Management of asymptomatic carotid stenosis in patients undergoing general and vascular surgical procedures

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Current available data do not seem to support the strategy for carotid endarterectomy prior to surgical intervention in patients with asymptomatic carotid stenosis. However, in patients with coronary artery disease, synchronous carotid endarterectomy and coronary artery bypass grafting should be considered where there is a proven surgical risk of <3% with unilateral asymptomatic stenosis >60% or bilateral carotid stenosis >75% on the same side as the most severe stenosis. Clarification of the optimal strategy requires an adequately powered, multicentre, randomised clinical trial.

Cerebrovascular accidents occurring during surgical procedures are rare, but the associated mortality and long term disability are high. Some investigators have demonstrated a significant correlation between the presence of carotid artery stenosis and perioperative stroke. The appropriate treatment of patients with known asymptomatic carotid stenosis undergoing surgical procedures is still unclear. Because of the lack of randomised trials, the results of the published papers are subjected to bias and have thus made it impossible to draw firm conclusions regarding the best management strategy.

The objective of this paper was to review the available evidence supporting and refuting the role of carotid artery disease in the pathophysiology of stroke after vascular and general surgery and to analyse the results of systematic reviews of staged and synchronous carotid reconstruction.

ASYMPTOMATIC CAROTID ARTERY STENOSIS

Ultrasound is the primary modality used to screen for the presence of carotid stenosis. In the Framingham Study, the prevalence of significant (>50%) carotid stenosis determined by duplex ultrasound in patients >65 years of age was 7% in women and 9% in men.1

Carotid artery lesions have an increased prevalence in patients with coronary and peripheral artery disease (PAD). The annual risk of ipsilateral stroke in patients with asymptomatic >50% carotid stenosis is approximately 2–3%.2–10 The risk of ischaemic stroke increases with the severity of stenosis.11 12 Mackey et al.13 found an annual rate of ipsilateral stroke of 1.4% among patients with a stenosis ≥50%, and 2.8% among patients with 80–99% carotid stenosis.

The results of trials assessing carotid endarterectomy (CEA) in patients with asymptomatic stenosis are still a matter of controversy.14 Several randomised trials have compared the efficacy and safety of CEA with best medical treatment in patients with asymptomatic carotid stenosis. A meta-analysis consisting of five trials (2440 patients with stenosis ≥50%), showed a significant reduction in the odds of ipsilateral stroke plus perioperative stroke or death, corresponding to a 2% absolute risk reduction over about 3.1 years in patients undergoing CEA. During the immediate postoperative period an increased prevalence of stroke and death among such patients was observed.15 The Asymptomatic Carotid Surgery Trial showed that in asymptomatic patients <75 years of age with ≥70% carotid stenosis, immediate CEA halved the 5 year stroke risk from ~12% to ~6%. Half of this 5 year benefit included either disabling or fatal strokes.16 The American Heart Association Stroke Council has stated that for CEA to be effective in asymptomatic patients, the target for combined perioperative death and stroke rate should be <3%.17 18

The advent of endovascular approaches for the treatment of carotid disease provides another potential mode of intervention. Most data regarding the performance of endovascular carotid procedures are based on case series, surveys, and enrolment of patients in voluntary registries.19–22 Several studies are now underway to further evaluate the potential role of carotid angioplasty and stenting in patients with asymptomatic (and symptomatic) carotid stenosis. The SAPPHIRE trial showed that among high risk patients with symptomatic and asymptomatic (>50% and >80% respectively) severe carotid artery stenosis, carotid stenting with the use of an embolic protection device was not inferior to CEA.23

CARDIAC SURGERY AND RISK OF STROKE

Strokes have been estimated to occur in 0.3–5.2% of patients after open heart surgery,24 1.3% after cardiac catheterisation,25 0.2–0.3% after percutaneous transluminal coronary angioplasty,26 1.4–11.0% after percutaneous transluminal aortic valvuloplasty,27 3.2–4.2% after percutaneous

Abbreviations: CAGB, coronary artery bypass grafting; CEA, carotid endarterectomy; PAD, peripheral artery disease; TIA, transient ischaemic attack
mitral valvuloplasty,^24^ 9.0% after cardiac transplantation,^25^ almost 9% in patients with coronary artery bypass grafting (CABG) >75 years of age, and nearly 16% after valve surgery.^26^ A prospective multicentre study found that in patients undergoing intracardiac surgery combined with coronary revascularisation, cerebral complications occurred in one of six patients.~27^ Bucerius et al^28^ analysed the rate of stroke in 16 184 patients undergoing cardiac surgery (CABG, beating heart CABG, aortic valve surgery, mitral valve surgery, double or triple valve surgery, CABG and valve surgery). The overall incidence of stroke was 4.6% but varied between surgical procedures: CABG 3.8%, beating heart CABG 1.9%, aortic valve surgery 4.8%, mitral valve surgery 8.8%, double or triple valve surgery 9.7%, CABG and valve surgery 7.4%. Prospective studies of consecutive patients undergoing CABG showed that the risk of major ischaemic stroke is 1–6%. Multiple factors have been associated with an increased risk of stroke in patients undergoing cardiac surgery: age older than 60 years, ≥50% carotid stenosis, prior stroke or transient ischaemic attack (TIA), history of congestive heart failure, valvular disease, repeat heart surgery, postoperative atrial fibrillation, bypass time of more than 2 hours, and prior myocardial infarction.~16–41^ THE STROKE RISK FOR CABG PATIENTS WITH CONCOMITANT ASYMPTOMATIC CAROTID ARTERY DISEASE The presence of stenosing carotid plaque is predictive of both coronary artery disease and acute coronary events.~32–41^ Indeed, Hedblad et al^32^ found that 50% of men with asymptomatic carotid artery stenosis had signs or symptoms of ischaemic heart disease. The vascular mortality rate in men with carotid artery disease and concomitant ischaemic heart disease was more than twice as high as in men with carotid stenosis without ischaemic heart disease. In 1546 consecutive CEAs performed in 1238 patients, angina pectoris was present in 17% (212/1238); a further 32% (396/1238) of patients had a history of myocardial infarction.~32^ Several studies have suggested that the stroke risk during CABG is related to the degree of carotid stenosis. In a meta-analysis, patients with no significant carotid disease had a 1.9% risk of stroke, increasing to 3% in predominantly asymptomatic patients with unilateral 50–99% stenosis, 5% in those with bilateral 50–99% stenoses and 7–11% in patients with carotid occlusion.~42^ Although these data suggest an association between significant carotid disease and post-CABG stroke, no data on the laterality of the events were available. The incidence of carotid artery disease and postoperative cerebrovascular complications were higher in patients who had had revascularisation for stenosis of the left main stem coronary artery.~43^ The risk of major cerebrovascular and cardiovascular complications of atherosclerosis is related more to the stability than to the extent of plaques. The surface morphology of the carotid plaques predicts the risk of coronary events independently of degree of carotid stenosis.~44^ In the European Carotid Surgery Trial and the North American Symptomatic Carotid Endarterectomy Trial, patients with irregular or ulcerated plaques in one or both carotid arteries were more likely to have had previous myocardial infarction than patients with smooth plaques. The aforementioned patients were also twice as likely to suffer a vascular death mainly due to coronary artery disease during follow up.~45–47^ THE MANAGEMENT OF ASYMPTOMATIC CAROTID ARTERY STENOSIS IN PATIENTS UNDERGOING CABG There is no consensus on the management of asymptomatic carotid stenosis in patients undergoing CABG. The efficacy of CEA before or combined with CABG remains controversial (table 1). A meta-analysis of 56 studies reviewed three operative strategies: simultaneous carotid surgery and CABG, carotid surgery followed by CABG, and CABG followed by carotid surgery in patients with symptomatic and asymptomatic carotid artery disease.~14^ Perioperative stroke rates were 10% if CABG preceded carotid surgery, and somewhat lower if carotid and coronary surgery were combined (6%) and if carotid surgery preceded CABG (5%). On the other hand, CEA followed by CABG showed the highest rates for perioperative myocardial infarction (11%) and death (9%), whereas simultaneous carotid surgery and CABG and CABG followed by CEA showed lower rates for perioperative myocardial infarction (5% and 3%, respectively) and death (6% and 4%, respectively).~14^ Another meta-analysis covering 16 studies with a total of 844 combined CABG/CEA patients and 920 staged procedures patients revealed a significantly increased risk in the composite endpoint, stroke, or death for patients undergoing combined procedures. The crude event rates for stroke were 6.0% v 3.2% for combined versus staged procedure, 4.7% v 2.9%, and 9.5% v 5.7% for stroke and death.~31^ Das et al^32^ performed an analytical overview of the strategies for the management of concomitant coronary

### Table 1: Meta-analyses on the risk of stroke, myocardial infarction (MI) and death in patients undergoing CEA and CABG simultaneously or staged

<table>
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<tr>
<th></th>
<th>n</th>
<th>Stroke (%)</th>
<th>MI (%)</th>
<th>Death (%)</th>
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<tbody>
<tr>
<td>Simultaneous CEA+CABG</td>
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<tr>
<td>Moore 1995^26^</td>
<td>584</td>
<td>6</td>
<td>5</td>
<td>6</td>
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<tr>
<td>Borger 1999^27^</td>
<td>844</td>
<td>6</td>
<td>–</td>
<td>4.7</td>
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<tr>
<td>Das 2000^28^</td>
<td>3295</td>
<td>3.9</td>
<td>–</td>
<td>4.5</td>
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<tr>
<td>Nayler 2003^29^</td>
<td>7853</td>
<td>4.6</td>
<td>3.6</td>
<td>4.6</td>
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<tr>
<td>Prior staged (CEA+CABG)</td>
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<tr>
<td>Moore</td>
<td>573</td>
<td>1.5</td>
<td>–</td>
<td>5.9</td>
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<tr>
<td>Das</td>
<td>917</td>
<td>2.7</td>
<td>6.5</td>
<td>3.4</td>
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<tr>
<td>Nayler</td>
<td>302</td>
<td>6.3</td>
<td>0.9</td>
<td>2.0</td>
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<tr>
<td>Reverse staged (CABG+CEA)</td>
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<tr>
<td>Moore</td>
<td>83</td>
<td>10</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Das</td>
<td>302</td>
<td>2.4</td>
<td>–</td>
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<tr>
<td>Nayler</td>
<td>10</td>
<td>3</td>
<td>4</td>
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<tr>
<td>CEA and CABG separately*</td>
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<td></td>
</tr>
<tr>
<td>Borger</td>
<td>920</td>
<td>3.2</td>
<td>–</td>
<td>2.9</td>
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*Borger^28^ reviewed papers reporting data for both staged and synchronous procedures; †not reported (meta-analysis included 56 reports), n, number of patients. MI, myocardial infarction.
artery disease and asymptomatic carotid artery stenosis (>50%). Four strategies were analysed: CABG in the presence of carotid stenosis, combined CEA and CABG, reverse (CABG + CEA <3 months) and prior staged (CEA + CABG <3 months). Comparative analysis indicated a significant reduction in stroke for prior versus combined procedures (1.5% v 3.9%, p = 0.007, odds ratio (OR) = 0.39, 95% confidence interval (CI) 0.2 to 0.7) with a higher mortality (5.9% v 4.5%, p = 0.1, OR = 1.41, CI 0.96 to 2.06). The stroke rate in the prior stage also remained significantly lower compared with the other two groups but when total risks for stroke and death were analysed, similar results were found among the groups: prior 7.4%, reverse stage 7.2%, combined 8.4% and 11.3% in CAVG in the presence of carotid stenosis.

In another systematic review,\(^\text{31}\) the outcomes following staged or synchronous procedures in several studies were analysed, with 94 studies having synchronous CEA+CABG and 24 staged CEA-CABG. About 60% of patients undergoing staged/synchronous procedures were neurologically asymptomatic, while 30–37% had bilateral 50–99% stenosis or contralateral occlusion. The majority of synchronous cases (72%) were New York Heart Association grade 3 or 4; 39% of these were classed as “urgent” while left mainstem disease was present in −25%. Operative mortality was highest in patients undergoing synchronous CEA+CABG (4.6%, 95% CI 4.1 to 5.2). Reverse staged procedures (CABG-CEA) were associated with the highest risk of both ipsilateral stroke (5.8%, 95% CI 0.0 to 14.3) and any stroke (6.3%, 95%CI 0.0 to 14.3). The risk of any operative stroke was lowest following staged CEA-CABG (2.7%, 95% CI 1.6 to 3.9). The risk of myocardial infarction was lowest following reverse staged procedures (0.9%, 95% CI 0.5 to 1.4) and highest in patients undergoing staged CEA-CABG (6.5%, 95% CI 2.9 to 10). Death and any stroke were highest in patients undergoing synchronous CEA+CABG (8.7%, 95% CI 7.7 to 9.8) and lowest following staged CEA-CABG (6.1%, 95% CI 2.4 to 9.2). However, the benefit conferred by staging the operation was reduced when the risk of myocardial infarction was subsequently included in the analysis (synchronous = 11.5%, 95% CI 10.1 to 12.9; staged CEA-CABG = 10.2%, 95% CI 7.4 to 13.1). A multistate population based study was undertaken to evaluate both the community wide outcomes of combined CEA and CABG and the risk for adverse events. In total, 10 561 CEAs were randomly selected, of which 226 procedures were performed in combination with CABG in the same operative event. Only 12% of patients undergoing CEA/CABG had had recent ipsilateral stroke or TIA, while 56% had had an asymptomatic carotid stenosis. The combined stroke and death rate was 17.7%. Proximal aortic arch atherosclerosis and symptomatic carotid stenosis were associated with stroke (p<0.05). Female sex, emergent operation, reperformed CABG, blood pressure on pump, total pump time, presence of left main disease and number of diseased coronaries were associated with higher mortality (p<0.05). Strokes appeared to be associated with operative events, but diagnosis was delayed and post-event carotid patency was not documented. Most strokes did not occur in the ipsilateral hemisphere of the CEA.\(^\text{31}\)

The aforementioned data do not support the strategy for CEA prior to CABG in patients with asymptomatic carotid stenosis. The patient subset with severe stenosis (especially >90%) or occlusion, or bilateral occlusive disease is likely to represent a special circumstance, especially in patients with poor collateral circulation.\(^\text{31}\) In some patients, the reduction in cerebral perfusion distal to a tight carotid stenosis or occlusion could be an important factor leading to the development of ischaemic stroke. In these patients, cerebral perfusion reserve ipsilateral to the carotid stenosis should be performed using: transcranial Doppler sonography or single photon emission computed tomography after administration of acetazolamide,\(^\text{133}\)Xe radionuclide CT, functional magnetic resonance imaging and positron emission tomography.\(^\text{56–58}\) Magnetic resonance spectroscopy showed that such patients have metabolic changes in the affected hemisphere, which are consistent with a chronic ischaemia in the absence of cerebral infarction.\(^\text{59}\) When the cerebral autoregulation is impaired, the simultaneous intervention (CEA/CABG) should be considered because patients with cerebral hyperfusion and ischaemic metabolic changes distal to severe carotid stenosis are probably at high risk for stroke during CABG. Unfortunately, no clinical trial has proven this hypothesis. In patients with bilateral >75% carotid stenosis, Caplan et al\(^\text{67}\) recommended simultaneous CAVG and CEA on the side of the more severe stenosis.

The American Heart Association (AHA) has published guidelines regarding the appropriateness of synchronous CAVG+CEA in CABG patients with asymptomatic occlusive carotid disease. The consensus view is that synchronous CAVG+CEA is “acceptable but not proven” in patients with unilateral >60% asymptomatic stenosis where there is a proven operative stroke and death risk of <3%. In those units with an operative stroke and death risk >3%, the guidelines qualified the appropriateness of synchronous procedures as uncertain.\(^\text{60}\)

In spite of the aforementioned AHA recommendations, the most favourable surgical management of patients with >60% asymptomatic carotid stenosis planning to undergo CABG remains unclear. Clarification of the optimal strategy requires an adequately powered, multicentre, randomised clinical trial.\(^\text{67}\)

Regarding new endovascular approaches, the SAPPHIRE trial showed that in high risk patients with asymptomatic severe (>80%) carotid artery stenosis, carotid stenting with the use of an embolic protection device was not inferior to CEA. Patients with previous CAVG were the major population enrolled in the study.\(^\text{68}\) This strategy could be an alternative procedure to CEA in the future.

**NON-CARDIAC SURGERY AND RISK OF STROKE**

Stroke after general surgical procedures is reported to be <1%.\(^\text{69}\) Parikh et al\(^\text{67}\) reported that 19 (0.08%) of 24 641 general and vascular surgical procedure patients suffered a perioperative stroke. The significant factors contributing to perioperative stroke included: hypertension, smoking, earlier neurological symptoms, and an abnormal rhythm on electrocardiogram. The most common factor for stroke was atrial fibrillation.

Perioperative stroke and other complications can be related to atherosclerosis, although there is no evidence that asymptomatic carotid artery stenosis predictably increases stroke risk during aortoiliac surgery.\(^\text{70–72}\) Barnes and Marszałek\(^\text{73}\) found in a prospective study that perioperative mortality in PAD patients was higher in the presence of carotid obstruction found by ultrasound. Deaths were primarily due to myocardial infarction. Gerraty et al\(^\text{74}\) described asymptomatic >50% stenosis or occlusion of the carotid in 53 patients, including 28 cases with >80% stenosis or occlusion, who had peripheral vascular procedures. There was no perioperative stroke on the side of carotid obstruction. Cardiac embolism, hypotension, and perioperative hypercoagulable state could have been the other stroke mechanism involved.

In order to define the management of patients with PAD and concomitant carotid stenosis, Bower\(^\text{75}\) reviewed the stroke risk in 121 patients undergoing both CEA and abdominal aortic reconstruction. Of these 59 had had an asymptomatic carotid stenosis at the time of the first
operation: 44 had had CEA before abdominal aortic reconstruction (group I) and 15 had had surgery before CEA (group II). In group II, two patients had a postoperative stroke and six developed TIAs in the interval between operations. Seven patients (47%) remained asymptomatic between the procedures. In comparison, only two (5%) of the 44 asymptomatic patients in group I developed TIAs in the interval between operations, and only one was on the CEA side. The other 42 (95%) patients remained asymptomatic. Additionally, in general elective surgery several studies have failed to demonstrate a correlation between severe asymptomatic carotid stenosis and incidence of perioperative stroke. Ropper et al. prospectively examined 735 unselected patients undergoing elective surgery to determine the incidence of carotid bruit and postoperative stroke. In 104 patients (14%) with bruits, only 1 had a stroke within 3 days after the operation, while in 631 patients without a bruit, 4 had a stroke within that time. The overall incidence of stroke was 0.7% and did not differ between the groups. The stroke risk related to asymptomatic carotid stenosis in patients undergoing non-cardiac surgery is low. There is no evidence to support prophylactic CEA.

CONCLUSION

At present, there are no clearly defined indications for managing asymptomatic carotid stenosis in patients undergoing general and vascular surgical procedures. Based on the data described, we suggest the following recommendations:

- In patients with asymptomatic internal carotid artery stenosis (>50%) planned to undergo general surgery, available data do not support performing CEA prior to surgical intervention.
- In patients with unilateral asymptomatic internal carotid artery stenosis (>60%) planned to undergo CABG, synchronous CEA+CABG is an acceptable option but has not yet been proven. Perioperative stroke and death risk must be <3% and life expectancy at least 5 years to justify the procedure.
- In patients with bilateral internal carotid artery stenosis (>75%) planned to undergo CABG, synchronous CEA on the side of the more severe stenosis + CABG is an acceptable option but has not been proven to date. Perioperative stroke and death risk must be <3% and life expectancy at least 5 years to justify the procedure.
- In patients with internal carotid artery stenosis (>60%), and contralateral occlusion planned to undergo CABG, available data do not support performing CEA prior to surgical intervention.
- In the aforementioned patients planned to undergo CABG, carotid stenting could be a therapeutic alternative but no study has examined this issue.

REFERENCES

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