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Controversies in Carotid Endarterectomy

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CONTENTS

| | |
|---|----|
| CONTROVERSIES IN CAROTID ENDARTERECTOMY..... | 3 |
| INDICATIONS..... | 3 |
| Symptomatic patients | 3 |
| Asymptomatic | 4 |
| SHUNT or NO SHUNT or SELECTIVE SHUNT..... | 5 |
| MONITORING | 7 |
| To Monitor or not to Monitor and if so, which Monitor?..... | 7 |
| ANAESTHETIC TECHNIQUE: REGIONAL vs GENERAL:..... | 9 |
| GA TECHNIQUE | 12 |
| REGIONAL | 14 |
| HAEMODYNAMIC CONTROVERSIES | 16 |
| QUO VADIS..... | 18 |
| REFERENCES | 19 |

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On the one hand, if patients with poor cerebral autoregulation show little improvement immediately after surgery, the arterial pressure should not be allowed to rise unduly in the postoperative period. On the other, if autoregulation is intact, the arterial pressure should be controlled with a view to the needs of the coronary circulation.

QUO VADIS

- ❖ Medical therapy has evolved significantly since the landmark CEA trials. Stroke risk reduction from current best medical therapy may exceed the small benefit from surgery in patients with asymptomatic disease or symptomatic patients with 50% to 69% stenosis.
- ❖ Patients presenting with a suspected TIA undergoing investigation and, if appropriate, surgery within 2 weeks of presentation.
- ❖ So what next with GALA? Do we need another megatrial powered enough to demonstrate or refute the small decrease in mortality while limiting the regional anaesthetic technique to a superficial cervical plexus block, with a low epinephrine concentration in the local anaesthetic solution and tight control of the perioperative haemodynamic variables? Or should we follow the recommendations from GALA: The anaesthetist and surgeon, in consultation with the patient, should decide which anaesthetic technique to use on an individual basis? Does Gala mean the end of CEA under LA in some centres?
- ❖ Increasing use of stents?
- ❖ Carotid surgery as day-case surgery?

CONTROVERSIES IN CAROTID ENDARTERECTOMY

Carotid endarterectomy (CEA)

- Performed to prevent embolic stroke in patients with atheromatous disease at the carotid bifurcation.
- Prophylactic operation: only yields benefit if the risks of surgery does not outweigh the benefit i.e. a reduction in the risk of stroke.

INDICATIONS

Symptomatic, Asymptomatic Patients or Both?

Symptomatic patients

- Have active plaque giving rise to emboli that cause transient ischaemic attacks (TIAs) and reversible ischaemic neurological deficits.
- Unequivocal evidence to support CEA in symptomatic patients with >70% carotid stenosis in the relevant carotid territory.
 - This is based particularly on two large studies, the North American Symptomatic Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST)
 - Both compared surgery with the best contemporary medical treatment.
 - > 70% stenosis or more: absolute risk reduction for the combined outcome of perioperative death or subsequent stroke more than 5 yr of 16% yielding a number needed to treat of 6.3.
 - 50 - 69% stenosis: benefit less marked with an absolute risk reduction of 4.6% more than 5 yr and a number needed to treat of 22.
 - 30–49% stenosis- CEA not beneficial to symptomatic patients

Rothwell et al found the absolute risk reduction with surgery in the group with 70% or more stenosis was diminished by the inclusion of patients with near occlusion, in whom surgery is less beneficial. When these subjects are excluded from this group of patients, there is a 30.2% absolute risk reduction of stroke in patients when surgery was performed **within 2 weeks** of their last event.

Explained by plaque morphology studies have shown that patients with recent symptoms are more likely to have:

1. acute plaque disruption
2. spontaneous embolization
3. overlying thrombus formation
4. abnormal levels of metalloproteinases within the plaque.

Patient with a progressing stroke of less than 24 h duration: Currently, there appears to be no benefit, with operative risk of stroke and death of 20% and is 4 times greater than patients with stable disease.

The categorization of patients as symptomatic and asymptomatic is perhaps an oversimplification, and operative risks depend on the specific clinical indication.

- The American Heart Association (AHA) Stroke Council have recommended that the perioperative risk should not exceed 5% for patients with TIA, 7% for patients with stroke, and 10% for patients with recurrent stenosis.

Asymptomatic

Have demonstrable disease at the carotid bifurcation but no history of a recent neurological event attributable to this lesion.

- Indications are controversial. Evidence is derived from three class-1 studies:
 - The Asymptomatic Carotid Atherosclerosis Study
 - The Veterans Affairs Study, and
 - The Asymptomatic Carotid Trial.
- A Cochrane review of CEA for asymptomatic carotid stenosis showed a 3% risk of perioperative stroke
- If surgery for asymptomatic carotid stenosis is to be profitable, need to identify those patients:
 - With a high risk of ipsilateral stroke
 - Reasonable life expectancy to justify CEA
 - Sufficiently low perioperative risk
- Several prognostic scoring systems have been developed The Halm score and the generic Revised Cardiac Risk Index were found to be superior to the Detsky index, Goldman index, American Society of Anesthesiologists index, and the Tu score in predicting medical and surgical complications.
- The Halm score identifies 3 independent predictors of poor outcome:
 1. the presence of contralateral disease
 2. 50% stenosis
 3. the presence of active coronary artery disease

Postoperative Hypotension

The anaesthetist may feel caught between the head and the heart. On one hand, the low systolic and mean arterial pressure may compromise myocardial perfusion and indeed predispose to internal carotid artery thrombosis. On the other, raising the arterial pressure across a carotid artery which is now no longer partially occluded by a stenosis may lead to excessive increases in cerebral perfusion. The conventional treatment in this setting is to render the patient normotensive with the use of fluids and vasopressors.

Transcranial Doppler monitoring should be used if available to monitor MCAv in patients who are given vasopressors for postoperative hypotension, especially patients who had severe bilateral stenosis or marked hypertension before surgery and so may be prone to hyperperfusion.

Marked Hypertension

Postoperative hypertension can plausibly be explained by a reduction in sensitivity of the carotid baroreceptor reflex. Surgery is associated with an acute deterioration in carotid baroreflex sensitivity, presumably because of the mechanical injury caused by surgery. Patients with bilateral disease had a more marked response to direct stimulation of the carotid sinus than those with unilateral disease and this was attributed to sensitization of the baroreflex response to compensate for the dysfunction of the contralateral side. After surgery, patients with bilateral disease had a more marked deterioration in baroreflex function.

Management here more clear cut. There is a concern that marked hypertension may injure both the heart by inducing myocardial ischaemia and the head by causing cerebral hyperperfusion, and arterial pressure reduction is appropriate.

Marked increases in middle cerebral artery velocity in association with increases in mean arterial pressure in symptomatic patients have been taken as markers of disordered static autoregulation after surgery. The immediate changes in static cerebral autoregulation after surgery are of direct relevance to the perioperative haemodynamic management of patients.

HAEMODYNAMIC CONTROVERSIES

Uncontrolled Hypertension

Treat?

- ✓ Significant association between a preoperative systolic blood pressure of >180mm Hg and postoperative stroke or death
- ✓ Diastolic hypertension (>110 mmHg) was found to be a predictor of adverse events.
- ✓ Significant association between a postoperative systolic blood pressure 220 mm Hg and postoperative stroke or death.
- ✓ A preoperative systolic blood pressure of >160 mm Hg was also a risk factor for postoperative hypertension.

Not to treat?

- ✓ The time course of adaptation of cerebral autoregulation to the lower arterial pressure is unclear. If the patient is subjected to anaesthesia and surgery before this, there could be an increased risk of stroke.
- ✓ The greatest benefit is seen from CEA if the operation is performed soon after presentation.
- ✓ Concerns that lowering the arterial pressure in patients with bilateral carotid stenosis may compromise cerebral perfusion.
- ✓ Although an association between poorly controlled arterial pressure and stroke has been demonstrated, no study has demonstrated that reducing the arterial pressure does indeed reduce operative risk.

It is reasonable to take the time to achieve good control of the arterial pressure in patients who have a preoperative systolic blood pressure consistently above 180 mm Hg or diastolic > 110mmHg, who do not have severe bilateral disease, and are not having frequent neurological events. It is probably appropriate to proceed to surgery even in the presence of marked hypertension in the patient who has severe bilateral disease and is having frequent TIAs.

Postoperative Hypertension and Hypotension

Common after CEA: hypertension in 25–58% of patients and hypotension in 8–10% of patients.

However, the utility and applicability of scoring systems in individual patients depend largely on quantifying institutional risk. Independent audit should ensure that institutional risk does not exceed the recommendations of the AHA Stroke Council. Any benefit would be negated in centers that have a higher than 3% perioperative risk.

Optimal management of the patient with combined coronary and carotid disease is controversial. The best evidence suggests that the risk of death or stroke is almost doubled if CABG and CEA are performed during a single anesthetic as opposed to a staged procedure.

SHUNT or NO SHUNT or SELECTIVE SHUNT

Cerebral blood supply:

- Eighty-to-ninety per cent via the two internal carotid arteries
- The remainder from the vertebrobasilar system.
- The Circle of Willis offers the brain considerable protection against the occlusion of one or another vessel, but it is incomplete in 15% of normal people.

The carotid shunt is essentially a length of plastic tubing which carries blood from the common carotid to the internal carotid artery to maintain cerebral blood flow in those patients who have a contralateral carotid stenosis or a compromised Circle of Willis.

It is important to appreciate the causes of perioperative stroke with CEA and their relative frequencies. Perioperative stroke can be divided into intraoperative (25%) and postoperative (75%).

Intraoperative :

- **Ischaemic (1/3)**
 - From inadequate cerebral perfusion after clamping of the carotid artery
 - Fairly uncommon cause of stroke.
- **Embollic (2/3)**
 - occur during manipulation of the carotid artery
 - Also occur as a result of technical defects in the endarterectomy site. A technically inadequate endarterectomy may also result in a delayed postoperative stroke.

Acute complications of shunt insertion

- Air embolization
- Plaque embolization
- Intimal tears
- Carotid dissection.
- Haematoma
- nerve injury
- infection
- Late carotid restenosis
-

A shunt only has the capacity to prevent ischemic stroke, whereas it may actually increase the risk of embolic stroke. Furthermore, for all these risks, flow through the shunt may be inadequate to meet cerebral oxygen requirements.

However, there are a group of patients in whom ischemia does cause perioperative stroke and placement of a shunt would relieve ischemia and translate to a reduction in stroke rate if the complications are minimized.

Three approaches to shunting have emerged:

- (1) Shunts in all patients (routine shunting)
- (2) No shunting
- (3) Selective shunting

Local policy: use selective shunting (with a 25% shunt rate)

There is a lack of good evidence to support the use of shunts. Both prospective randomized trials and retrospective studies have been unable to show a clinically significant difference in any outcome measure between patients who were routinely shunted compared with patients who were not shunted.

To advocate selective shunting, it would be critical to develop objective tests that would accurately identify those patients at risk for intraoperative ischemia.

The conversion rate to general anaesthesia was also higher with deep/combined block (odds ratio 5.15, $P < 0.0001$) suggesting that deep block is 5 times more likely to 'fail'. From analysis of 2500 cases and 30 yr of publications, it appears that no single instance of a serious complication related to placement of a superficial/intermediate block has ever been formally described.

Limitation: Only two of the studies in the analysis were randomized controlled trials (RCTs) Nonetheless, the strongest evidence came from RCTs.

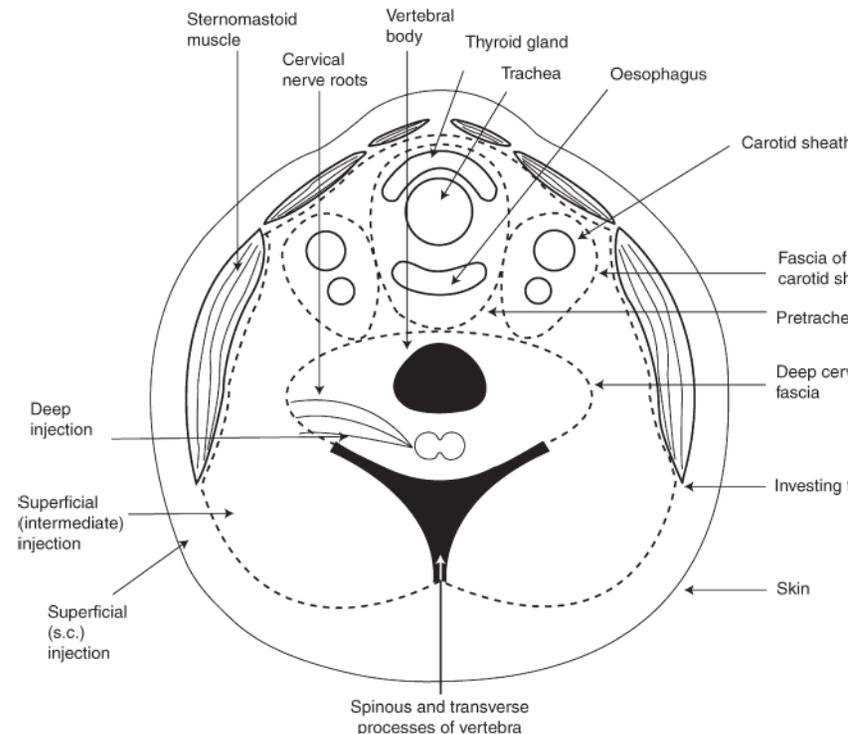


Fig 1 Drawing of a cross-section of the neck at the C4 vertebral level

REGIONAL

Posterior paravertebral block:

Single-injection; performed at the C4 level has been used as an alternate to the cervical plexus block.

Cervical epidural anaesthesia

Good operating conditions.

Significant risk of major anaesthetic complications including dural puncture, epidural venepuncture and respiratory muscle paralysis. Also difficulty to perform in the elderly

Cervical plexus block

Deep:

Consists of identifying the transverse processes of upper cervical vertebrae C2–C4 and injecting local anaesthetic directly into the deep (prevertebral) cervical space. Either as three separate injections or as a single injection.

Superficial:

Incorporates a variety of procedures. The simplest is a subcutaneous(s.c.) infiltration of local anaesthetic along the posterior border of sternocleidomastoid muscle.

An '**intermediate**' block is one where the injecting needle pierces the investing fascia of the neck, deep to the s.c. layer, but superficial to the deep cervical (prevertebral) fascia.

A '**combined** block', consists of a deep injection and a superficial or intermediate injection.

Pandit et al conducted a systematic review of published papers to assess the complication rate associated with superficial (or intermediate) and deep (or combined deep plus superficial/intermediate) cervical plexus block.

Deep/combined block was associated with a 2 times higher serious complication rate related to the injecting needle when compared with the superficial/intermediate block (odds ratio 2.13, P=0.006). Complications with the deep block included intrathecal or vertebral artery injection, respiratory problems related to phrenic nerve paralysis, and Horner's syndrome

MONITORING

To Monitor or not to Monitor and if so, which Monitor?

EEG

- Reflects only cortical events and does not disclose ischaemia in deeper structure
- The raw EEG is difficult to interpret compared with the processed EEG
- processed EEG easier to interpret but considerable information is lost during its conversion
- The BIS monitor is not suitable as it primarily detects frontal lobe activity.

SSEP

- Are no more specific or sensitive than the EEG.
- May be superior in patients whose baseline EEG is not easily interpretable because of a previous stroke.

Stump Pressure

- the perfusion pressure transmitted around the Circle of Willis upon clamping of the common and external carotid arteries
- wide range of proposed thresholds for the stump pressure, ranging between 25 and 70 mmHg
- Studies suggest stump pressure to be specific but not sensitive at identifying patients with cerebral ischaemia upon carotid cross-clamping. Stump pressure of 50 mm Hg had sensitivity 29.8% and specificity 98.6% for the prediction of neurological changes necessitating shunt placement. For a stump pressure of 40 mm Hg, the values were sensitivity of 56.8%; specificity, 97.4%.
- Local policy - a pressure > 50 mmHg is regarded as adequate.

JvO2

- Sensitivity, specificity, and intervention thresholds not determined

TCD (Transcranial Doppler)

- The thin petrous temporal bone provides an acoustic window that allows Doppler ultrasound detection of blood flow in the middle cerebral artery.

- beneficial for assessing hemodynamic ischemia, shunt function, embolic phenomenon, and the hyperperfusion syndrome
- Limitations : Probe has to be placed relatively near to the surgical site; skilled operator; acoustic window may not be found in between 10 and 20% of subjects

NIRS

- Regional cerebral oxygenation (rSO₂), a composite measure of predominantly arterial venous and capillary oxygenation.
- Unacceptably low sensitivity and specificity.
- There is not a well-defined biologic zero: studies in dead subjects give an average rSO₂ value of 51%, compared with a value of 68% in normal controlled subjects

What does the evidence say?

Nascet: no difference in the stroke rate in centers that used monitoring and those that did not (adjusted risk ratio, 1.0 [0.6-1.6]). The ECST trial had similar findings.

Awake patient (CEA under Local Anaesthesia)

- Gold standard for neurologic monitoring.
- Requires constant verbal contact ensuring patient orientation and movement of the contralateral side (a squeaky toy or a fluid filled bag connected to a pressure transducer may be helpful).
- Used to limit shunt insertions to patients with insufficient blood supply, as shown by an altered state of consciousness or contralateral motor weakness or seizure during a clamping test under regional anaesthesia.
- Only effective form of monitoring that will detect 100% of patients who would require a shunt. Sensitivity or capability to identify patients who require a shunt (as shown by a change in neurological status) under regional anaesthesia is 59–91%, and the specificity or capability identify patients who do not is 57–99%.

Isoflurane

- Neuronal protection (experimental evidence)

Xenon

- Experimental
- both pre- and post-insult neuroprotection

Volatile vs TIVA

- Comparable reductions in cerebral blood flow and metabolic rate in contrast to the flow metabolism decoupling with higher concentrations of sevoflurane.
- Preserved cerebral autoregulation under propofol–remifentanyl anaesthesia.
- Internal carotid artery pressure on the site of surgery was lower with sevoflurane and this was attributed to the vasodilatation induced by this drug compared to propofol.
- Propofol may offer a degree of neuroprotection as with the volatile agents.
- Post-insult neuroprotection (postconditioning) by anaesthetic drugs.

Barbiturates

The evidence does not support the use of barbiturates as a cerebral protectant for permanent focal ischemia. However, during transient focal ischemia there is evidence to support barbiturate therapy. One point for barbiturates is just prior to carotid artery cross-clamping, however significant cardiovascular depression and delayed awakening can occur.

Etomidate

There is evidence in animals that worsens ischemic injury while thiopental improves injury. Accordingly, etomidate is not recommended for use as a cerebral protectant.

Dexmedetomidine

Studies in animals suggest that is neuroprotective. Although in human volunteers dexmedetomidine decreases CBF and may increase the incidence of shunt placement during awake CEA.

Bottom line: There is no hard data to favour any particular general anaesthetic technique but issues of cerebral blood flow, ischaemic preconditioning and pre and post insult neuroprotection needs to be considered. A technique that optimizes brain perfusion, minimizes myocardial stress, and allows for a rapid recovery is recommended together with the maintenance of normocarbica, normoglycaemia and HCT – 30%.

- Intraoperatively management
 - Use of cardioactive drugs like statins.
3. The study is underpowered to exclude an absence of stroke or death reduction. To exclude a reduction of mortality from 1.5% to 1.1% (an incidence similar to that seen in nonrandomized studies), the study would have needed about 25 000 patients ($\alpha=0.05$ two-tailed, $\beta=0.2$).

GA TECHNIQUE

LMA vs ETT

Laryngeal mask may be inserted if there is a need to convert from regional to general anesthesia. However, endotracheal tube provides definitive airway control as airway access during surgery can be difficult.

Volatile Agents

Sevoflurane:

Arguably agent of choice

- Rapid recovery; less vasodilatation than isoflurane at the same anaesthetic depth.
- Produces concomitant reductions in cerebral metabolic blood flow and cerebral metabolic rate. (at concentrations of 1.0 MAC) At concentrations above this increases in regional cerebral blood flow noted.
- Static autoregulation is well maintained at 1.2 MAC. Dynamic autoregulation is impaired even with concentrations of volatile anaesthetic agents of 1.0 MAC, although this effect is more marked with isoflurane than with sevoflurane.
- The response of the cerebral circulation to carbon dioxide is maintained. In an in vitro study, preconditioning and neuronal protection demonstrated.

Desflurane

- Marked vasodilatation (in animal models) increasing cerebral blood volume, and thence intracranial pressure.

Nitrous oxide

- Avoid. Increases the cerebral metabolic rate and produces a concomitant increase in middle cerebral artery blood flow velocity (MCAv).
- Increased cerebral blood flow.

ANAESTHETIC TECHNIQUE: REGIONAL vs GENERAL:

Regional anaesthesia was thought to be associated with more appropriate and less frequent shunt use, fewer cardiorespiratory complications, and preserved cerebrovascular autoregulation. Another possible benefit of local anaesthesia could be the increase in systemic blood pressure that occurs after carotid clamping under local anaesthesia and its effect in maintaining cerebral perfusion.

Under general anaesthesia, the choice is either risking thrombus dislodgement from an unnecessary shunt (if all patients are systematically shunted) or failure to detect brain ischaemia. Furthermore, there is the risk of insertion of an unnecessary shunt (if a selective shunt insertion technique is used).

Regional anesthesia was therefore hypothesized to be associated with a significant decrease in stroke and cardiac morbidity.
And then came GALA!

The General Anaesthesia versus Local Anaesthesia for Carotid Endarterectomy (Lancet 2008)

- Large multicentre trial (95 centres from 24 countries) with data from 3526 patients collected over 8 years designed to compare the risk of stroke, MI, and death after carotid endarterectomy under either GA or LA.
- The first patient was randomized in 1999.

Findings:

The two groups did not significantly differ for quality of life, length of hospital stay, or the primary outcome (stroke, myocardial infarction, or death between randomization and 30 days after surgery).

Even when added to the randomized trials in the Cochrane review, there is still no clear answer, with GALA dominating the analysis by providing 86% of the patients:

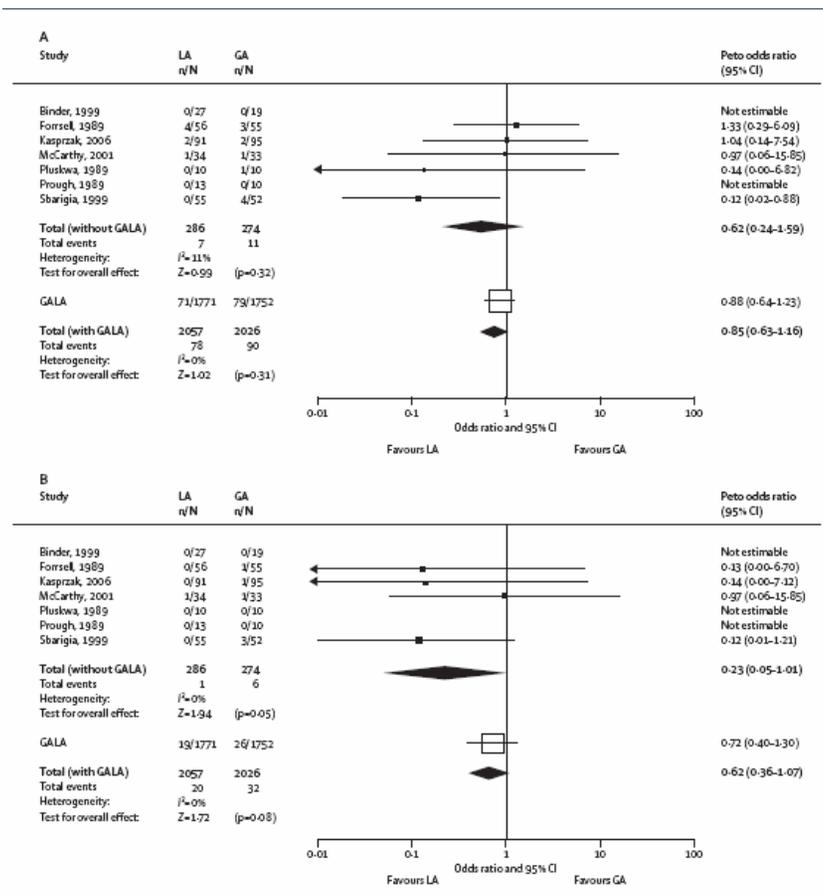


Figure 3: Cochrane review for outcome of stroke or death (A) or for outcome of death (B)

For the pro-local group, this was not good. The expected reduction in stroke or mortality with local anaesthesia at 30 days was not statistically significant. Worse, a non-significant increased rate of myocardial infarction (local vs. general anaesthetic: 0.5% vs. 0.2%; effect difference 0.3% [95% CI -0.2% to 0.8%]) was reported.

Reasons postulated:

- Pain and anxiety under local might increase the risk of myocardial ischaemia. Blood concentrations of noradrenaline (possibly

indicating high anxiety or insufficient analgesia) and systolic arterial blood pressure were higher in these patients.

- If the concentration of adrenaline added to the local anaesthetic is high (1:200 000 or higher), a 15% increase in heart rate will occur.

Thus the non-significantly increased incidence of myocardial infarction in GALA could, unfortunately, be real. Furthermore:

- Conversion to general anaesthesia may still be needed (1.4% of patients in the GALA study), which is not without risk, particularly if done in a hurried, uncontrolled way. Access to the airway is compromised by the surgical drapes, and anaesthetic-induced hypotension might cause cerebral hypoperfusion.
- Not all patients are psychologically able to tolerate procedures while awake.
- Needle damage to vulnerable structures (vertebral artery during deep cervical-plexus block, intravascular injection, and phrenic-nerve block) and might cause haematoma. In this study, 4.4% of patients under local anaesthesia had complications that led to cancellation of surgery or conversion to general anaesthesia.
- Perhaps surgery was more hurried during local anaesthesia

The good news, however was that local anaesthesia reduced the need for shunt insertion (14% vs. 43%, $p<0.001$). Unfortunately, we do not know if the reduced shunt insertion rate had any effect on the rate of restenosis at 1 year.

Bad news for the Pro- GA group:

- GA associated with a slightly higher risk than local anaesthesia of perioperative stroke, myocardial infarction, or death but this was not statistically significant.
- Patients with contralateral-carotid occlusion: risk of stroke seemed higher during surgery under general anaesthesia than under local anaesthesia, although again this was not statistically significant.

Limitations of the study:

1. The absence of blinding might have caused bias in the recognition or assessment of outcomes.
2. Absence of strict standardization of anesthetic and surgical techniques such as
 - The regional anaesthetic technique used : cervical epidural versus deep cervical plexus block versus superficial cervical plexus block
 - the local anaesthetic solution used in GALA was not standardized
 - The use and indication for shunts