affected carotid artery and therefore cannot be attributed to the stenosis alone. However, similar data in noncardiac, nonneurosurgical patients are currently lacking. The risk of perioperative stroke in patients with intracranial cerebral artery stenosis is unknown, but these patients carry a much higher risk (15% each yr) of stroke in the nonsurgical setting, and therefore possibly in the perioperative period, too.

Type of Surgery

The nature of surgery also has some bearing on perioperative stroke. For example, hip arthroplasty and peripheral vascular surgery are associated with a higher incidence than knee arthroplasty or general surgery. Head and neck surgery increases the risk for stroke to 0.2–5%. Patients undergoing neck dissection for cancer typically present with multiple medical comorbidities that already increase their risk for stroke. In addition, external beam radiation accelerates atheromatous changes in arteries. It is therefore not surprising that manipulation of these diseased vascular structures could result in plaque rupture, embolism, and vasospasm.

Other procedures that potentially compromise cerebral perfusion may also increase the risk of stroke. Pohl and Cullen reported four cases of strokes and ischemic spinal cord injury in patients after shoulder surgery in the beach-chair (nearly 90 degrees upright) position. Two patients had posterior fossa infarcts, one had disseminated cerebral and temporal infarcts, and one had a unilateral watershed infarct. The authors could only speculate on mechanisms and suggested that postural hypotension and extreme rotation, or hyperflexion of the neck, resulted in a decrease in cerebral blood flow and potentially aggravated thromboembolic mechanisms. A study measuring cerebral oximetry in the sitting position found a high incidence, 80% of patients, with a more than 20% decrease in saturation, but no adverse neurologic consequences. This may reflect the small sample size and the need for cerebral saturation to be reduced for a relatively long time, perhaps up to 50 min at less than 50% saturation to produce an adverse outcome. Despite studies using surrogate endpoints, the risk of stroke after shoulder surgery in beach-chair position remains undefined.

β-Blockers and Hypotension

A meta-analysis by Bangalore et al. found an increased risk of nonfatal stroke, hypotension, and bradycardia with the use of β-blockers in patients undergoing noncardiac surgery. The recent PeriOperative Ischemic Evaluation trial (POISE) car-
ried the greatest weight in the analysis. Although there is an association among \( H_9 \)-blocker use, hypotension, and stroke, this cannot be assumed to be a direct cause and effect. Many aspects remain unclear. There are substantial variations in drug choice, drug dose, and regimen; definitions of outcomes including definition of hypotension; and patients’ surgical and medical risks. Previous studies have shown that hypotension may not increase the risk of perioperative stroke even in patients with extracranial carotid artery stenosis. Importantly, it is unclear in studies, including POISE, whether the hypotension occurred immediately before the stroke or after. POISE reports “clinically significant hypotension,” defined as a systolic blood pressure of less than 100 mmHg for an unspecified time, as an “intraoperative and postoperative predictor” of stroke (see table 4), but the results do not state the temporal relationship between hypotension and the stroke, and also fail to specify if the hypotension was intraoperative or postoperative. Postoperative hypotension occurring on the ward is likely to be prolonged and therefore potentially more detrimental than intraoperative hypotension, which is usually easily detected. There is consensus that patients chronically on \( H_9 \)-blockers should be kept on their drugs through the perioperative period, and that caution is needed when these agents are begun immediately before surgery.

It is unclear whether the stroke rate is increased with other antihypertensive or sympatholytic agents, such as clonidine and dexmedetomidine. The introduction of these drugs in the perioperative period could increase vulnerability to cerebral ischemia, as the compensatory mechanisms to cope with hypotension are attenuated because of hypovolemia and blood loss. Clinical trials will be needed to address this. The POISE 2 trial, which is expected to be completed in 2014, includes a clonidine arm and more detailed reporting on intra- and postoperative blood pressure (personal communication, Table 2.

<table>
<thead>
<tr>
<th>First Author</th>
<th>Period of Study</th>
<th>Patient Population</th>
<th>Risk Factors</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parikh¹⁰</td>
<td>1987–1992</td>
<td>Noncardiac, noncarotid artery</td>
<td>Hypertension</td>
<td>—</td>
<td>0.025</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Smokers</td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prior stroke</td>
<td></td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Arrhythmia</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>Limburg¹¹</td>
<td>1986–1996</td>
<td>Selected patients at risk of perioperative stroke</td>
<td>Prior stroke</td>
<td>14.3 (3.3–63)</td>
<td>0.0004</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic obstructive pulmonary disease</td>
<td>8.8 (2.5–30.5)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Kikura¹²</td>
<td>2005</td>
<td>General surgery patients</td>
<td>Age older than 70 yr</td>
<td>20.2 (7.3–56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age 50–69 yr</td>
<td>3.7 (1.2–11)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Hyperuricemia</td>
<td>3.5 (1.2–9.8)</td>
<td>0.01</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Prior ischemic stroke</td>
<td>2.4 (1.4–4.1)</td>
<td>0.002</td>
</tr>
<tr>
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<td></td>
<td>Cancer</td>
<td>1.6 (1.0–2.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Parvizi¹³</td>
<td>2004–2005</td>
<td>Patients undergoing hip or knee arthroplasties</td>
<td>Age equal to or older than 70 yr</td>
<td>23.6 (8.6–58.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>High risk surgery</td>
<td>1.5 (1.1–2.2)</td>
<td>0.02</td>
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<td></td>
<td>Diabetes mellitus</td>
<td>2.2 (1.4–3.3)</td>
<td>0.006</td>
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<td></td>
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<td></td>
<td>Coronary artery disease</td>
<td>2.3 (1.3–4.1)</td>
<td>0.003</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Prior congestive heart failure</td>
<td>1.7 (1.1–2.7)</td>
<td>0.03</td>
</tr>
<tr>
<td>Kikura¹⁴</td>
<td>1991–2006</td>
<td>Patients undergoing noncardiac, noncarotid surgery</td>
<td>History of atrial fibrillation</td>
<td>5.5 (2.8–10.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prior stroke</td>
<td>7.1 (4.6–11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Popa¹⁵</td>
<td>1998–2002</td>
<td>Patients older than 65 yr undergoing major hip surgery</td>
<td>History of atrial fibrillation</td>
<td>2.2 (1.3–3.7)</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>Hip fracture</td>
<td>3.8 (1.9–7.4)</td>
<td>&lt;0.001</td>
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<td>Age older than 75 yr</td>
<td>2.2 (1.2–4.2)</td>
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<td>Aspirin use</td>
<td>1.8 (1.1–3.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Bateman¹⁶</td>
<td>2002–2004</td>
<td>Patients older than 18 yr undergoing hemicolecction, hip replacement, or lung surgery</td>
<td>Renal impairment</td>
<td>3.0 (2.5–3.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>History or current atrial fibrillation</td>
<td>2.0 (1.7–2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prior stroke</td>
<td>1.6 (1.3–2.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Valvular heart disease</td>
<td>1.5 (1.3–1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Current congestive heart failure</td>
<td>1.4 (1.2–1.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Diabetes mellitus</td>
<td>1.2 (1.0–1.4)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

* Odds ratios not calculated in this study. † Patient population overlapped in these two reports. ‡ Hazard ratios calculated.

CI = confidence intervals.
Stroke Prevention – Risk Modification

Timing Elective Surgery after a Recent Stroke

Acute stroke impairs cerebral autoregulation so that cerebral blood flow becomes passively dependent on perfusion pressure. The injured brain is therefore vulnerable to even modest hypotension. The impairment in cerebral autoregulation is not limited to the affected stroke hemisphere, but appears to be an overall phenomenon that occurs to the same extent after both anterior and posterior circulation strokes. Failure of cerebral autoregulation and vasomotor response to carbon dioxide has been demonstrated within 8 h after ictus and lasting for 2–6 months. Ideally, enough time should be allowed for autoregulation to be restored before elective surgery, as well as abatement of the inflammatory response. Previous investigators have recommended delaying nonurgent surgery for 1–3 months after stroke. If surgery needs to take place sooner, blood pressure should be meticulously monitored, and one could make a reasonable argument for monitoring for cerebral ischemia using transcranial Doppler or neurophysiology (e.g., electroencephalography and evoked potentials).

Preoperative Carotid Artery Revascularization

In patients with high-grade (more than 70% stenosis) symptomatic carotid artery stenosis, revascularization in the form of carotid artery stenting or endarterectomy should be offered before nonurgent elective surgery. However, in accordance with the 2009 European Society for Vascular Surgery guideline, carotid endarterectomy is contraindicated for patients with less than 50% stenosis. Revascularization for patients with asymptomatic carotid artery stenosis is much more controversial. Some evidence suggests that intensive medical therapy offers superior secondary stroke prevention compared with carotid endarterectomy or stenting. This includes smoking cessation, blood pressure control, anticoagulation for atrial fibrillation, and administration of lipid lowering and antiplatelet therapy. In contrast, the recently published 10-yr follow-up of the European Asymptomatic Carotid Surgery Trial found a benefit favoring surgery in asymptomatic patients with more than 60% stenosis. The implications for preoperative carotid endarterectomy were not addressed.

Perioperative Management of Atrial Fibrillation

Patients with preexisting atrial fibrillation who have received antiarrhythmic or rate-controlling agents should continue therapy throughout the perioperative period. Intravenous formulations should be used if necessary. Correction of postoperative electrolyte imbalances and fluid volume is important, as electrolyte disturbances and dehydration increase atrial activity and predispose the arrhythmia. Although no randomized controlled trial is available to specifically address the problem of anticoagulation for postoperative atrial fibrillation, the American College of Chest Physicians recommends that heparin therapy be considered for high-risk patients or those with a previous history of stroke or transient ischemic attack, and to continue anticoagulation therapy for 30 days after the return of normal sinus rhythm. The Effectiveness of Bridging Anticoagulation for Surgery study, which compares dalteparin with a placebo, is expected to be completed by 2013. For patients with new onset atrial fibrillation, echocardiography and cardioversion are appropriate.

Perioperative Management of Patients on Oral Anticoagulant Therapy

Patients who are on oral anticoagulant therapy pose a common and challenging perioperative problem. There is a need to balance the risk of a thromboembolic event during interruption of oral anticoagulant therapy against the risk of bleeding. However, there is a paucity of data to inform decisions regarding perioperative antithrombotic therapy. Consequently, there is little consensus on the optimal management strategy. Nevertheless, three approaches to oral anticoagulation management have been suggested: (1) to continue warfarin therapy, (2) to withhold warfarin therapy for some time before and after the procedure, or (3) to temporarily withhold warfarin therapy while also providing a short acting, or bridging, anticoagulant during the perioperative period.

For procedures that carry a low risk of bleeding, continuation of warfarin therapy is probably safe. However, in patients undergoing major surgery or invasive procedures, interruption of antithrombotic therapy is typically required to avoid bleeding. The risk stratification and bridging anticoagulant approaches adopted by the 2008 guidelines of the American College of Chest Physicians should advise clinical practice (table 3).

Perioperative Management of Patients on Antiplatelet Drugs

Withdrawing antiplatelet therapy given for secondary prevention of stroke exposes patients to an increased risk of recurrent ischemic stroke. This may be related to the rebound or prothrombotic effect associated with antiplatelet withdrawal in addition to the prothrombotic effect of surgery. On the other hand, continuing antiplatelet therapy may increase the risk of major bleeding. Unfortunately, there are currently no data to guide the management, and clinical practice has been variable. The situation is more problematic when antiplatelet drugs are given for previous placement of intracranial stents. Withholding antiplatelet in these patients may confer higher risks of stroke. The POISE 2 trial, a large randomized control trial evaluating the risks and benefits of continuing antiplatelet therapy, has recently started recruiting patients, and should be completed by 2014. This study

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Given such complexity, the absence of outcome data defining a blood pressure threshold for stroke in general surgical patients, and the relative infrequency of purely hemodynamic strokes, it is not surprising that there is no consensus on appropriate perioperative blood pressure targets. A common practice is to maintain mean or systolic blood pressures within 20% of baseline, which is usually the blood pressure measured immediately before entry to the operating room. This reference value is above the patient’s usual awake blood pressure and even further increased above their sleep values. Such a relatively conservative approach to intraoperative blood pressure management is justifiable in patients at high risk for perioperative strokes. In healthy patients, blood pressures that approximate sleep levels are likely quite acceptable, i.e., 25–35% decrease from immediate preoperative baseline.

**Other Contributing Factors**

Beyond avoidance of severe hyperglycemia and hypoglycemia, both of which are detrimental, there is no consensus on the perioperative target glucose values to enhance clinical outcomes. Although an earlier study of patients in the surgical intensive care unit found a survival benefit following strict glucose control, or glucose concentrations 4.4–6.1 mM, compared with traditional management, or glucose concentrations 10–11.1 mM, evidence from recent randomized controlled trials and meta-analyses suggest that there is no benefit to overall mortality with strict glycemic control compared with traditional management. In fact, an increased incidence of stroke was found with strict intraoperative glucose control in cardiac surgery patients. The American Diabetes Association and the American Association of Clinical Endocrinologists have published a joint consensus statement defining a target range of 7.8–10 mM among critically ill patients. Pending results from prospective trials in patients undergoing major surgery, this seems a reasonable aim for all surgical patients.
Patients with previous stroke are often taking statin and other lipid-lowering drugs for secondary stroke prevention. Discontinuation of statin therapy can be harmful and may acutely impair vascular function. Statin withdrawal in patients with acute stroke was associated with an 8.7-fold increase in the risk for early neurologic deterioration. Discontinuation of statin therapy should be continued throughout the perioperative period in at-risk patients. Instituting statin therapy should be continued perioperatively or immediately at stroke onset has yet to be convincingly shown in randomized trials to be of benefit. Statin withdrawal in patients with acute stroke was associated with an 8.7-fold increase in the risk for early neurologic deterioration. Thus, statin therapy should be continued throughout the perioperative period in at-risk patients. Instituting statin therapy should be continued perioperatively or immediately at stroke onset has yet to be convincingly shown in randomized trials to be of benefit.

Recent stroke
Defer elective surgery for longer than 3 mo, risk factor modification. For urgent surgery, meticulous blood pressure monitoring and maintenance. Consider monitoring for cerebral ischemia with transcranial doppler or neurophysiological monitoring.

Carotid stenosis
For symptomatic, high grade (more than 70% stenosis), revascularization recommended prior to elective surgery. Revascularization is contraindicated for less than 50%, symptomatic stenosis. There is still controversy about the best management of asymptomatic stenosis, but more than 60% stenosis is increasingly being operated on.

Atrial fibrillation
Continue antiarrhythmic therapy perioperatively, correct electrolyte disturbances and dehydration. For postoperative atrial fibrillation in patients at high risk of stroke, consider heparin therapy and continue heparin for 30 days after return of sinus rhythm.

Patients on oral anticoagulation
See guidelines outlined in Table 3.

Patients on antplatelets
No good evidence to guide practice. Maintain on aspirin if possible.

Hyperglycemia
Maintain blood glucose within normal range.

Hypertension
Intraoperative blood pressure targets on awake resting range.

Perioperative stroke
Early diagnosis aided by noncontrast computed tomography of the brain, consider thrombolysis on a case-by-case basis. Correct postoperative hypotension and fever; transfer to an acute stroke unit for general supportive care and prevention of complications.

Table 4. Issues Concerning Prevention and Early Management of Perioperative Stroke

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Early Management of a Perioperative Stroke

Important elements in early management are identifying at-risk patients and early diagnosis (table 4). Nursing staff initially detect the vast majority of perioperative strokes, as most strokes are not acute intraoperative events but are diagnosed during the postoperative period and later hospital stay. However, routine surgical nursing care does not include a useful neurologic examination. There is extensive research and clinical experience with the use of the National Institutes of Health Stroke Scale and the Canadian Neurologic Scale. These do not take long to do, but require some training, making it unlikely that they would be widely adopted. Wide integration of simpler scales would be a step in the direction of earlier detection. There is also a need to shorten the time from nursing diagnosis to neurologist’s assessment, without waiting for the surgical team to complete the day’s operating room activities. An increasing number of medium- to large-sized medical centers have an “Acute Stroke Team” that is managed by neurologists and who respond rapidly if a stroke is suspected. Emergency noncontrast scanning of the brain is the primary diagnostic brain-imaging study for evaluation of patients with suspected stroke, and the goal is to complete the computer tomography examination within 25 min of the provisional diagnosis being made. Noncontrast computer tomography accurately discriminates ischemic stroke from intracranial hemorrhage and nonvascular causes of neurologic symptoms, such as tumors. It is, however, relatively insensitive in detecting acute and small cortical or subcortical infarctions, especially in the posterior fossa. Multimodal computer tomography and magnetic resonance imaging may provide additional information that will improve diagnosis of ischemic stroke. However, emergency treatment of stroke should not be delayed to obtain multimodal imaging studies.

General supportive care and prevention of complications are also important to patients with perioperative stroke. This may be best achieved by moving the surgical patient to an Acute Stroke Unit, where management is coordinated by stroke neurologists. Partial airway obstruction, hypoventila-
tion, aspiration pneumonia, and atelectasis are common causes of hypoxia that may worsen the brain injury. Both hypertension and hypotension are associated with poor outcome after stroke. Urgent correction of common postoperative causes of hypotension, including volume depletion, blood loss, myocardial ischemia, or arrhythmias, may improve neurologic outcomes. Although there are data from small clinical trials suggesting that drug-induced hypertension could be used for the treatment of selected patients with acute ischemic stroke, there are no data from large clinical trials, and current consensus does not recommend this treatment.113 Intentional hemodilution does not improve functional outcome and is not recommended for the treatment of acute stroke.113 The source of any fever should be ascertained and treated, as fever is associated with poor neurologic outcome after acute stroke.115,116 Both myocardial ischemia and cardiac arrhythmias are potential complications, and the current American Heart Association guidelines recommend that patients with acute ischemic stroke should have cardiac monitoring for at least the first 24 h and that any serious arrhythmia should be actively treated.113

Unfortunately, much of the emergency advanced treatment of acute stroke, such as pharmacologic thrombolysis, mechanical recanalization of occluded arteries, and heparin administration, are not suitable for patients after surgery. The current American Heart Association guidelines consider major surgery within 14 days of stroke a contraindication to intravenous thrombolysis. However, given the benefit to be gained, on a case-by-case basis, patients who suffer a perioperative ischemic stroke may be eligible for intravenous thrombolysis. Intravenous thrombolysis is another option for treatment, either alone or in conjunction with intravenous thrombolysis, and may be safely administered to patients within 6 h of symptom onset. Currently, aspirin is the only oral antiplatelet agent that has been found beneficial in the treatment of acute ischemic stroke, and should be used in the perioperative period whenever deemed safe.113

In conclusion, perioperative stroke is more common than generally acknowledged. Increased awareness and management of predisposing risk factors with early detection should result in improved outcomes. Prospective studies of overt and covert stroke in the perioperative period are needed in order to inform incidence, pathophysiology, prevention, and treatment.

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