Review Articles

Perioperative stroke. Part I: General surgery, carotid artery disease, and carotid endarterectomy

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Although stroke, defined as a focal neurological deficit lasting more than 24 hr, is uncommon in the perioperative period, its associated mortality and long-term disability are high. No large-scale data are available to identify the importance of recognized risk factors for stroke in the perioperative period. A review of the literature shows that the incidence and mechanism of its occurrence are influenced by the presence of cardiovascular disease and the type of surgery. The most common cause of perioperative stroke is embolism. In non-cardiac surgery, the incidence of perioperative stroke is higher among the elderly. Properly administered, controlled hypotension is associated with minimal risk of stroke. Cerebral vasospasm may be the cause of focal cerebral ischaemia in eclamptic patients, and the aggressive treatment of hypertension may exacerbate the neurological damage. The risk of stroke associated with carotid endarterectomy is closely related to the preoperative neurological presentation, and the experience of the surgical/anaesthetic team. Symptomatic cerebrovascular disease, acute stroke, asymptomatic carotid lesions, preoperative assessment of risk, local and general anaesthesia, cerebral protection and monitor-

ing during carotid endarterectomy are discussed with reference to reducing the risk of perioperative stroke. Adequate monitoring and protection have minimized the risk of ischaemia from carotid clamping, and the major mechanism of stroke is embolization.

Même si l'apoplexie, définie comme un déficit neurologique focal d'une durée supérieure à 24 heures, est rare en période périopératoire, elle est associée à une mortalité et une morbidité chronique élevée. Aucune donnée à grande population n'est disponible afin d'identifier l'importance des facteurs de risques reconnus pour l'apoplexie en période périopératoire. Une revue de la littérature démontre que l'incidence et le mécanisme de sa survenue sont influencés par la présence de maladie cardiovasculaire ainsi que du type de la chirurgie. La cause la plus fréquente de l'apoplexie périopératoire est l'embolie. En chirurgie non cardiaque, l'incidence de l'apoplexie périopératoire est élevée chez les gens âgés. L'hypotension contrôlée, adéquatement administrée, est associée avec un risque minime d'apoplexie. Le vasospasme cérébral peut être la cause de l'ischémie cérébrale focale chez les patientes en éclamptie, et le traitement agressif de l'hypertension peut exacerber les lésions neurologiques. Le risque d'apoplexie associé à l'endartérectomie carotidienne est étroitement relié à l'état neurologique préopératoire et l'expérience de l'équipe chirurgicale-anesthésique. Les maladies cérébrovasculaires symptomatiques, l'apoplexie aiguë, les lésions carotidiennes asymptomatiques, l'évaluation du risque préopératoire, l'anesthésie générale et locale, la protection cérébrale et la surveillance lors de l'endartérectomie carotidienne sont discutées particulièrement en rapport avec la diminution du risque d'apoplexie périopératoire. La surveillance adéquate et la protection ont diminué le risque d'ischémie dû au clampage carotidien et le mécanisme majeur d'apoplexie demeure l'embolisation.

Key words

BRAIN: infarction;

COMPLICATION: stroke, perioperative;

EMBOLISM: cerebral.

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Stroke occurring in the perioperative period is a devastating complication, as illustrated by the following three cases.

Case #1

A 75-yr-old man was admitted for transurethral resection of a hypertrophic prostate gland. He had chronic obstructive pulmonary disease, extensive peripheral vascular disease with previous aorto-bifemoral bypass graft, hypertension, atherosclerotic heart disease, and chronic atrial fibrillation. He had a history of "mild stroke" consisting of weakness of the left arm and leg some 15 yr previously, and from which he had completely recovered. Bruits were noted in both sides of the neck and groin. His medications included digoxin, hydrochlorothiazide, and sulfinpyrazone. Preoperative ECG showed atrial fibrillation with ventricular rate of 100 per minute, infrequent premature ventricular contractions, left ventricular hypertrophy and evidence of old antero-septal infarction. A spinal anaesthetic using 12 mg tetracaine produced cutaneous analgesia to T₁₀. The intraoperative course was stable, with blood pressure maintained close to the preoperative level of 150/90 mmHg. Five hours after surgery, he had a major bleed at the surgical site, which resulted in a decrease of blood pressure to 60/50 mmHg,

and he was transfused with three units of packed red cells, two units of plasma, and two litres of crystalloid solutions, followed by cystoscopy and fulguration for haemostasis. He developed weakness of the left arm and leg at the time of the hypotension. By the time of discharge from hospital two weeks later, he had partially recovered from the weakness in the left leg. His left arm was still very weak when seen eight years later, when he was readmitted for unrelated problems.

Case #2

A 70-yr-old man with recurrent transient ischaemic attacks, which presented as weakness of the right arm and leg, and angiographic demonstration of tight stenosis of the left internal carotid artery at its origin, was admitted for left carotid endarterectomy. The CT head scan showed the presence of multiple small old infarctions in the left frontal, parietal and occipital lobes. He also had hypertension, non-insulin dependent diabetes, atherosclerotic heart disease with angina and a history of myocardial infarction in the remote past. His medications included ASA, isosorbide dinitrate, propranolol, and hydrochlorothiazide. The preoperative blood pressure was 140/70 mmHg. He received a general anaesthetic consisting of thiopentone, succinylcholine, fentanyl, isoflurane, nitrous oxide and pancuronium. The systemic blood pressure was labile during the intraoperative course, requiring small doses of ephedrine to maintain his blood pressure above 115/50 mmHg. Intraoperative EEG showed asymmetry prior to induction of anaesthesia, and there was no change during carotid artery cross-clamping. A shunt was not used. The EEG monitoring was discontinued ten minutes after release of the carotid clamps. During skin closure, the blood pressure suddenly increased to 210/110 mmHg briefly. At the end of the procedure, he was very drowsy, his speech was slurred, and his right arm and leg were weak. The CT scan showed a small haematoma of the internal capsule. Digital subtraction angiography showed that the endarterectomized artery was patent. The stroke was the result of a hypertensive intracerebral bleed. By the time he was discharged three weeks later, his speech had improved, but he still had marked weakness of the right side of the body.

Case #3

An 82-yr-old man presented with recurrent carcinoma of the larynx which had been controlled with radiotherapy two years before admission. During the two years, he experienced three episodes of reversible ischaemic neurological deficits involving the left eye and the right arm and leg. He also had chronic atrial fibrillation, and non-insulin dependent diabetes. He was taking digoxin and ASA. He had a total laryngectomy with isoflurane, nitrous oxide

and fentanyl anaesthesia. During surgery, he developed one brief episode of rapid atrial fibrillation at 120 bpm. On emergence from anaesthesia, he had a right hemiplegia. He could "mouth" words, and showed no obvious evidence of aphasia. The CT scan one week after surgery showed multiple bilateral cerebral, lacunar and cerebellar infarcts. Presumably these were embolic in origin, and the infarct in the region of the left posterior caudate radiata was responsible for the right hemiplegia. Although he was probably cured of his cancer, his postoperative course was slow and difficult because of his hemiplegia and lack of communication as a result of the laryngectomy. Six weeks after surgery, he was transferred to a rehabilitation care facility.

These strokes occurred either in the intraoperative or the postoperative period. Pre-existing cerebrovascular disease and haemodynamic instability were responsible in the first and second cases, and cardiogenic embolization probably was responsible in the third.

Strokes associated with general surgical procedures are uncommon and are rarely reported.¹ The purpose of this paper is to review the incidence and mechanisms of perioperative stroke in various situations encountered in the surgical patients.

General overview

Stroke is defined as a focal neurological deficit which has a sudden onset and which persists for longer than 24 hr. Global cerebral ischaemic syndromes caused by hypoxaemia or ischaemia are not considered. The overall incidence of perioperative stroke is low. In 1986, Cohen *et al.* published the outcome of a nine-year post-anaesthetic followup program, involving 112,721 anaesthetics at the Health Sciences Centre in Winnipeg. Perioperative stroke was not listed as a separate complication.² Although stroke in the perioperative period is uncommon, the acute mortality is high – from 16 to 50%^{3,4} and many of the survivors have long-term disability, resulting in pain and suffering to both the patients and their families.^{5–7}

There are two mechanisms of stroke: (1) occlusion of a cerebral artery (thrombotic or embolic), which causes brain infarction, and (2) spontaneous rupture of an intracranial artery, which causes bleeding either in the brain parenchyma or in the subarachnoid space. Based on the data from the National Pilot Stroke Data Bank (1982) and the Harvard Stroke Series (1978), the ratio of infarcts to haemorrhage is about 4:1, and embolism accounts for approximately one-third of all strokes.⁸

The major risk factors for stroke identified by the special subcommittee of the Council on Cerebrovascular Disease of the American Heart Association were transient ischaemic attacks, cerebral infarction, hypertension, car-

diac abnormalities, other consequences of atherosclerosis and diabetes mellitus.⁹ Solzi *et al.* identified age, hypertensive heart disease, peripheral vascular disease, diabetes, myocardial infarction and atrial fibrillation as the most important risk factors.¹⁰ Herman *et al.* reported that transient ischaemic attacks (TIA), cardiac arrhythmias, myocardial infarction, diabetes mellitus, other heart conditions, and high blood pressure are the most important risk factors after adjusting for age and sex.¹¹ The risk for stroke can be decreased by treatment of hypertension, cardiac disease, TIA, high haematocrit and possibly diabetes mellitus.¹²

These factors are also potential risk factors for perioperative stroke. However, large scale data are not available to identify the importance of the individual risk factors as the cause of perioperative stroke. The incidence of perioperative stroke varies with the type of surgical procedure.⁴ For this review, perioperative stroke is considered in the following situations:

- 1 General surgery,
- 2 Carotid artery disease and carotid endarterectomy,
- 3 Cardiac surgery,
- 4 Perioperative cardiogenic embolic stroke.

General surgery

Stroke associated with general surgery

It is difficult to gain an accurate incidence of central nervous complications associated with general surgery without a prospective study of a large number of patients. The neurological deficit may be mild or transient, and may escape detection or recording in the clinical chart. The incidence depends on the size and duration of sampling, the patient population with different coexisting medical conditions, the type of surgery and anaesthetic technique, and the accuracy of observation. Perioperative stroke is uncommon in general surgery which includes urological, gynaecological, obstetrical, orthopaedic, and peripheral vascular procedures. In one survey by Hart,⁴ the incidence of perioperative stroke was 0.07% in 24,500 general surgical procedures. Since stroke is a relatively uncommon complication of general surgery, it is difficult to predict those patients who are at risk.

AGE

There are reasons why the elderly patient may be more prone to perioperative stroke. Arteriosclerosis and hypertension are more common, and the autoregulatory range of cerebral blood flow may be more restricted than in the young population. In addition, atheroma formation in the carotid artery is an aging process. Indeed, the incidence of perioperative stroke in elderly patients may be between 0.4 and 3.3%.¹³

TABLE 1 Incidence of perioperative neurological deficits in elderly patients undergoing non-cardiac surgery

Author	Patients	Cases	Periop stroke/TIA
Knapp ¹⁴	>50 yr male	8,984	0.38%
Stephen ¹⁵	>70 yr	1,207	0.5%
Wilder ¹⁶	>80 yr	207	3.4%
Hosking <i>et al.</i> ¹⁷	>90 yr	185	3.2%

The risk appears to increase with age (Table 1). In Knapp's series of 8,984 male patients over 50 yr old, the incidence of perioperative stroke was 0.38%.¹⁴ Stephen reviewed 1207 surgical procedures in 1000 patients over 70 years. The perioperative stroke rate was 0.5%, and one-third of these were fatal.¹⁵ Wilder studied 207 patients over 80 years undergoing non-cardiac surgery. Stroke occurred in seven patients (3.4%), and six of the seven patients died.¹⁶

However, more recent studies show a lower perioperative mortality and morbidity in elderly patients. In the retrospective study by Hosking *et al.* in patients over 90 yr at the Mayo Clinic, TIAs occurred in 2.9% of 103 patients who had general anaesthesia, in 5.3% of 38 patients who had regional anaesthesia for total hip arthroplasty, in none of the 13 patients who had general anaesthesia, and in 3.2% of 31 patients who had regional anaesthesia for transurethral resection of the prostate. Thus, neurological deficits occurred in 3.2% of a total of 185 patients.¹⁷

HYPOTENSION

Cerebral complications may result from hypotension if the delivery of oxygen and nutrients is compromised. However, this is more likely to result in diffuse rather than focal injury. To study how often brain infarcts were caused by hypotensive episodes, Torvik and Skullerud examined the brains from 135 patients who had been resuscitated after cardiac arrest and who subsequently died from one day to several weeks after the episode. If hypotension was a major cause of brain infarcts, it would have been expected that patients with severe cerebral atherosclerosis would have a high incidence of brain infarcts in addition to signs of diffuse cerebral anoxia, while patients without cerebral atherosclerosis primarily would have shown signs of diffuse cerebral anoxia. Seven patients (5.2%) in this series had cerebral infarcts. The incidence of cerebral infarction did not correlate with the severity of cerebral atherosclerosis.¹⁸ Therefore this study did not support the concept that hypotension was a major factor in the production of brain infarcts in elderly atherosclerotic patients. Furthermore, the risk of precipitating brain infarction by lowering the blood pressure in

hypertensive patients may not be much greater in atherosclerotic than in nonatherosclerotic subjects.

DELIBERATE HYPOTENSION

Thirty years ago, patient selection and control and monitoring of blood pressure during hypotensive anaesthesia were less than ideal.¹⁹ Consequently, cerebral thromboses were reported. A postal survey in 1953 by Hampton and Little revealed 46 deaths in 21,125 hypotensive anaesthetics (0.2%), the commonest cause of death being cerebral thrombosis.²⁰ Little reported 47 cases of cerebral thrombosis in 27,930 hypotensive anaesthetics, of which 18 were fatal.²¹ Way and Clarke had two deaths in 50 prostatectomies. One was an 82-yr-old man with preoperative congestive heart failure, who developed profound hypotension resulting in massive thrombosis of the middle cerebral artery. The other was an 81-yr-old man with a history of hypertension, who had a stroke five days after surgery.²² Grace used deliberate hypotension for prostatectomy in 1000 patients, which resulted in five fatal cerebral thromboses. Three of these occurred in a group of 40 patients with cerebro-vascular disease.²³ On the other hand, Linacre had no cerebral complications in 1000 mostly middle-aged patients having gynaecological surgery.²⁴ Larson reported a 0.85% mortality rate in 13,264 cases.²⁵ Prys-Roberts *et al.* reported two cases of cerebral damage in 15 patients undergoing hypotensive anaesthesia induced with halothane. One patient developed hemiplegia and the other had extensive cerebral and cerebellar infarction.²⁶

With better selection of patients and improvement in techniques, Kerr reported no morbidity or mortality in 700 cases.²⁷ In a survey of 20,558 hypotensive anaesthetics (mean BP 60 to 80 mmHg) in one institution over a 30-year period from 1950 to 1979, there were only three cases of focal neurological deficit.²⁸ When hypotension was carefully controlled to a mean of 50 to 60 mmHg, no difference in postoperative cerebral function using psychometric tests was found between patients randomly allocated to hypotensive and non-hypotensive group.²⁹⁻³¹ Pinaud *et al.* showed that during craniotomy for cerebral aneurysm in patients with good neurological function, mean regional cortical cerebral blood flow in the non-operated hemisphere remained unchanged despite a major nitroprusside-induced reduction in blood pressure to 40 mmHg.³²

Unlike "shock" states associated with severe decreases in organ perfusion, and acid-base and metabolic changes, brain perfusion is well maintained by autoregulatory mechanisms during deliberate hypotension.³³ The risks of brain damage are minimal with deliberate hypotension provided that hypotensive anaesthesia is carefully administered. However, potential complications in other organ

systems also have to be considered. Patients with cerebrovascular disease, hypotension, ischaemic heart disease, renal disease, hypovolaemia, or anaemia are not suitable candidates. The degree of hypotension should be limited to a mean of 60 mmHg, and rapid reduction of arterial pressure or excessive hypocarbia should be avoided. Arterial pressure monitoring is considered mandatory, and some have recommended that EEG should be used.³⁴

MECHANISMS OF PERIOPERATIVE STROKE IN GENERAL SURGERY

Hart and Hindman studied the mechanisms of perioperative cerebral infarction in general surgical procedures.⁴ In their retrospective study, the incidence of perioperative stroke in 24,500 general surgical procedures was 0.07%. Patients over 65 yr of age had a higher incidence of 0.22%. The majority of strokes, 83%, occurred in the postoperative period, and were unrelated to hypotension. Cardiogenic embolism was suspected as a common cause of stroke (42%), with atrial fibrillation being present in 33% at the time of stroke. However, carotid bruit or evidence of carotid occlusive disease were not predictive of perioperative stroke. These authors suggested that altered coagulability in the postoperative period probably played a major role.

Kelley and Kovacs examined in-hospital cerebral ischaemia prospectively.³⁵ In a group of 171 patients with cerebral ischaemia, 26 (15.2%) developed symptoms while in hospital. Cerebral ischaemia occurred in the perioperative period in 12 patients, unsuccessful cardioversion in one and coronary angiography in another. Twelve of the 14 patients had procedures related to cardiovascular or peripheral vascular disease. Thus the majority of in-hospital events were due to embolic stroke.

Stroke associated with obstetrics and pregnancy

Cerebrovascular disease is rare in patients of childbearing age. Perioperative stroke associated with obstetrics or surgery during pregnancy is usually related to cerebral aneurysm, arteriovenous malformation or preeclampsia. If an arteriovenous malformation or aneurysm ruptures during pregnancy, emergency craniotomy may be required. In stable patients with unruptured aneurysms, the pregnancy should be brought to term and craniotomy performed electively after the delivery of the baby.³⁶ Vaginal delivery or Caesarean section in a patient with cerebral aneurysm is a challenge to the anaesthetist. Epidural anaesthesia for forceps delivery or Caesarean section is a suitable technique for minimizing the hypertensive responses to stress and Valsalva manoeuvre.³⁷

Preeclamptic patients are at risk for intracerebral bleeding. Focal neurological abnormalities are rare in preeclampsia or eclampsia, and most reports are of

patients with temporary cortical blindness. Focal signs in eclampsia are most commonly due to cerebral haemorrhage and less commonly due to ischaemic infarction.^{38,39}

A few reports have appeared recently of focal cerebral ischaemia in the peripartum period,⁴⁰ and complicating eclampsia.^{41,42} Vasospasm appears to be the cause of these neurological manifestations. Indeed, cerebral angiographic studies in toxemia have demonstrated severe cerebral arterial vasospasm.^{43,44} These findings suggest that aggressive treatment of hypertension is likely to exacerbate neurological damage. It would appear that the most appropriate treatment would be a cerebral vasodilator agent such as nimodipine in conjunction with other antihypertensive agents. Magnesium sulphate, which has long been advocated for treating toxemia of pregnancy, may exert its beneficial effect by opposing calcium-dependent arterial constriction.⁴⁵

Carotid artery disease and carotid endarterectomy

Carotid reconstruction and endarterectomy were first performed in the early 1950s,⁴⁶⁻⁴⁹ after the recognition of the relationship between occlusive disease of the extracranial carotid arteries and cerebrovascular insufficiency,^{50,51} and the use of arteriography for the diagnosis of carotid artery thrombosis.⁵² In less than 40 yr, carotid endarterectomy proliferated markedly, and has become the third most common operation performed in the United States.⁵³⁻⁵⁵

Intimal thickening and plaque formation at the carotid artery bifurcation may be asymptomatic. However, if the collateral perfusion is inadequate, the plaque may give rise to symptoms either by reducing blood flow,⁵⁶ or, more frequently, by producing emboli.^{57,58} Cerebrovascular insufficiency may present as transient hemispheric ischaemic attacks, amaurosis fugax, reversible ischaemic neurological deficit, or stroke. The source of obstruction and embolization can be removed by carotid endarterectomy.⁵⁹ Unfortunately, however, cerebral angiographic investigations and the operation itself sometimes cause stroke.

With improvements in angiographic equipment and operator dexterity, the risks of cerebral angiography have gradually decreased over the past 20 yr.⁶⁰⁻⁶⁹ The overall risk of neurological complication is about 4%, and a disabling stroke occurs in about 1% of patients.^{70,71} The risks associated with cerebral angiography must be considered when evaluating the risks of carotid endarterectomy.

Stroke associated with carotid endarterectomy

There are many reports on the morbidity and mortality associated with carotid endarterectomy. Some of these are summarized in Table II.⁷²⁻¹⁰⁷ The neurological compli-

TABLE II Mortality and CNS morbidity associated with carotid endarterectomy

Author	Cases (asymptomatic %)	Shunt use	CNS monitor	CNS complications		
				Transient	Permanent	Mortality
<i>Local anaesthesia</i>						
Perry (1970) ⁷²	77 (*)	*	SvO ₂	2.6	3.9	2.6
Erwin (1980) ⁷³	21 (*)	38.1%	N,SP	9.5	0	0
Whittemore (1980) ⁷⁴	96 (11.5%)	Routine	N	2.1	1.0	1.0
Steed (1982) ⁷⁵	359 (rarely)	3.9%	N	4.2	1.7	0
Gableman (1983) ⁷⁶	54 (0)	20%	N	1.9	3.7	0
Luosto (1984) ⁷⁷	111 (8.1%)	14.4%	N,SP	0	1.8	0.9
Hafner (1988) ⁷⁸	1,200 (23.6%)	9.4%	N	0.9	0.9	0.7
<i>General anaesthesia</i>						
Bloodwell (1968) ⁷⁹	374 (8.1%)	No shunt	None	-4.8-		5.6
DeWeese (1971) ⁸⁰	349 (14.3%)	4.9%	None	5.4	15.8	7.4
Hays (1972) ⁸¹	297 (*)	19.9%	SP	3.7	4.3	0.7
Howe (1974) ⁸²	73 (*)	Routine	None	0	0	0
Akl (1975) ⁸³	77 (22.0%)	1.3%	SP	2.6	5.2	2.6
Lindberg (1975) ⁸⁴	104 (4.8%)	66%	EEG	9.6	5.8	7.7
Matsumoto (1977) ⁸⁵	130 (*)	*	EEG	4.6	1.5	1.5
Stanford (1978) ⁸⁶	187 (0)	72.7%	None	2.7	2.1	0
Hertzer (1978) ⁸⁷	260 (36.2%)	59.6%	SP	2.7	1.9	1.2
Haynes (1979) ⁸⁸	276 (5.1%)	Routine	None	2.5	0.4	1.1
Ennix (1979) ⁸⁹	1,546 (21.3%)	*	*	*	1.7	2.1
Carmichael (1980) ⁹⁰	467 (7.3%)	0.9%	None	1.1	1.9	0.2
Whitney (1980) ⁹¹	1,197 (14.6%)	No shunt	None	1.2	2.3	1.8
Watson (1981) ⁹²	177 (20.9%)	60.5%	None	1.7	4.0	0.6
Schiro (1981) ⁹³	200 (32.0%)	Routine	None	1.5	1.0	0.5
White (1981) ⁹⁴	252 (17.5%)	87%	SP	2.0	2.0	2.00
Sundt (1981) ⁹⁵	1,145	44.6%	EEG, rCBF	1.7	2.2	1.5
Gableman (1983) ⁷⁶	46 (18.0%)	83.0%	None	13.0	4.3	2.2
Muuronen (1984) ⁹⁶	128 (0)	*	*	-12.5-		3.1
Brott (1984) ⁹⁷	431 (50.1%)	*	*	4.2	8.6	2.8
TCSG (1986) ⁹⁸	358 (3%)	*	*	5.0	4.5	1.5
Fode (1986) ⁹⁹	3,328 (17.2%)	43.8%	SP, EEG	2.5	4.2	2.0
Jenkins (1987) ¹⁰⁰	419 (2.6%)	74.9%	EEG	4.5	5.0	1.4
Nunn (1988) ¹⁰¹	651 (0)	Routine	None	0.9	1.5	0.8
Friedmann (1988) ¹⁰²	688 (18.3%)	Routine	None	-4.5-		1.0
Rubin (1988) ¹⁰³	8,535 (12.4%)	*	*	0.2	1.1	1.6
Kirshner (1989) ¹⁰⁴	1,035 (21.4%)	24.8%	EEG	2.3	3.5	1.4
<i>Mixed local and general anaesthesia</i>						
Bland (1970) ¹⁰⁵	613 (*)	No shunt	None	-9.0-		2.9
Peitzman (1982) ¹⁰⁶	314 (4.0%)	7.6%	N, EEG	0.9	2.2	0.9
Till (1987) ¹⁰⁷	389 (39.8%)	*	*	*	1.5	2.3

*Data not available. SvO₂, Venous oxygen saturation. EEG, Electroencephalography. N, Neurological examination. SP, ICA stump pressure. rCBF, Regional cerebral blood flow.

cation rates of these series are not strictly comparable because of the differences in: (1) the selection of patients based on neurological presentation, (2) the data collection: prospective versus retrospective chart reviews, (3) the nature of the series: personal, institutional, multicentre or community study, (4) the sample size, (5) the duration of study: varying from months to over 20 years, (6) the duration of followup: perioperative period versus hospital stay, (7) the definition of "transient," "pro-

longed," "permanent," "minor" and "major" deficits, and (8) the cause of mortality, some of which were due to myocardial infarction rather than stroke.

Many recent large series on carotid endarterectomy have achieved very low perioperative stroke and mortality rates of less than 2%.^{78,89,95,101,103} Brott and Thalinger reported a different picture in their review of all carotid endarterectomies performed in the greater Cincinnati metropolitan area during 1980. Among the 431 proce-

dures performed in 16 hospitals, the perioperative stroke rate was 8.6%, and mortality rate was 2.8%. The disturbing finding was that the stroke rate among asymptomatic patients was 5.6%, and half of the procedures were performed in asymptomatic patients.⁹⁷ The risk in asymptomatic patients should have been minimal.⁹⁴

The specific mechanisms that cause perioperative stroke in carotid endarterectomy have been the subject of many studies. In Brott and Thalinger's survey, 57% of the strokes occurred in the postoperative period.⁹⁷ The major mechanism appeared to be thrombogenic-embologenic problems at the operative site. The Toronto Cerebrovascular Study Group reviewed the outcome of 358 carotid endarterectomies performed in the neurosurgical units of the University of Toronto in 1982. The mortality rate was 1.5%, and the perioperative stroke rate was 3.9%. The majority (82%) of the strokes occurred in the postoperative period. The major mechanism was embolic rather than haemodynamic. The authors stressed the importance of careful operative technique and the use of anticoagulants and antiplatelet agents.⁹⁸ A review of 419 carotid endarterectomies done at Vancouver General Hospital showed an overall mortality rate of 1.4%, and a stroke (both major and minor) rate of 5%. The causes of the 21 major and minor strokes were embolic in 14, ischaemic in three, thrombosis in two, major haemorrhage from arteriotomy site in one, and hypertensive cerebral haemorrhage in one patient.¹⁰⁰

Steed *et al.* studied carotid endarterectomy performed under regional anaesthesia, which provided a unique opportunity to determine the time of onset of a neurological deficit and to deduce its likely cause. Of 366 patients, 345 (96%) tolerated carotid clamping and did not require shunting. Stroke occurred in six patients (1.7%) and TIA in 15 patients (4.3%). Neurological deficits occurred during carotid dissection in three patients, during carotid occlusion in one patient, upon release of carotid artery cross-clamp in two patients, and during the first five postoperative days in 15. They concluded that the likely cause of the perioperative strokes were thromboembolic in 20, and cerebral anoxia in only one patient.⁷⁵ Krul *et al.*, using CT scan to study the pathogenesis of 34 ischaemic strokes associated with carotid endarterectomy, found that 68% were due to intraoperative or postoperative thromboembolism, and 21% were haemodynamically induced.¹⁰⁸

In the report of Sundt *et al.*, 36% of the neurological deficits occurred intraoperatively, and 64% occurred postoperatively. The major cause of intraoperative deficits was embolization and occasionally hypoperfusion. Similarly embolization was the major mechanism of stroke during the postoperative period.⁹⁵ However, hyperperfusion subsequent to endarterectomy played a

major role in postoperative stroke among the neurologically unstable patients with tight stenosis.¹⁰⁹ Caplan *et al.* reported two cases of fatal intracranial haemorrhage due to uncontrolled postoperative hypertension in patients who had preoperative hypertension, severe carotid stenosis and recent stroke. They postulated that the tight stenosis protected the distal cerebral bed from systemic hypertension, and its removal increased the pressure in the previously protected capillary bed, which became prone to rupture in the presence of postoperative hypertension.¹¹⁰ Towne and Bernhard examined the relationship between postoperative hypertension and neurological deficits following carotid endarterectomy in their series of 253 cases. They found that the incidence of neurological deficits was 10.2% in patients who developed hypertension and only 3.4% in those who did not.¹¹¹

Based on these reports, it appears that most of the factors determining the occurrence of perioperative stroke are within surgical control. Selection of patients for carotid endarterectomy should take into consideration the neurological, angiographic and medical risks. The risk of surgery should be balanced against that of not operating. Embolic rather than haemodynamic factors appear to be the major mechanism of perioperative stroke, and meticulous surgical technique is necessary.

However, anaesthetists can help to minimize the risk of perioperative stroke in this operation by actively participating in all phases of their management. In the preoperative period, the risk factors should be identified. Hypertension should be controlled, and patients with coronary artery disease should be investigated and prepared to the optimal state. During the intraoperative period, appropriate use and interpretation of cerebral monitoring to identify the patients who need shunting, and maintenance of cardiac function and cerebral perfusion for optimal cerebral protection are our primary responsibility. In the postoperative period, one should aim for early emergence to allow neurological assessment. Continual close monitoring of neurological assessment is crucial. Hypertension should be prevented and treated promptly. These will be discussed in more detail.

Assessment of risks associated with carotid endarterectomy

The Mayo Clinic group assigned grades of risks to patients based on medical, neurological and angiographically defined risk factors that may influence the outcome of carotid endarterectomy; and, in particular, the risk of perioperative stroke associated with this procedure (Table III).^{112,113}

While many of these factors have also been found by others to increase the risk of perioperative stroke, some, such as age,¹¹⁴ and intracranial vascular disease,^{115,116}

TABLE III Preoperative risk factors and classification of risks in carotid endarterectomy (Sundt TM Jr *et al.*)

<i>Medical risk factors</i>
Angina pectoris
Myocardial infarction within past six months
Severe hypertension >180/110
Chronic obstructive pulmonary disease
Age >70 yr
<i>Neurological factors</i>
Progressive neurological deficit
Deficit <24 hr old
Frequent daily TIA
Deficits secondary to multiple cerebral infarctions
<i>Angiographically defined risk factors</i>
Stenosis of internal carotid artery in siphon area
Extensive involvement of internal carotid artery
High bifurcation of artery and short and thick neck
Occlusion of the opposite internal carotid artery
Soft thrombus extending from an ulcerative lesion
<i>Grade 1 Risk</i>
Neurologically stable patients with no associated risk factors
<i>Grade 2 Risk</i>
Neurologically stable patients with no major medical risks but with significant angiographically defined risks
<i>Grade 3 Risk</i>
Neurologically stable patients with major medical risk factors
<i>Grade 4 Risk</i>
Neurologically unstable patients
<i>Grade 5 Risk</i>
Patients with symptomatic complete occlusion of internal carotid artery, regardless of other factors

have not. Nonetheless, the overall mortality and morbidity, such as myocardial infarction and neurological deficits, correlate quite well with this classification. The results based on an analysis of 1104 procedures showed that the combined morbidity and mortality in grades 1 to 4 were 1, 2, 4 and 9% respectively, and the incidence of neurological deficits were 1, 2, 2.6 and 4.5%.⁹⁵ In an analysis of 282 consecutive carotid endarterectomies done in the same institution from 1982 to 1984, it was shown that the risk of complications in grade 1 and 2 patients was 0%. The single nonfatal cardiac complication occurred in a patient with a grade 3 risk. All minor and major strokes and deaths occurred in grade 4 risk patients, with a total morbidity and mortality rate of 7.8% in this group.¹¹⁷

Salenius *et al.* from Finland identified the following risk factors for early cerebral complications in carotid endarterectomy: advanced age, type II diabetes mellitus, elevated serum triglycerides, high-grade stenosis or occlusion of the contralateral carotid artery, and second operation performed for bilateral disease or recurrent stenosis.¹¹⁸

The experience of the surgical team also influences the outcome of this operation.^{99,103} The surgeons performing carotid endarterectomy should evaluate their own results.^{119,120} The upper limits of morbidity and mortality that should prompt individual peer review have been defined by an Ad Hoc Committee on Carotid Surgery Standards of the Stroke Council, American Heart Association.¹²¹ The 30-day mortality rate from all causes for all carotid endarterectomies should not exceed 2%. The upper limit of combined morbidity and mortality due to stroke during or after carotid endarterectomy is adjusted according to the indications for surgery. The limit is 3% in asymptomatic patients, 5% for TIA, 7% for ischaemic stroke, and 10% for recurrent carotid disease in the same artery after endarterectomy.

Neurological presentation

The indications for carotid endarterectomy have evolved since it was first performed. The most suitable patients for surgery are those who present with transient hemispherical ischaemic attacks, amaurosis fugax, reversible ischaemic neurological deficits, or minor stroke with good functional recovery, and also have an appropriate angiographically demonstrated internal carotid plaque.^{101,122,123}

There is a 25 to 40% chance of a stroke within five years of onset of TIAs.¹²⁴⁻¹²⁷ Carotid endarterectomy can decrease this risk to between three and 14%.^{59,101,128,129} Salenius *et al.* recently reported the results of 44 surgically and 40 non-surgically (mostly with anticoagulants) treated patients with carotid stenosis documented by angiography. All patients, except four in the surgical group, had either TIA or stroke. They found that the operated patients had a lower incidence of cerebrovascular complications than the nonoperated patients (31.7% vs 55.0%) during a median follow-up period of over 123 months. However, the survival of the patients was similar, due mostly to myocardial infarction.¹³⁰

Preoperative CT scan studies showed that silent cerebral infarction was a common preoperative finding, and was present in 18 to 20% of patients for elective carotid endarterectomy.¹³¹⁻¹³³ Graber *et al.* found that 14 out of 79 asymptomatic patients had unexpected preoperative silent cerebral infarction. Four of these 14 patients (28.6%), compared with only one of 66 patients (1.5%) with a normal scan, had postoperative neurological deficit.¹³¹ These authors suggested that CT scanning of potential carotid endarterectomy patients was of benefit to predict more accurately the risk of postoperative neurological deficit. However, more recent studies failed to show a relationship between the presence of a silent cerebral infarction and perioperative neurological morbidity.^{132,133}

TABLE IV Surgical management of patients with acute stroke due to carotid thromboembolism

<i>Clinical presentation</i>	<i>Angiography & surgery</i>
Fixed neurological deficits; and depressed levels of consciousness	Not indicated
Unstable, fluctuating, mild to moderate deficits; and no alteration of consciousness	As soon as possible
Completed mild to moderate stroke; fixed or progressively improving deficits	Delay for 2 to 6 weeks; or operate when neurological recovery has reached a plateau

ACUTE STROKE

The management of patients with acute stroke is controversial. Early experiences showed that the operative morbidity and mortality during the acute phase were very high,^{80,134,135} and that intracranial haemorrhage might follow successful revascularization.^{110,136-138} However, more recently, selected patients with acute strokes have been successfully managed by surgery.¹³⁹⁻¹⁴⁵ The indications for surgery have been redefined,¹⁴⁶⁻¹⁴⁹ and depend on both the severity and the early course of the neurological deficit (Table IV).

The patients fall into three groups. The first consists of patients with fixed neurological deficits and depressed levels of consciousness. Cerebral infarction presumably has already occurred and is irreversible. Angiography and surgery are not indicated. The second consists of a few patients presenting with unstable and fluctuating, mild to moderate neurological deficits due to thromboembolism from carotid plaque, and without alteration of consciousness. Emergency angiography followed by emergency endarterectomy may reverse these deficits. If the perioperative blood pressure is carefully controlled, the risk of postoperative haemorrhagic infarction is low.¹⁴¹ Good neurological recovery with this aggressive approach has been reported.^{140,141,143,150} Nevertheless, the perioperative morbidity is much higher than in patients who are neurologically stable. On the other hand, the risk of not operating may be even greater.¹⁴³ A third group includes those who have completed strokes with mild to moderate fixed deficits, and those who appear to be progressively improving. Experience showed that surgery performed within two weeks of the onset of stroke was associated with high morbidity and mortality,^{135,137,138,151} and arteriograms in patients suspected of carotid artery disease should be delayed. Endarterectomy, if indicated, should be delayed for two to six weeks.^{152,153} Surgery should be delayed even longer in hypertensive patients.¹¹⁰ However, Piotrowski *et al.* recently showed evidence that carotid endarterectomy after acute stroke could be performed with no increase in morbidity or

mortality as long as the neurological recovery had reached a plateau. In a series of 140 patients who had carotid endarterectomy performed between 1978 and 1988, 82 were operated on within six weeks of stroke, and 47 were operated upon at varying times after six weeks. There was no significant difference of cerebrovascular events (1.2% vs 4.2%) and deaths (1.3% vs 2.1%) between the two groups of patients with respect to the timing of carotid endarterectomy.¹⁵⁴

Not infrequently, patients with recent strokes undergo surgery unrelated to their cerebrovascular disease. The general principles outlined above may also be applied to their management. After a stroke, regional cerebral blood flow may be unstable for weeks or even months. Changes of regional cerebral blood flow occur and adjustments, with luxury perfusion and hypoperfusion in and around the area of infarction, do not necessarily correlate with the clinical neurological outcome.¹⁵⁵⁻¹⁵⁷ Haematological disorders, with platelet hyperfunction and enhanced thrombin activity, are present for many weeks following an ischaemic stroke or a transient ischaemic attack.¹⁵⁸⁻¹⁶¹ In addition, systemic blood pressure changes continue for weeks in response to brain ischaemia.¹⁶² Haemodynamic instability in the perioperative period may affect the recent cerebral infarction unfavourably.

In the absence of symptoms, endarterectomy on a chronically occluded internal carotid artery is not indicated. Surgery on patients whose symptoms do not fit the diseased carotid artery is not likely to be beneficial.¹⁶³ The immediate and late surgical results depend largely on the preoperative neurological presentation. The more severe the neurological deficits from the previous stroke, and the more neurologically unstable the patient, the less favourable the outcome.^{99,104}

ASYMPTOMATIC CAROTID DISEASE

The best results, as expected, are obtained in asymptomatic patients with demonstrated carotid plaques.⁹⁴ However, the management of these patients is controversial.

Asymptomatic cervical bruit is found in 4% of people over the age of 45, and is more common as age advances.^{164,165} A cervical bruit may be caused by conditions other than carotid artery disease, and it does not reflect the degree of stenosis or the nature of the plaque.^{166,167} The overall correlation between demonstrable carotid disease and bruits is about 60%.¹⁶⁸ Non-invasive tests are useful to screen asymptomatic bruits for haemodynamically significant carotid lesions.¹⁶⁹⁻¹⁷¹

Since patients with asymptomatic carotid bruits are more likely to have ischaemic stroke than an age- and sex-matched population with no bruit,^{172,173} prophylactic carotid endarterectomy has been recommended.^{174,175} Rapid progression of carotid plaque or plaques with deep

TABLE V Perioperative stroke in the territory of asymptomatic carotid disease (bruit or stenosis) in non-cardiac surgery

Authors	Surgery	Stroke (cases)	
		Asymptomatic bruits	No bruits
Treiman <i>et al.</i> ¹⁹⁸	Abdominal aortic	0% (33)	1.3% (156)
Carney <i>et al.</i> ³	Aortoiliac	0% (30)	1.9% (213)
Evans <i>et al.</i> ¹⁹⁹	Major vascular	0% (92)	0.8% (496)
Dorazio <i>et al.</i> ¹⁷²	Major surgery	0% (94)	—
Ropper <i>et al.</i> ¹⁹⁷	Non-neurologic	0% (72)	0.6% (631)
		Carotid stenosis	No stenosis
Barnes <i>et al.</i> ²⁰¹	Peripheral vascular	0% (23)*	1.0% (102)
Turnipseed <i>et al.</i> ²⁰⁰	CABG, PVR	5% (62)+§	4% (98)
Kartejmer <i>et al.</i> ²⁰⁶	Major CV surgery	17%‡§	1%
Gutierrez <i>et al.</i> ²⁰⁷	Peripheral vascular	16% (19)‡	0% (355)

*Doppler ultrasound with spectral analysis.

†Doppler imaging and spectral analysis.

‡Oculoplethysmography screening.

§Includes patients with cerebrovascular symptoms.

ulcerations or considerable stenosis, in particular, appear to be associated with higher risks of stroke, and surgery is even more justified.^{176–181} Norris and Zhu used continuous-wave directional Doppler ultrasound examination to quantify the degree of carotid stenosis in 500 patients with asymptomatic cervical bruits. During a mean followup period of 52 months, there were 40 TIAs and 11 ischaemic strokes. The frequency of ischaemic cerebral events was maximal at 75–90% stenosis.¹⁸² It appeared that there was a critical degree of carotid stenosis at which stroke risk became maximal. The authors suggested that this represented a window of therapeutic opportunity. In experienced hands, prophylactic surgery may reduce the occurrence of TIAs and stroke.^{183–186} The role of carotid endarterectomy in asymptomatic carotid stenosis is being investigated in multicentre prospective trials.^{187–189}

The risk to the patients with asymptomatic lesions is for stroke without warning.¹⁹⁰ Stroke can occur without prior TIAs, but the incidence is low.^{191,192} Once a TIA occurs, the risk of stroke increases sharply. It is therefore logical to manage asymptomatic patients conservatively, by controlling hypertension, treating concomitant cardiac disease, and using platelet anti-aggregation agents such as aspirin. Surgery is recommended only when TIAs occur in the followup period.^{193,194} Endarterectomy in asymptomatic patients should be done only by experienced surgeons with documented low operative stroke and death rates.^{168,195,196}

ASYMPTOMATIC CAROTID LESIONS IN PREOPERATIVE PATIENTS

Asymptomatic carotid bruit is present in about 10%

of surgical patients presenting for major surgery, in 16% for peripheral vascular surgery, and in 8% for CABG.^{3,197–201} Prophylactic carotid endarterectomy is sometimes performed in these patients before other major surgery to minimize the risk of stroke.^{202–205}

However, while a cervical bruit associated with symptomatic cerebrovascular disease may predispose the patient to perioperative stroke, several studies have shown that the presence of asymptomatic cervical bruit did not increase the risk of stroke following peripheral vascular reconstructions and other major surgery (Table V).

Treiman *et al.* reported no perioperative stroke following abdominal aortic operation in 33 patients with asymptomatic bruits, and a 1.3% stroke rate in 156 patients with no bruit.¹⁹⁸ Carney *et al.* also had no strokes following aortoiliac reconstruction in 30 patients with asymptomatic bruits, and a 1.9% stroke rate in 213 patients with no bruit.³ Similarly, Evans and Cooperman reported no perioperative stroke associated with major vascular surgery in 92 patients with asymptomatic bruits, and a 0.8% stroke rate in 496 patients with no bruit.¹⁹⁹ Dorazio *et al.* reported that 53 patients with asymptomatic bruits underwent a total of 94 major operations, and no patient developed stroke or transient neurological deficits.¹⁷² Ropper *et al.* prospectively studied 735 unselected patients over the age of 55 having all types of non-neurologic elective surgery.¹⁹⁷ There were four perioperative strokes among 631 patients free of bruits (0.6%), and one stroke in 104 patients with bruits (1%). However, none of the 72 patients with asymptomatic bruits had neurological complications.¹⁹⁷

Carotid stenosis may be present in the absence of symptoms. In a prospective study by Barnes *et al.* 125

asymptomatic patients for peripheral vascular reconstructions were evaluated using Doppler ultrasound with spectral analysis. There was one perioperative stroke among 23 patients with severe carotid stenosis, but was contralateral to the side of stenosis, and one stroke in 102 patients without carotid stenosis.²⁰¹ Turnipseed *et al.* used Doppler imaging and spectral analysis of flow to screen patients admitted for elective coronary artery bypass or peripheral vascular reconstruction for presence of carotid lesions. One-third of the 160 patients for peripheral vascular reconstructions had previous cerebrovascular symptoms. There were seven strokes, three of which occurred in 62 patients with carotid stenosis (5%), and four in 98 patients without carotid stenosis (4%). However, most of the strokes were not focal, suggesting diffuse cerebral ischaemia.²⁰⁰

Kartchner and McRae reported quite different results from their retrospective review of oculoplethysmography (OPG) screening for functional impairment of cerebral blood perfusion in 234 patients undergoing major cardiovascular surgery. They found a perioperative stroke rate of 1% in patients with normal OPG, and 17% in those with OPG studies indicating internal carotid stenosis of more than 60%.²⁰⁶ However, the report did not indicate how the patients were chosen for OPG, and more than 50% of the patients had previous cerebrovascular symptoms. Their study did not specifically examine asymptomatic patients with OPG-demonstrated carotid lesions. Nevertheless, their findings were supported by Gutierrez *et al.* who also used OPG to evaluate 300 patients without neurological symptoms prior to 374 elective peripheral vascular procedures. There were no perioperative strokes in 280 procedures in patients with no bruits, or 75 procedures on patients with non-haemodynamically significant bruits. However, three strokes occurred after 19 procedures (16%) in patients with haemodynamically significant bruits.²⁰⁷ Thus, there appears to be a subgroup of patients with asymptomatic carotid bruits associated with haemodynamically significant lesions, who are at risk. These patients should be further evaluated with cerebral angiography, and the decision for prophylactic carotid endarterectomy should be based on the individual patient and the surgeon/anaesthetic team.

For most patients with asymptomatic cervical bruit, or noninvasive evidence of carotid obstruction, routine prophylactic carotid endarterectomy before major surgery is not justified.²⁰⁸ Nonetheless, the presence of asymptomatic carotid disease does identify the patient at high risk of myocardial infarction, whether or not surgery is performed,^{3,201,202,209–211} and of late postoperative neurological deficits such as TIAs.^{212,213} The management of asymptomatic bruits and carotid artery disease in cardiac surgery will be discussed in Part II of this review.

Anaesthetic techniques for carotid endarterectomy

While both regional and general anaesthesia can produce similar perioperative neurological outcomes, regional anaesthesia usually results in less cardiovascular morbidity and a shorter hospital stay in this high-risk population.²¹⁴

REGIONAL ANAESTHESIA

Regional anaesthesia, using superficial cervical plexus block with infiltration of deeper layers, combined superficial and deep cervical plexus blocks^{74,215,216} or cervical epidural anaesthesia,^{217,218} allows monitoring of neurological function for evidence of inadequate cerebral perfusion. The level of consciousness, speech, and the strength of contralateral hand grip, can be assessed throughout the procedure. Routine shunting is generally not necessary.⁷⁸ Postoperative hospital stay is shortened.⁷⁶ The expertise of the anaesthetist is crucial for the patient's comfort and cooperation during carotid endarterectomy under regional block.¹⁰⁶ Restlessness and fatigue are not uncommon even in the presence of an adequate block.²¹⁹ The use of regional anaesthesia can reduce, but not eliminate, perioperative morbidity usually associated with general anaesthesia.²²⁰ Hypertension during carotid occlusion, as a result of baroreceptor activity, is common.^{77,221} Intraoperative or postoperative cerebral embolization and thrombosis can still occur, and can cause neurological deficits.^{77,106,222} The occurrence of intraoperative embolization may occasionally escape detection by neurological monitoring in the awake patient, only to manifest as a postoperative deficit.²²³

GENERAL ANAESTHESIA

The variables which affect cerebral blood flow and cerebral oxygen consumption, such as arterial blood pressure, ventilation, oxygenation, and depth of anaesthesia are better controlled by general anaesthesia.

Most anaesthetists prefer a balanced anaesthetic technique using a combination of volatile anaesthetic agent, nitrous oxide, narcotic, and muscle relaxant. The cerebral blood flow changes during carotid endarterectomy have been studied under general anaesthesia using different agents.^{224–227} Halothane produces cerebral vasodilatation with an increase in cerebral blood flow and increased intracranial pressure. On the other hand, isoflurane reduces cerebral oxygen consumption, preserves the normal cerebral energy state, and has minimal effect on intracranial pressure.^{228–233} Messick *et al.* showed that the critical regional cerebral blood flow, below which EEG signs of cortical ischaemia occur, was less during isoflurane anaesthesia ($10 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$) than during halothane anaesthesia (previously reported as $18\text{--}20 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$).²²⁶ Michenfelder *et al.*, from their

retrospective study of 2010 carotid endarterectomies performed using inhalational anaesthesia, with EEG and CBF monitoring, reached the same conclusion. The critical CBF was $10 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$ with isoflurane anaesthesia (703 cases), $15 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$ with enflurane anaesthesia (840 cases), and $20 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$ with halothane anaesthesia (467 cases). The EEG ischaemic changes occurred in 18% of cases performed with isoflurane, 26% with enflurane, and 25% with halothane anaesthesia. Patients with ischaemic changes received shunts immediately and there was no difference in the neurological outcome between the three anaesthetics.²³¹ This suggests that relative to halothane and enflurane, isoflurane does offer some cerebral protection for transient incomplete regional cerebral ischaemia during carotid endarterectomy. However, this has been challenged by Young *et al.* who demonstrated that, although cerebral blood flow was different with different anaesthetic agents, there were no differences in cerebral metabolic rate.²²⁷ They believed that the choice of anaesthetic agent with comparable anaesthetic regimens should not be made on the basis of "metabolic suppression," but on the basis of other cardiovascular considerations. Isoflurane may induce coronary steal phenomena in patients with coronary atherosclerosis.^{234–237} However, perioperative myocardial infarction is not more common in patients anaesthetized with isoflurane than with halothane or enflurane for carotid endarterectomy.²³⁸ The use of high-dose narcotic anaesthesia may provide haemodynamic stability, but it reduces the sensitivity of intraoperative EEG monitoring.^{239,240}

The selection of agents and techniques should aim for rapid and smooth emergence. Since neurological function in patients under general anaesthesia cannot be assessed directly, cerebral perfusion should be monitored using EEG or other techniques, so that corrective measures such as insertion of a shunt or treatment of hypotension can be instituted when inadequate perfusion during carotid occlusion is detected.

Cerebral protection during carotid endarterectomy

Meticulous control of systemic blood pressure during both the intraoperative and postoperative periods is essential, as hypertension and hypotension may increase neurological morbidity.^{9,110,111,241} Since the incidence of coronary artery disease is common among these patients,^{242,243} and myocardial infarction is a major cause of perioperative morbidity and mortality,^{95,113,244} the anaesthetic techniques chosen should produce minimal cardiac stress. Indeed, myocardial infarction is responsible for 40 to 60% of all perioperative deaths following this operation.^{95,243,245}

Intraoperative neurological complications are mainly

TABLE VI Brain protection during carotid endarterectomy

Reduction of oxygen demand

- General anaesthesia
- Hypothermia
- Barbiturates

Improvement of oxygen delivery

- Hyperbaric oxygenation
- Hypercarbia
- Acetazolamide infusion
- Induced systemic hypertension
- Temporary bypass shunting

due to embolization and ischaemia. The risk of embolization is primarily related to the surgical technique. The risk of ischaemia depends on the state of collateral circulation which is inadequate in 10 to 30% of patients.^{225,246} Many methods of brain protection have been used to compensate for the reduction of cerebral blood flow during carotid artery occlusion (Table VI).^{247,248}

Reduction of cerebral oxygen requirements may be achieved with general anaesthesia, hypothermia, or barbiturates. The ability of some anaesthetic agents to depress cortical electrical activity and reduce oxygen consumption may increase the tolerance to cerebral ischaemia in animals and humans.^{249–255} The role of isoflurane was discussed earlier in this review. Hypothermia, either systemic,⁴⁸ or in the ICA circulation,^{256,257} is time-consuming, and often complicated by cardiac arrhythmias.²⁵⁸

Barbiturates reduce cerebral utilization of oxygen by decreasing cerebral functional activity.^{259–257} Thiopentone therapy has been used to protect the brain during carotid artery clamping for patients at risk.²⁶² However, neither the dose nor the benefit has been established in prospective clinical trials^{263–265} or animal experiments.²⁶⁶ One regime is to administer repeated boluses of thiopentone, to a total dose of approximately 3 g, for maintaining a burst suppression pattern in the EEG during the entire duration of carotid clamping.²⁶² A more common method is to administer thiopentone ($4\text{--}5 \text{ mg} \cdot \text{kg}^{-1}$) as a single bolus prior to carotid clamping. This results in only a brief period of elevated blood thiopentone concentrations and transient EEG burst suppression, and is inadequate to cover the duration of carotid artery occlusion.²⁶⁵ The incidence of stroke due to cerebral anoxia is small.⁷⁵ The routine use of a single bolus of thiopentone prior to carotid clamping does not appear to be indicated or beneficial.^{264,265} Thiopentone treatment may be of value when, in the presence of inadequate perfusion as demonstrated by monitoring, insertion of a shunt is not technically feasible, or when the EEG abnormalities cannot be corrected by shunt insertion. In

these situations, thiopentone is given in sufficient dosage to maintain EEG burst suppression or isoelectricity during the duration of occlusion, and then discontinued. Cardiovascular support by vasopressors may be necessary during thiopentone treatment. Markowitz *et al.*, using barbiturate-induced coma, successfully reversed the neurological deficits in three patients presenting with evolving strokes immediately after carotid endarterectomy and demonstrated to have patent carotid arteries.²⁶⁷

Improvement of oxygen delivery to the brain may be achieved by the use of hyperbaric oxygenation, hypercarbia, acetazolamide infusion, induced systemic hypertension, or a bypass shunt.

Hyperbaric oxygenation has limited applications, and few institutions have walk-in hyperbaric chambers.^{268,269} The increased amount of dissolved oxygen may improve oxygen delivery only if perfusion is present, and is of no benefit in total ischaemia.

Hypercarbia causes cerebral vasodilatation and increases total cerebral blood flow (CBF). This property has been used for cerebral protection during carotid endarterectomy.^{79,270,271} However, hypercarbia, by dilating normal cerebral vessels with an increase in regional CBF (rCBF), may actually shunt blood away from ischaemic areas where the vessels are already maximally dilated ("intracerebral steal").²²⁵ Furthermore, hypercarbia causes intense sympathetic stimulation, increasing myocardial oxygen demand and predisposing to cardiac arrhythmias. On the other hand, hypocarbia may have a beneficial effect by constricting normal cerebral vessels and diverting blood flow to ischaemic areas ("reverse cerebral steal"). However, the cerebrovascular responses to PaCO₂ levels in a given patient is unpredictable. One should aim at maintaining normocarbica or mild hypocarbia during carotid endarterectomy.

Cerebral vasodilatation may be produced by carbonic acid accumulation in the brain tissue using an infusion of acetazolamide,²⁷² but the technique itself may have potential harmful effects on ischaemic brain tissue.^{273,274}

Induced hypertension appears to be a logical method of increasing CBF.²⁷⁵⁻²⁷⁷ Since the vessels in the ischaemic areas of the brain lose their autoregulatory function and are maximally dilated, induced hypertension may increase blood flow to these areas, provided that collateral circulation is available to deliver the blood. However, if the collateral circulation is poor, induced hypertension will not be able to improve perfusion significantly.^{225,278} Because of the marginal benefit achieved in patients with poor collateral circulation, the associated increased myocardial workload, and the risk of cerebral haemorrhage and oedema, drug-induced hypertension is not a suitable routine technique for cerebral protection during carotid endarterectomy. Instead, maintenance of adequate sys-

temic perfusion pressure, and avoidance and prompt treatment of hypotension are essential.

Many surgeons routinely use a temporary bypass shunt to ensure adequate cerebral perfusion when the carotid artery is clamped.^{93,279} On the other hand, there are others who believe that shunts are rarely necessary, and that their use may actually cause embolization.^{91,280-282} In a randomized prospective study of 138 carotid endarterectomies in 118 consecutive symptomatic patients, the use of intraluminal shunt was found to reduce significantly the risk of intraoperative neurological deficit. In the 24 hr after surgery, there was no stroke in 63 procedures in which a shunt was used, and an 8% stroke rate in 75 procedures in which a shunt was not used.²⁸³ However, these procedures were performed under general anaesthesia, and cerebral perfusion was not monitored. It appears that shunts should be used selectively for patients with inadequate perfusion when demonstrated by intraoperative monitoring,^{248,284-286} and for those who had preoperative cerebral infarction in whom the monitoring techniques may not be sensitive enough to detect hypoperfusion.²⁸⁷

Monitoring of cerebral perfusion

Preoperative tests are available for predicting haemodynamic consequences of cross-clamping during carotid endarterectomy. These include angiogram,²⁸⁸ transcranial Doppler ultrasonography,²⁸⁹ and EEG monitoring during digital compression of the common carotid artery.^{290,291}

Many techniques have been devised to assess the adequacy of cerebral perfusion during surgery (Table VII). While some are research tools and are not commonly available, they illustrate the ingenuity of the approach to this important aspect of management.

Neurological assessment during regional anaesthesia, discussed earlier in this review, is an effective monitor during carotid endarterectomy.^{73,284}

Techniques that utilize special equipment and technical expertise to monitor cerebral haemodynamics such as regional cerebral blood flow,^{113,225,292-296} carotid artery blood flow,^{297,298} oculoplethysmography,²⁹⁹ supraorbital photoplethysmography,³⁰⁰ and transcranial Doppler ultrasonography^{301,302} are not generally available. Regional cerebral blood flow measurements, because they are non-continuous, may not detect complications caused by embolization, hypotension, or ischaemia at all times during the operation, and thus may not correlate well with the neurological outcome.

The ICA stump pressure is easy to measure, and may be used to estimate the perfusion pressure in the vessels supplying the brain on the side of carotid occlusion.^{81,286,303-308} The stump pressure is determined by

TABLE VII Monitoring of cerebral perfusion during carotid endarterectomy

*Neurological assessment of the awake patient**Cerebral haemodynamic variables*

- Internal carotid artery stump pressure
- Regional cerebral blood flow
- Carotid artery blood flow
- Oculoplethysmography
- Supraorbital photoplethysmography

Middle cerebral artery blood velocity and emboli

- Transcranial Doppler ultrasonography

Cerebral oxygenation

- Jugular venous oxygen saturation
- Conjunctival oxygen tension

Cerebral electrical activity

- Electroencephalography
- Computerized EEG analysis
- Somatosensory cortical evoked responses

Anatomical patency of the endarterectomized artery

- Operative arteriography
- Ultrasound imaging and flow analysis
- Retinal artery pressure measurement
- Ocular pneumoplethysmography (OPG-Gee)

the pressure transmitted through the circle of Willis, which is dependent upon the systemic BP and the adequacy of the collateral circulation, and by the cerebrovascular resistance. Since cerebrovascular resistance is influenced by anaesthetic agents, the anaesthetic technique should be taken into consideration when interpreting stump pressure value.³⁰⁸ In patients with a neurological deficit prior to operation, the stump pressure may not be reliable for detecting inadequate perfusion, and a shunt should be used.³⁰⁵

If the metabolic rate is constant, the difference in the oxygen content between the arterial and venous blood is inversely proportional to the regional blood flow. The jugular venous oxygen saturation, in association with fully saturated arterial blood, has been used to reflect CBF during carotid endarterectomy.³⁰⁹⁻³¹³ However, the jugular venous oxygen saturation is a poor indicator of regional cerebral ischaemia, because it only reflects the average of the hemispheric perfusion, and part of the venous drainage is from the opposite half of the brain.^{72,292} The conjunctival oxygen tension of the eyes has been used during carotid occlusion to reflect the corresponding ophthalmic arterial supply, and thus the adequacy of collateral perfusion.³¹⁴ However, this technique may not be a reliable indicator of CBF during carotid surgery.³¹⁵

EEG MONITORING

Changes in the EEG correlate well with changes in

rCBF.^{224,296} Under halothane anaesthesia, the normal rCBF is 40–50 ml · 100 g⁻¹ · min⁻¹. When the rCBF is maintained above 30 ml · 100 g⁻¹ · min⁻¹, no EEG abnormalities are seen. EEG changes occur in most patients when the rCBF decreases below 23 ml · 100 g⁻¹ · min⁻¹, and certainly in all patients when it reaches a threshold of 18 ml · 100 g⁻¹ · min⁻¹. The EEG abnormalities which indicate inadequate cerebral perfusion include suppression of background fast frequencies, slowing, and voltage attenuation. These ischaemic changes are apparent even in the presence of pre-existing focal EEG abnormalities.^{296,316} Slowing of the EEG is evident at less severe flow reductions (12–18 ml · 100 g · min⁻¹), and flattening occurs at extreme reduction of rCBF (7–15 ml · 100 g⁻¹ · min⁻¹).^{113,316} This close relationship between EEG and rCBF makes the EEG a valuable monitor for evaluating cerebral perfusion, and continuous EEG monitoring is commonly used for detecting cerebral ischemia during carotid endarterectomy.^{95,318-321} The sensitivity of the EEG for detecting focal ischaemia is dependent upon a stable anaesthetic depth and a constant level of ventilation. A continuous 16-channel EEG tracing is initiated before the induction of anaesthesia and continued until the patient is awake.^{95,224} If there are no persisting focal EEG changes intraoperatively, the patient will not have new postoperative neurological deficit on emergence from anaesthesia. The presence of persisting focal EEG changes usually indicates an ischaemic event, and may serve as a warning for instituting corrective measures such as the insertion of a shunt or correction of hypotension. However, since neurological damage is dependent upon the degree as well as the duration of ischaemia, these abnormalities may not necessarily indicate irreversible cerebral damage.³²¹ In a multicentre study, the use of EEG monitoring was found to be associated with a lower incidence of neurological deficits. The total stroke and death rate was 3.5% among 973 patients monitored with EEG, 5.5% of 176 patients monitored with stump pressure, and 7% of 1908 patients who had no cerebral perfusion monitoring during carotid endarterectomy.⁹⁹ It must be realized, however, that the electrical activity on the surface of the brain may not reveal ischaemia in the deeper regions.³²²

Constant attention by trained personnel is required to detect ischaemic changes in the raw EEG. The task of monitoring can be simplified greatly by the use of computer-processed EEG. Power spectrum analysis, by a complex mathematical Fourier transformation of EEG signal sampled at epoch lengths varying from 2 to 32 sec, can present most of the information present in the original complex EEG in a simple and easily recognized pattern.^{323,324} The amplitude and frequency of the EEG over time can be displayed by compressed spectral array (CSA)

or density-modulated spectral array (DSA). The CSA display looks like hills and valleys. The amplitude is plotted against the frequency, and each updated epoch is slightly shifted, producing a three-dimensional effect. The DSA display uses variations in density or size of lines or dots to represent the amplitude at a given density. To simplify the power spectrum analysis, further one-dimensional descriptors such as median power frequency (the frequency below which 50% of the total EEG power is present), peak power frequency (the frequency with the greatest amount of power) and spectral edge frequency (the frequency below which a specified percentage, such as 90 or 95%, of the total power is contained) have been proposed. The power spectrum analysis is based on frequency. There are other techniques of EEG analysis, such as aperiodic analysis (each waveform being mapped in relation to its frequency, amplitude, and time of occurrence, rather than averaging a large number of waveforms over a given epoch), zero-crossing frequency analysis (the number of times each cycle of EEG crosses the isoelectric line), and voltage analysis, that are based on time.

The Cerebral Function Monitor (CFM) (Devices Limited, Hertfordshire) was the first commercially produced EEG processor. It was a one-channel EEG filter-amplifier, which filtered out frequencies below 2 Hz and above 15 Hz, amplified and displayed the average peak voltage on a recorder at a slow speed. The CFM was found to be insensitive for detecting subtle ischaemic changes during carotid endarterectomy.²²³ Cucchiara *et al.* found that the CFM was not as good as the standard 16-channel EEG for detecting cerebral ischaemia. The sensitivity was somewhat better when both electrodes were placed over the hemisphere at risk than when the two electrodes were placed on opposite sides of the head.³²⁵ Artru and Strandness recently reported a case in which delayed carotid shunt occlusion was detected by an updated CFM (Model 970, Critikon Inc., UK, Ascot) using four bilaterally placed electrodes.³²⁶

The power spectrum analysis has been found to be a sensitive and easy-to-interpret technique for detecting ischaemic changes during carotid endarterectomy. Chiappa *et al.* compared on-line power spectrum analysis, using four-second epochs from four channels, to conventional EEG recording in 35 patients during carotid endarterectomy. The power analysis was displayed in the CSA format, with the two channels from each hemisphere combined by simple averaging. The information was shown in four columns. Two columns displayed the power spectrum of the right and left hemispheres. The third showed the frequency difference between the two hemispheres. The fourth showed the total amplitude of the EEG from each hemisphere in each four-second epoch,

so that one could easily see which hemisphere had the highest amplitude activity by simply comparing the relative length of the lines. In no instance did the conventional EEG reveal a significant pattern not seen with the computerized EEG, and the computer always made the EEG changes more readily apparent to all OR personnel than did the conventional EEG.³¹⁶ Rampil *et al.* found automated EEG useful for predicting gross neurologic outcome following carotid endarterectomy in 78 procedures in patients without preoperative neurological deficits. They used a single-channel EEG, with one electrode placed frontally on the side of the operation, and the other placed over the opposite mastoid. The power spectral analysis, using two-second epochs, was displayed using the DSA, and the spectral edge frequency. The loss of high frequency activity was used to identify serious ischaemic EEG events. No neurological deficit occurred postoperatively in 71 procedures in which there were either no EEG changes or in which the changes lasted less than 10 min. However, new deficits developed following all seven procedures in which EEG events persisted longer than 10 min.³²⁷

The Lifescan EEG monitor (Neurometrics, San Diego, CA) with two bipolar-channels, uses aperiodic analysis and displays the processed EEG, together with the 90% edge frequency, on a colour screen. This monitor has been assessed for use in carotid endarterectomy. Spackman *et al.* used three-colour printouts of the Lifescan screen for interpretation separately by three anaesthetists after surgery. The interpreters were blinded to the results of the rCBF and 16-channel EEG which were also used. Nine of the 50 patients showed EEG changes at the time of occlusion with rCBF of $9 \text{ ml} \cdot 100 \text{ g}^{-1} \cdot \text{min}^{-1}$ or less. There was variation in the interpretation among the three anaesthetists and only 56 to 89% of the ischaemic changes were diagnosed using the Lifescan monitor printouts.³²⁸ Silbert *et al.* presented two cases of eventful carotid endarterectomy under local anaesthesia. In one case, the changes in the edge frequency displayed by the Lifescan EEG monitor during carotid clamping corresponded to the deterioration of neurological functions. In the other case, however, the monitor failed to detect cerebral hypoperfusion that could be detected by the loss of power of the contralateral hand.³²⁹

Computerized EEG systems are simple and convenient to use. The display can be presented in a format so that people not familiar with the EEG can interpret ischaemic changes easily. However, there are inherent disadvantages. The use of fewer channels and the selective EEG information displayed may reduce the sensitivity and specificity that are associated with the conventional 16-channel EEG recording. When two- or four-channel systems are used, the limited choice of electrode place-

ment may not be able to detect all focal ischaemia. In systems using power spectrum analysis, the epoch length greatly affects their sensitivity.³³⁰ The sensitivity in detecting ischaemia also varies with the method of analysis.^{329,331}

Whereas the EEG records the spontaneous electrical activity of the cortex, evoked potential (EP) is a recording of the electrical activity produced by a stimulus. The EP is much smaller than the spontaneous EEG, and is made apparent by summing the response to 100–250 repetitive stimulations, and treating the EEG as background noise. Somatosensory evoked potential (SEP) has been used to monitor cerebral perfusion during carotid endarterectomy.^{332–337} The SEPs were recorded from a cervical and a parietal electrode placed above the ipsilateral hemisphere in response to stimulation of the opposite median nerve. Dinkel and Kamp, in a series of 378 cases, demonstrated a high sensitivity and specificity of SEP monitoring in the early detection of ischaemia after carotid clamping, and relied on the SEP findings for shunt indication.³³⁶ However, it must be realized that the SEP monitors only a small part of the CNS pathway, and cannot be expected to identify damage to another part of the brain.

The function of the various monitoring techniques is for detecting inadequate cerebral perfusion to identify patients who require shunting at the time of carotid occlusion,^{285,286,319,336} for assessing the function of the shunt when placed,³²⁶ for indicating the need for supportive measures such as vasopressor use, and for choosing the appropriate anaesthetic techniques.³³⁸ It is important to realize that no single monitoring technique is absolutely reliable in detecting cerebral ischaemia and in predicting postoperative neurological complications in all patients. Many intraoperative neurological complications are not due to ischaemia secondary to carotid occlusion, but to ischaemia secondary to embolization which may occur either intraoperatively or postoperatively. The monitoring techniques available may not be sensitive enough to detect small emboli.²²³ In addition, in patients who have suffered stroke, stump pressure and EEG may not be reliable indicators of inadequate cerebral perfusion, and a temporary shunt should be used regardless, even if no ischaemia patterns are shown.^{287,305}

In an effort to minimize neurological complications further, some surgeons use various techniques to assess the adequacy of the endarterectomy and to detect technical problems in the operating room or in the early postoperative period. These include operative arteriography,^{339–344} ultrasound imaging and flow analysis,^{345–348} retinal artery pressure measurement,^{113,294,349} and ocular pneumoplethysmography (OPG-Gee).^{350,351}

The use of these techniques enables the surgeon to correct technical defects before they produce neurological deficits.

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