Symptomatic Carotid Stenosis

Written by A.Ross Naylor* — 2020

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SUMMARY

Patients suffering a transient ischaemic attack (TIA) or minor ischaemic stroke and who have a 50-99% ipsilateral stenosis benefit from optimisation of risk factors, implementation of best medical therapy and an expedited carotid intervention. The concept that one is delivering optimal care, provided a carotid intervention is performed within 6 months of the index symptom, should now be considered obsolete. Compelling data show that the highest risk period for suffering a stroke is the first 7-14 days after the index TIA/minor stroke and that carotid endarterectomy (CEA) confers maximum stroke prevention benefit if performed as soon as possible.

Carotid artery stenting (CAS) has emerged as a less invasive alternative to CEA. However, with current stent technology, randomised controlled trials (RCTs) suggest that CAS is associated with significantly higher 30-day rates of death/stroke (compared with CEA) and especially when CAS is performed in the first 7-14 days after onset of symptoms. It remains to be seen whether newer stent technologies (e.g. Transcarotid arterial revascularisation (TCAR)) can lessen procedural risks in the early time period after onset of symptoms. After the 30-day peri-operative period has elapsed, RCTs suggest that there is no difference in rates of late ipsilateral stroke between CEA and CAS.

INTRODUCTION

Definition of stroke

The World Health Organization defines stroke as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24-hours (or leading to death), with no apparent cause other than a vascular origin”. A transient ischaemic attack (TIA) carries the same definition, but with a time frame of <24 hours. The 2017 European Society for Vascular Surgery (ESVS) guidelines on the management of carotid disease also used an updated definition for stroke, based on functional imaging but (to-date) this has not been accepted into everyday clinical practice.

Burden of Stroke

Globally, stroke is responsible for 5.5 million deaths annually (second after ischaemic heart disease). There are 13.7 million new stroke cases in the world each year and approximately 80 million stroke survivors at any one time. In Europe, death rates following stroke within member states varies from 30:100,000 to 170:100,000, while the number of European Union (EU) citizens living with stroke as a chronic condition is predicted to undergo a 25% increase from 3.718 million in 2015 to 4.631 million by 2035, largely through an increasingly ageing population. When indirect costs are added to the direct costs of treating stroke, EU health systems (and carers) spend about 45 billion Euros on stroke care each year. www.strokeeurope.eu (accessed 4th February 2020). Haemorrhagic stroke is significantly less common than ischaemic stroke, but it carries a much
higher mortality rate. Globally, the number of deaths following an ischaemic stroke in 2016 was 2.7 million, compared with 2.8 million after haemorrhagic stroke.

Aetiology of Stroke

Approximately 20% of strokes are haemorrhagic (intracranial haemorrhage (ICH), sub-arachnoid), while 80% are ischaemic. Of the ischaemic strokes, 20% will be vertebrobasilar, while 80% affect the carotid territory. The TOAST classification of ischaemic stroke includes 5 categories; (1) thrombosis/embolism due to atherosclerosis of a large artery; (2) cardiac embolism; (3) blockage of a small intracranial artery (lipohyalinosis, fibrinoid degeneration, microatheroma); (4) other determined causes (arteritis, dissection) and (5) undetermined causes (e.g. two possible causes, no cause identified, incomplete investigations). Excluding VB strokes, approximately half of ischaemic carotid territory strokes will have a non-carotid aetiology (cardiac embolism, small vessel disease, arteritis). Of the remaining 50% with a suspected carotid thromboembolic origin, about two thirds will not have an ipsilateral 50-99% carotid stenosis.

The aetiology of ischaemic stroke may, however, be changing. In the UK, the annual number of CEA procedures in recently symptomatic patients has declined by 25% over 6-years, despite no change in guidelines regarding interventions in symptomatic patients. Declining CEA rates have also been reported in the United States and Canada. Data from rapid access TIA clinics suggest that total carotid plaque volume in recently symptomatic patients (using Duplex ultrasound (DUS)) has declined by 24% between 2002 and 2014, in conjunction with a 30% decrease in the incidence of carotid stenoses >60% and a 36% decrease in stenoses >80%. These temporal changes in plaque morphology, stenosis severity and declining CEA rates may reflect reductions in smoking rates, along with an increasing likelihood that a greater proportion of the population are prescribed statins, antiplatelet agents and antihypertensive therapy (for primary/secondary cardiovascular risk control), compared with historical cohorts and so may be less likely to suffer a stroke due to embolisation from a previously asymptomatic carotid stenosis. The potential for temporal changes in stroke aetiology should not come as a surprise. If a similar audit had been carried out in the 1970-1980s, a significant proportion of strokes would have been due to embolism from rheumatic valvular heart disease, which is now very rarely observed.

Principles of managing stroke/TIA

The clinician should ask five questions when faced with a patient in whom a cerebrovascular event is suspected. First; were the symptoms consistent with a diagnosis of stroke/TIA and what was the likely vascular territory? Second; which investigations should be performed to establish the likeliest cause. Third; have the patient’s risk factors been corrected? Fourth; has ‘optimal medical therapy’ (OMT) been prescribed? And fifth; is there any need for a carotid intervention (CEA/CAS)?

TIA/stroke symptoms

It has become traditional to ascribe the term ‘recently symptomatic’ as including any patient who has suffered a carotid or VB territory stroke/TIA in the preceding 6 months. This is a somewhat arbitrary definition, as it was originally the main criterion for inclusion within the landmark randomised controlled trials (RCTs) which compared OMT with CEA in the 1980s/1990s. There is little scientific evidence that a patient with symptoms of 5-months duration has a significantly higher risk of secondary stroke, compared to someone whose TIA happened 7-months before hand. As will be seen, this 6-month threshold for being defined as ‘recently symptomatic’ should be considered obsolete, as modern day treatments (interventional and medical) should now be implemented as soon as possible after onset of symptoms.

Typical carotid territory symptoms include (i) hemi-sensory deficit (numbness, paraesthesia of face/arm/leg); (ii) hemi-motor deficit (weakness of face/arm/leg, or limb clumsiness), and (iii) evidence of higher cortical dysfunction (dysphasia/aphasia, visuospatial problems). Amaurosis Fugax (transient monocular blindness) refers to a temporary loss of vision in one eye and is another ‘carotid territory’ symptom. If bilateral visual loss occurs, this is a VB event involving the visual cortex in the occipital lobe. Occasionally, monocular visual loss can be permanent, due to irreversible retinal infarction (analogous to an ischaemic stroke). Ocular ischaemia syndrome is rare and involves a spectrum of clinical features due to sustained ocular
hypoperfusion (progressive visual loss, painful eye, dilated conjunctival/episcleral vessels, rubeosis iridis, retinal haemorrhages, microaneurysms). In very rare patients, entering a brightly lit room can cause a temporary 'whiteout' loss of vision.\textsuperscript{12}

The VB territory includes the brainstem, cerebellum, occipital lobes and (in most patients) the inferior temporal lobes and most of the thalami. Accordingly, thrombosis or embolisation into these areas can give rise to a spectrum of vertigo, ataxia, eye movement disorders, bilateral limb weakness, complete visual loss (cortical blindness) and hemianopia. In a series of 407 patients with VB stroke, the most common symptoms were dizziness (47%), unilateral limb weakness (41%), dysarthria (31%), headache (28%) and nausea/vomiting in (27%). The most frequent signs were: unilateral limb weakness (38%), gait ataxia (31%), unilateral limb ataxia (30%), dysarthria (28%) and nystagmus (24%).\textsuperscript{13}

The term ‘non-hemispheric symptom’ is applied to patients presenting with isolated syncope (blackout, drop attack), isolated presyncope (faintness), isolated dizziness, isolated double vision and isolated vertigo. These should not be considered to be VB or carotid symptoms unless accompanied by more classical symptoms from these territories.

‘Crescendo TIAs’ involve multiple TIAs within a short time period, with full recovery in between. The exact number and/or frequency has never been defined, but ESVS have adopted a threshold of >3 events in seven days.\textsuperscript{14} ‘Stroke-in-evolution’ refers to a fluctuating deficit (never fully back to normal) or a progressively worsening neurological deficit.

**Investigation of suspected stroke/TIA**

(a) \textbf{First line} All patients should have baseline bloods checked, including; urea/electrolytes (to exclude renal impairment/failure), lipids (raised total cholesterol, elevated low-density lipoprotein cholesterol, elevated triglycerides), glucose (exclude new diagnosis of diabetes, poor control of diabetes), full blood count (exclude blood dyscrasias, myeloproliferative disorders, leukaemia/lymphoma, thrombocytosis), plasma viscosity (may be raised in certain arteritis pathologies), chest x-ray (exclude lung tumour, cardiomegaly) and ECG (arrhythmias, left ventricular hypertrophy). More specialised investigations (thrombophilia screening, autoantibodies, homocysteine levels, echocardiography and 24-hour tapes) should be reserved for selected cases, especially in younger patients.

(b) \textbf{Functional brain imaging.} Computed Tomographic (CT) and/or Magnetic Resonance (MR) brain imaging should be performed as soon as possible after onset of symptoms. The first aim is to differentiate between an haemorrhagic or ischaemic aetiology, while the second aim is to identify non-atherosclerotic intracranial pathologies (benign/malignant tumours, aneurysms, arterio-venous malformations), which may have been responsible for the event. The location of an acute infarction will also be informative (watershed, cortical, lacunar).

(c) \textbf{Imaging of the extracranial and intracranial arteries.} When the landmark RCTs (comparing CEA+OMT versus OMT alone) were recruiting, all patients underwent intra-arterial angiography. At the time, angiography was the ‘gold-standard’ for diagnosing both the location and severity of atherosclerotic lesions affecting the carotid and vertebral arteries. However, the two most important RCTs (The European Carotid Surgery Trial (ECST) and the North American Symptomatic Carotid Endarterectomy Trial (NASCET)) used different methods for measuring stenosis severity \textbf{Figure 1}.\textsuperscript{14}
Figure 1: ECST and NASCET methods for measuring stenosis severity*
* ECST = Method used by the European Carotid Surgery Trial
NASCET = Method used by the North American Symptomatic Carotid Endarterectomy Trial

Figure 1, high resolution.
Both used the residual luminal diameter within the stenosis as the numerator.16 In ECST, the denominator was the estimated vessel diameter, where the residual luminal diameter was measured (usually the carotid bulb). In NASCET, the denominator was the diameter of a disease free ICA segment above the stenosis, where the vessel walls were approximately parallel. Accordingly, both methods will provide different values (regarding stenosis severity) for the same stenosis. In practice, a 50% NASCET stenosis is equivalent to a 75% ECST stenosis, while a 70% NASCET stenosis approximates to an 85% ECST stenosis.

However, angiography was associated with a 1-2% risk of procedural stroke and has now been replaced by a range of non-invasive imaging modalities, including DUS, CT angiography (CTA) and MR angiography (MRA). DUS is usually the ‘first-line’ investigation for imaging the extracranial carotid arteries. It is operator dependent and (because units no longer perform comparative angiography), vascular centres now use a variety of peak systolic velocity (PSV), end-diastolic velocity (EDV) and velocity ratios within (between) the internal carotid artery (ICA) or common carotid artery (CCA) to determine stenosis severity (Table 1).17 DUS can anticipate the likelihood of proximal inflow disease (damped proximal CCA waveform), or distal stenotic/occlusive disease (high resistance distal waveform) and the presence of these features mandates corroborative imaging with either CTA or MRA.
The main advantage of CTA and MRA is the simultaneous ability to image the aortic arch, supra-aortic vessels, the carotid bifurcation, distal ICA and the intracranial circulation. Imaging these regions is not always necessary if a patient is being considered for CEA, but it is mandatory if the patient is being considered for CAS. In a Health Technology Assessment meta-analysis, DUS, MRA and CTA were equivalent for detecting significant ICA stenoses. In modern day practice, intra-arterial digital subtraction angiography is now only indicated where there are discrepancies on non-invasive imaging.

The 2017 ESVS Carotid Guidelines recommend that “DUS (as first-line), CTA and MRA are recommended for evaluating the extent and severity of extracranial carotid stenoses” (Class I, Level A). In addition, the guidelines advise that when CEA is being considered, it is recommended that DUS stenosis measurement be corroborated by CTA/MRA, or by a repeat DUS performed by a second operator (Class I, Level A). If, however, CAS is being considered, ESVS guidelines recommend that any DUS study be followed by CTA/MRA, which will provide additional information on the status of the aortic arch, as well as the intracranial circulation (Class I, Level A).

**Risk factor control**

Ten modifiable risk factors account for around 90% of acute ischaemic strokes, the most important being hypertension, raised cholesterol, smoking, obesity, atrial fibrillation and diabetes mellitus (DM). In a meta-analysis of 32 studies, smoking was associated with a significant increase in late ischaemic stroke (Relative Risk Increase (RRI) 1.9 (95%CI 1.7-2.2)). In another meta-analysis, moderate or high levels of physical activity were associated with a 25% relative risk reduction (RRR) in ischaemic stroke, possibly via reductions in blood pressure (BP), body weight and effects on other risk factors. In a meta-analysis of 25 studies involving 2 million people, obesity was associated with a significant increase in stroke prevalence (RRI 1.64 (95%CI 1.36-1.99)). The 2017 ESVS guidelines recommend that a healthy diet, smoking cessation and physical activity are recommended for all patients with symptomatic carotid disease (Class I, Level B).

<table>
<thead>
<tr>
<th>% stenosis</th>
<th>PSV ICA cm/sec</th>
<th>PSVICA/PSVCCA ratio</th>
<th>St Mary’s ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50%</td>
<td>&lt;125</td>
<td>&lt;2</td>
<td>&lt;8</td>
</tr>
<tr>
<td>50-69%</td>
<td>≥125</td>
<td>2.0-4</td>
<td>8-10</td>
</tr>
<tr>
<td>60-69%</td>
<td>11-13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70-79%</td>
<td>≥230</td>
<td>≥4</td>
<td>14-21</td>
</tr>
<tr>
<td>80-89%</td>
<td>≥400</td>
<td>≥5</td>
<td>≥30</td>
</tr>
<tr>
<td>near-occlusion</td>
<td>high, low – string flow</td>
<td>variable</td>
<td>variable</td>
</tr>
<tr>
<td>occlusion</td>
<td>no flow</td>
<td>not applicable</td>
<td>not applicable</td>
</tr>
</tbody>
</table>

NASCET = North American Symptomatic Carotid Endarterectomy Trial; PSV = peak systolic velocity

ICA = internal carotid artery; CCA = common carotid artery; EDV = end diastolic velocity.

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Implementing Optimal Medical Therapy

The 2017 ESVS Carotid Guidelines provide a comprehensive review of the evidence supporting decisions regarding what constitutes OMT.2 The next section provides a summary of the main recommendations, as well as any changes in practice since 2017.

https://vimeo.com/452137392

(a) Antiplatelet therapy The 2017 ESVS guidelines recommended clopidogrel monotherapy or combination aspirin+dipyridamole in recently symptomatic patients not undergoing CEA or CAS (Class I, Level A).2 Patients scheduled for CAS, should receive dual antiplatelet therapy (DAPT) with aspirin (75-325mg daily) and clopidogrel (75mg daily). Clopidogrel should be started 3 days prior to CAS or as a single 300mg loading dose in urgent cases. Aspirin and clopidogrel should be continued for at least 4 weeks after stenting and then clopidogrel or aspirin monotherapy should be continued indefinitely (Class I, Level B).2

In patients scheduled for CEA, it was recommended that all should receive antiplatelet monotherapy, with lower dose aspirin (75-325mg) being preferable to higher doses (>625mg). It was also suggested that treatment with aspirin+clopidogrel or aspirin+dipyridamole ‘may be considered’ in patients with ipsilateral 50-99% stenoses in order to prevent early recurrent events in patients awaiting expedited CEA (Class IIb, Level C).2 However, the guidelines were unable to recommend routine DAPT in patients awaiting CEA (or who were being treated medically), because there was no compelling evidence that DAPT conferred additional benefit over monotherapy, in addition to concerns that DAPT would increase bleeding complications after CEA.

The updated 2022 guidelines will likely revise the latter recommendation in light of meta-analyses of three large RCTs, which compared outcomes following treatment with aspirin monotherapy versus aspirin + clopidogrel DAPT, where therapy was started as soon as possible after onset of symptoms.23 The meta-analyses showed significant reductions in non-fatal recurrent ischaemic and haemorrhagic stroke, moderate/severe functional disability and poor quality of life. Moreover, DAPT only needed to be continued for 10-21 days after onset of symptoms. Thereafter, all patients should revert to clopidogrel monotherapy, unless contraindicated. Figure 2 presents a DAPT algorithm for use in recently symptomatic patients undergoing expedited CEA and in those being treated medically. More details regarding the rationale for prescribing DAPT in patients awaiting CEA and in patients treated medically, dosing strategies and choice of DAPT (aspirin and clopidogrel versus aspirin and dipyridamole) are detailed in a recent review.24
(b) Lipid lowering treatment

Statins appear to confer benefit in terms of stroke prevention in the long term and in reducing 30-day death/stroke rates after CEA. No RCTs have specifically addressed the role of statins in patients with recent onset TIA/minor stroke and who have significant carotid disease. However, two RCTs are worthy of further mention. SPARCL randomised 4,731 patients with a history of TIA/stroke (966 with a median ICA stenosis of 51%) to 80mg atorvastatin or placebo.\(^{25}\) Patients with carotid stenoses who were randomised to atorvastatin had a 33% RRR in fatal/non-fatal stroke, as well as a 42% RRR in cardiovascular events. The Heart Protection Study reported on a subgroup analysis of 3,280 patients (within the overall cohort of 20,536) who had presented with a TIA, or non-disabling ischaemic stroke and who were randomised to 40mg of simvastatin daily versus placebo. Simvastatin conferred a 20% RRR in stroke, MI or vascular death (p=0.001).\(^{26}\)

A number of observational studies in CEA and CAS patients have reported that starting statin therapy pre-operatively is associated with significant reductions in 30-day death/stroke and/or myocardial infarction (MI). The evidence is presented in more detail in the 2017 ESVS carotid guidelines.\(^{2}\) It is speculated that statins may reduce morbidity/mortality via their pleiotropic effects in reducing inflammation, direct plaque stabilisation and a general reduction in the inflammatory response to surgery.

The ESVS guidelines recommend that recently symptomatic patients should start statin therapy prior to CEA/CAS and that statins should not be acutely stopped during the peri-operative period, because this can increase the risk of stroke or MI (Class I, Level B).\(^{27}\) Statin therapy is also recommended for the prevention of long-term stroke, MI and other cardiovascular events in patients with symptomatic carotid disease (Class I, Level A).\(^{27}\)

(c) anti-hypertensive therapy

As with statins, no RCT has evaluated the role of anti-hypertensive therapy in reducing late stroke in patients with symptomatic carotid stenoses. However, a meta-analysis of 13 blood pressure treatment studies in patients with a history of stroke reported a significant RRR in late stroke associated with antihypertensive therapy (34% (95%
There has been confusion as to whether it is appropriate to reduce blood pressure (BP) in recently symptomatic patients awaiting expedited CEA. A Cochrane review concluded that there was insufficient evidence to support lowering BP during the acute phase of stroke, because there was no improvement in functional outcome, but this study did not specifically include patients awaiting CEA. However, in patients being considered for early CEA, a balance needs to be struck. This is because systolic BP >180mmHg is an independent predictor for stroke after CEA.

Accordingly, the 2017 ESVS recommend that caution should be exercised in significantly reducing blood pressure immediately prior to CEA/CAS in the early time period after onset of symptoms, but that uncontrolled hypertension (>180/90mmHg) should be treated prior to proceeding to CEA or CAS (Level IIa, Class C). In addition, antihypertensive treatment is recommended for CEA/CAS and medically treated patients with hypertension and symptomatic extracranial internal carotid artery carotid stenoses in order to maintain long-term blood pressure <140/90mmHg (Class I, Level A).

(d) management of diabetes Diabetes doubles the risk of stroke and 20% of diabetic patients will die from a stroke. In meta-analyses, however, there was no evidence that tight glycaemic control reduced stroke risk, but it did reduce other diabetes-related complications. The UK Prospective Diabetes Study observed that tight BP control (mean BP 144/82mmHg) was associated with a 44% RRR in stroke (95%CI 11-65, p=0.013), compared with patients who had less tight BP control (mean BP 154/87mmHg). The 2017 ESVS carotid guidelines recommend that in diabetic patients, strict glycaemic control is recommended in order to reduce late diabetic related complications (Class I, Level C), and that in diabetic patients with symptomatic carotid stenoses, the target blood pressure should be <140/85mmHg (Class I, Level B).

Is there any need for a carotid intervention?

Carotid disease is one of the most evidence-based subspecialties in vascular surgery and a large number of RCTs have defined current practice.

RCTs comparing medical therapy with CEA

Three large, multi-centre RCTs (ECST, NASCET and the Symptomatic Veterans Affairs Co-operative Study (SVACS)) randomised 6092 recently symptomatic patients (defined as having suffered symptoms <6 months of randomisation) and who had 0-99% stenoses of the ipsilateral internal carotid artery (ICA) to OMT or OMT plus CEA. The Carotid Endarterectomy Trialists Collaboration (CETC) thereafter undertook a meta-analysis of individual patient data from the three constituent RCTs and the 5-year data are presented in Table 2. In this meta-analysis, all pre-randomisation angiograms were remeasured using the NASCET measurement system. CEA did not confer benefit (over OMT) in patients with 0-30% or 31-49% stenoses. CEA conferred a small, but significant reduction in late stroke in patients with 50-69% stenoses (ARR=7.8%; RRR=28%), while maximum benefit was observed in patients with 70-99% stenoses (ARR=15.6%; RRR=48%). There was no obvious benefit in patients with subocclusion.
Table 2. Individual patient meta-analysis of the 5-year risk of any stroke (including the peri-operative risk) from pooled ESCT, NASCET and SVACS Trial data*

<table>
<thead>
<tr>
<th>Stenosis severity (NASCET)</th>
<th>n=</th>
<th>5-year risk of any stroke (Incl. perioperative)</th>
<th>ARR @5 years</th>
<th>RRR @5 years</th>
<th>NNT to prevent one stroke @5 years</th>
<th>No. of strokes prevented per 1000 CEAs @ 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CEA + BMT</td>
<td>BMT alone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-30%</td>
<td>1746</td>
<td>18.4%</td>
<td>15.7%</td>
<td>-2.7%</td>
<td>no benefit</td>
<td>no benefit</td>
</tr>
<tr>
<td>31-49%</td>
<td>1429</td>
<td>22.8%</td>
<td>25.5%</td>
<td>+2.7%</td>
<td>no benefit</td>
<td>no benefit</td>
</tr>
<tr>
<td>50-69%</td>
<td>1549</td>
<td>20.0%</td>
<td>27.8%</td>
<td>+7.8%</td>
<td>28%</td>
<td>13</td>
</tr>
<tr>
<td>70-99%</td>
<td>1095</td>
<td>17.1%</td>
<td>32.7%</td>
<td>+15.6%</td>
<td>48%</td>
<td>6</td>
</tr>
<tr>
<td>Near occlusion</td>
<td>262</td>
<td>22.4%</td>
<td>22.3%</td>
<td>-0.1%</td>
<td>no benefit</td>
<td>no benefit</td>
</tr>
</tbody>
</table>

ESCT = European Carotid Surgery Trial; NASCET = North American Symptomatic Carotid Endarterectomy Trial; SVACS = Symptomatic Veterans Affairs Co-operative Study; ARR = absolute risk reduction in stroke; RRR = relative risk reduction in stroke; NNT = number needed to treat to prevent one stroke at 5 years; CEA = carotid endarterectomy; BMT = best medical therapy.

* Data derived from the Carotid Endarterectomy Trialists Collaboration

Table 2, high resolution.

Important subgroup analyses (OMT vs CEA)

One of the advantages of performing an individual patient meta-analysis involving a large number of patients, was that it permitted meaningful subgroup analyses to establish who gained the most (and the least) benefit from CEA. Clinical predictors of an increased risk of stroke on BMT included; increasing age, male sex, recent symptoms, hemispheric TIA/stroke, cortical (versus lacunar) stroke and increasing medical co-morbidities. Imaging predictors of an increased risk of stroke on BMT included; irregular stenoses, increasing stenosis severity, contralateral occlusion, tandem intracranial stenoses and a failure to recruit intracranial collaterals.
One of the most important of these predictive features (and which has changed practice around the world) was recognition of the need to intervene early after onset of symptoms. There is now compelling evidence that the highest risk period for recurrent stroke is the first 7-14 days after onset of symptoms. Contemporary natural history studies report that the incidence of recurrent stroke after the index TIA ranges from 5-8% at 48 hours, 4-17% at 72 hours, 8-22% at 7 days and 11-25% at 14 days. In addition, CETC have shown that CEA confers maximum benefit if performed as soon as possible after symptom onset. Table 4 details the ARR, number needed to treat to prevent one stroke at 5-years (NNT) and the number of strokes prevented per 1000 CEAs at 5-years, stratified for stenosis severity and sex of the patient. The table clearly shows that the sooner the patient undergoes CEA after symptom onset, the greater the number of ipsilateral strokes prevented in the long term. In addition, there is also evidence that females do not gain the same benefit as males. Males appear to continue to derive benefit from CEA, even if delayed by 12 weeks, especially in those with 70-99% stenoses. However, the data would suggest that CEA confers little obvious long-term benefit in females with 50-69% stenoses when CEA is performed >2 weeks, and there was no obvious benefit after 4 weeks in symptomatic females with 70-99% stenoses.
Table 4. Absolute risk reduction conferred by CEA in the 5-year risk of ipsilateral carotid territory ischaemic stroke (including peri-operative risk) in patients with a NASCET 50-69% and 70-99% stenosis, stratified for delay from index event to randomisation and sex

<table>
<thead>
<tr>
<th>Time since randomisation</th>
<th>50-69% stenosis</th>
<th>70-99% stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ARR</td>
<td>NNT</td>
</tr>
<tr>
<td><strong>All Patients</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 weeks</td>
<td>14.8%</td>
<td>7</td>
</tr>
<tr>
<td>2-4 weeks</td>
<td>3.3%</td>
<td>30</td>
</tr>
<tr>
<td>4-12 weeks</td>
<td>4.0%</td>
<td>25</td>
</tr>
<tr>
<td>&gt;12 weeks</td>
<td>-2.9%</td>
<td>nb</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 weeks</td>
<td>15.2%</td>
<td>7</td>
</tr>
<tr>
<td>2-4 weeks</td>
<td>6.8%</td>
<td>15</td>
</tr>
<tr>
<td>4-12 weeks</td>
<td>5.0%</td>
<td>20</td>
</tr>
<tr>
<td>&gt;12 weeks</td>
<td>6.3%</td>
<td>16</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 weeks</td>
<td>13.8%</td>
<td>7</td>
</tr>
<tr>
<td>2-4 weeks</td>
<td>-5.7%</td>
<td>nb</td>
</tr>
<tr>
<td>4-12 weeks</td>
<td>-2.2%</td>
<td>nb</td>
</tr>
<tr>
<td>&gt;12 weeks</td>
<td>-21.7%</td>
<td>nb</td>
</tr>
</tbody>
</table>

ARR = absolute risk reduction (%); CEA = carotid endarterectomy; NASCET = North American Symptomatic Carotid Endarterectomy Trial; NNT = number of CEA performed to prevent one stroke at 5 year; CVA/1000 = number of ipsilateral strokes prevented at five years by performing 1000 CEA; nb = no benefit conferred by CEA.

*Data derived from CETC with pre-randomisation angiograms re-measured using NASCET method.

The combination of there being a much higher risk of stroke in the first 7-14 days after onset of symptoms, in conjunction with the fact that CEA confers maximum benefit if performed <2 weeks became the key drivers behind the world-wide drive towards offering carotid interventions within the first 7-14 days after onset of symptoms.

RCTs comparing CEA with CAS

Twenty RCTs have compared outcomes following CEA versus CAS or carotid angioplasty, though not all were in symptomatic patients. Figure 3 details 30-day risks in 10 RCTs (n=5797 patients) comparing CEA with CAS (excluding carotid angioplasty). CAS was associated with significantly higher rates of ‘any stroke’, ‘death/any stroke’, ‘death/disabling stroke’ and ‘death/stroke/MI’. In Figure 4, similar outcome data are presented for 4754 patients in the four largest RCTs that randomised >500 patients. In this analysis, CAS was associated with significantly higher rates of ‘any stroke’, ‘death/stroke’ and ‘death/stroke/MI’. In summary, whether one included all RCTs, or only the largest ones, CAS was consistently associated with higher rates of 30-day ‘any stroke’; death/stroke and death/stroke/MI, compared with CEA.
### Figure 3. 30-day outcomes following CAS versus CEA in 10 RCTs which included 5797 symptomatic patients.
Reproduced with permission from Batchelder et al.
CAS = carotid artery stenting; CEA = carotid endarterectomy; OR = odds ratio; 95%CI = 95% confidence intervals; RCTs = randomised controlled trials; MI = myocardial infarction.

<table>
<thead>
<tr>
<th></th>
<th>Death</th>
<th>Stroke</th>
<th>Death/Stroke</th>
<th>Disabling Stroke</th>
<th>Death/Disabling stroke</th>
<th>MI</th>
<th>Death/Stroke/MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>9 RCTs n=4257</td>
<td>9 RCTs n=5535</td>
<td>10 RCTs n=5754</td>
<td>6 RCTs n=4835</td>
<td>5 RCTs n=3534</td>
<td>6 RCTs n=3980</td>
<td>6 RCTs n=3719</td>
</tr>
<tr>
<td></td>
<td>1.4% (0.9-2.0)</td>
<td>4.6% (3.2-6.37)</td>
<td>5.08% (3.7-6.9)</td>
<td>1.8% (1.1-3.1)</td>
<td>3.2% (2.5-4.1)</td>
<td>1.6% (1.0-2.3)</td>
<td>5.1% (4.1-6.30)</td>
</tr>
<tr>
<td>CAS</td>
<td>1.9% (1.4-2.6)</td>
<td>8.5% (5.8-12.14)</td>
<td>9.3% (6.8-12.6)</td>
<td>3.28% (1.6-6.7)</td>
<td>5.21% (3.0-8.9)</td>
<td>0.8% (0.5-1.4)</td>
<td>8.4% (5.0-13.8)</td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1.38 (0.81-2.34)</td>
<td>1.73 (1.38-2.18)</td>
<td>1.71 (1.38-2.11)</td>
<td>1.35 (0.91-1.99)</td>
<td>1.42 (1.00-2.02)</td>
<td>0.50 (0.24-1.02)</td>
<td>1.61 (1.21-2.14)</td>
</tr>
</tbody>
</table>

- **Significant benefit favouring CEA**
- **No significant difference between CAS and CEA**

### Figure 4. 30-day outcomes following CEA versus CAS in 4 randomised trials which randomised >500 symptomatic patients. Reproduced with permission from Batchelder et al.
CAS = carotid artery stenting; CEA = carotid endarterectomy; OR = odds ratio; 95%CI = 95% confidence intervals; RCTs = randomised controlled trials; MI = myocardial infarction.

<table>
<thead>
<tr>
<th></th>
<th>Death</th>
<th>Stroke</th>
<th>Death/Stroke</th>
<th>Disabling Stroke</th>
<th>Death/Disabling stroke</th>
<th>MI</th>
<th>Death/Stroke/MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>3 RCTs n=3413</td>
<td>4 RCTs n=4754</td>
<td>4 RCTs n=4754</td>
<td>4 RCTs n=4754</td>
<td>3 RCTs n=3413</td>
<td>3 RCTs n=3551</td>
<td>2 RCTs n=3031</td>
</tr>
<tr>
<td></td>
<td>0.9% (0.5-1.47)</td>
<td>4.8% (4.0-5.7)</td>
<td>5.5% (4.7-6.5)</td>
<td>2.4% (1.8-3.1)</td>
<td>3.2% (2.5-4.2)</td>
<td>1.0% (0.3-3.1)</td>
<td>5.2% (4.2-6.5)</td>
</tr>
<tr>
<td>CAS</td>
<td>1.2% (0.48-2.92)</td>
<td>7.8% (6.8-9.0)</td>
<td>8.7% (7.6-9.9)</td>
<td>3.3% (2.6-4.1)</td>
<td>4.3% (3.4-5.4)</td>
<td>0.7% (0.4-1.3)</td>
<td>8.0% (5.9-10.7)</td>
</tr>
<tr>
<td>OR (95%CI)</td>
<td>1.67 (0.88-3.17)</td>
<td>1.66 (1.32-2.10)</td>
<td>1.61 (1.29-2.01)</td>
<td>1.39 (0.98-1.97)</td>
<td>1.38 (0.96-1.98)</td>
<td>0.51 (0.25-1.07)</td>
<td>1.60 (1.19-2.14)</td>
</tr>
</tbody>
</table>

- **Significant benefit favouring CEA**
- **No significant difference between CAS and CEA**
However, once the 30-day peri-operative period has elapsed, meta-analyses suggested that there was no significant difference in 5 and 9-year rates of ipsilateral stroke. In a Carotid Stent Trialists Collaboration (CSTC) meta-analysis of 4754 symptomatic patients\(^{44}\), 5-year ipsilateral stroke was 3.1% (95%CI 2.3-4.1) after CEA and 3.2% after CAS (95%CI 2.3-4.2) (HR 1.06 (95%CI 0.73-1.54)), equating to an average annual ipsilateral stroke rate of 0.6% (95%CI 0.46-0.79) after CEA and 0.64% (95%CI 0.49-0.83) after CAS. The 9-year rate of ipsilateral stroke was 3.9% (95%CI 2.7-5.8) after CEA and 4.5% (95%CI 3.2-6.2) after CAS (ARR at 9-years = 0.5% (95%CI -1.6-2.7)).

**Important subgroup analyses (CEA vs CAS)**

The magnitude of the 30-day rate of death/stroke will, therefore, determine which treatment method (CEA or CAS) confers the maximum reduction in late stroke. Because of the large number of patients randomised within the 20 RCTs comparing CEA with CAS (n=9861), it is possible to perform meaningful subgroup analyses to identify clinical and/or imaging features that predict an increased risk of 30-day death/stroke after CEA or CAS\(^{45}\).

There was no association between increased rates of 30-day death/stroke following CEA/CAS and the following clinical/imaging features; side of lesion, BMI, pre-existing ischaemic heart disease; stenosis severity, the use of cerebral protection devices (or not) during CAS, pre-dilatation of the stenosis (or not) during CAS and post-dilatation of the stented stenosis (or not) during CAS\(^{45}\). There were minor increases in 30-day death/stroke for females after CAS and in patients with elevated pre-operative diastolic BPs in CEA patients\(^{45}\).

There were, however, a small number of pre-operative predictors for increased rates of 30-day death/stroke following CAS in the RCTs. These included; (i) age >70 years; (ii) performing CAS within 7-14 days of symptom onset, (iii) the presence of sequential plaques or remote lesions beyond the carotid bulb, (iv) plaque length >13mm, (v) the use of open cell stents, (vi) the use of 2 or more stents during CAS and (vii) an Age Related White Matter Change (ARWMC) score >7\(^{45}\).

**(i) increasing age** A CSTC meta-analysis of all four major RCTs (4289 symptomatic patients) reported that age had no effect on death/stroke after CEA, but there was a progressive increase in death/stroke with increasing age after CAS (Table 5)\(^{46}\). When compared to CEA (column 3, table 5), a threshold of 70-years was statistically significant. Above 70 years of age, CAS patients incurred significantly higher rates of death/stroke. Below the age of 70; CAS had very similar 30-day death/stroke rates to CEA.
In an earlier section, the rationale for performing carotid interventions as soon as possible after symptom onset was detailed. As a consequence, every guideline of practice now advises that CEA (CAS) should be performed within 14 days of symptom onset. In order to determine the comparative safety of CEA/CAS within this time-frame, CSTC undertook a meta-analysis of 30-day outcomes in 2839 patients randomised within the three European RCTs and observed that 30-day death/stroke was significantly higher when CAS was performed <7-days of symptom onset (9.4%), versus 2.8% after CEA (OR 3.4 (95%CI 1.01-13.1) p=0.03). 30-day death/stroke also remained significantly higher when CAS was performed 8-14-days after symptom onset (8.1%), versus 3.4% after CEA (OR 2.42 (95%CI 1.0-5.7) p=0.04).

Table 6 details the results of a second meta-analysis (n=4138) which now included symptomatic patients randomised within CREST. This meta-analysis was slightly different to the earlier one, as it only analysed outcome data for 0-7 days and >7 days after symptom onset. 30-day death/stroke after CAS <7-days of symptom onset was 8.4%, versus 1.3% after CEA (OR 6.51 (95%CI 2.0-21.21; p=0.002). 30-day fatal/disable stroke was also significantly higher when CAS was performed <7-days of symptom onset (3.1%), versus 0.4% after CEA (OR 8.38 (95%CI 1.09-64.76) p=0.04).
The CAS procedures in these meta-analyses were mainly transfemoral. It may be that newer stent technologies (such as TCAR) may be associated with lower procedural risks, but no published series has ever provided 30-day death/stroke data in patients undergoing TCAR within 7-14 days of symptom onset.

(iii) Plaque features

CREST evaluated various plaque features on pre-randomisation angiograms in 438 CEA and 1240 CAS patients. Sequential lesions and remote lesions extending beyond the bulb, were associated with significantly higher death/stroke rates after CAS (5.8%), vs 0.7% after CEA (OR 9.01 (95%CI 1.2-6.78). In addition, plaque length >13mm was associated with a 6.1% death/stroke rate after CAS, versus 1.9% after CEA (OR 3.42 (95%CI 1.19-9.78). CREST also analysed 1531 ‘lead in’ and 1121 trial patients undergoing CAS and showed that when one stent was deployed, the rate of peri-operative stroke was 4% in 2545 patients, versus 15% where >2 stents were deployed (OR 2.9 (95%CI 1.49-5.64). Patients with >2 stents were significantly more likely to have ulcerated plaques (p=0.006), be older (p=0.01) and have longer lesion lengths (p=0.02), the latter (presumably) tying in with recognition that stenoses >13mm in length were associated with higher procedural stroke rates.

(iv) Pre-existing white matter lesions on Magnetic Resonance Imaging (MRI)

The International Carotid Stenting Study (ICSS) scored the severity of pre-operative white matter lesions (WMLs) using the Age Related White Matter Changes (ARWMC) score. The median pre-operative score was 7. A subgroup of ICSS patients (CAS=536; CEA=500) were then stratified for whether the ARWMC score was <7 or >7.

In CEA patients, there was no relationship between the pre-operative ARWMC score and peri-operative stroke. However, in CAS patients, peri-operative stroke was significantly increased in patients with an ARWMC score >7, compared to those with a score <7 (HR 2.76 (95%CI 1.17-6.51). Higher rates of disabling stroke were also observed in CAS patients whose ARWMC score was >7 (HR 3 (95%CI 1.1-8.36).

When comparing CEA with CAS, in patients with an ARWMC score >7, CAS was associated with significantly higher stroke rates (HR 2.98 (95%CI 1.29-6.93), p=0.011). There was no difference in procedural stroke in CEA/CAS patients with an ARWMC <7. ICSS concluded that CAS should be avoided in patients with extensive WMLs on pre-operative MRI.
What do the 2017 ESVS guidelines advise regarding management?

The guidelines made the following recommendations regarding the selection of recently symptomatic patients for carotid interventions and whether CEA or CAS might be the preferred option.

Carotid endarterectomy is recommended in patients reporting carotid territory symptoms within the preceding 6-months and who have a 70-99% carotid stenosis, provided the documented procedural death/stroke rate is <6% (Class I, Level A).

CEA should be considered in patients reporting carotid territory symptoms within the preceding 6-months and who have a 50-69% carotid stenosis, provided the documented procedural death/stroke rate is <6% (Class IIa, Level A).

It is recommended that most patients who have suffered carotid territory symptoms within the preceding 6-months and who are aged >70 years and who have 50-99% stenoses should be treated by CEA, rather than CAS (Class I, Level A).

When revascularisation is indicated in patients who have suffered carotid territory symptoms within the preceding 6-months and who are aged <70 years, CAS may be considered an alternative to endarterectomy, provided the documented procedural death/stroke rate is <6% (Class IIb, Level A).

When revascularisation is considered appropriate in symptomatic patients with 50-99% stenoses, it is recommended that this be performed as soon as possible, preferably within 14 days of symptom onset (Class I, Level A).

Patients who are to undergo revascularisation within the first 14 days after onset of symptoms should undergo CEA, rather than CAS (Class I, Level A).

Challenging scenarios in symptomatic patients

The preceding sections have described how best to manage most recently symptomatic patients, but there are a number of clinical scenarios where management decisions may be more complicated. Examples include: (i) the optimal timing of carotid interventions after intravenous thrombolysis, (i) the optimal timing of carotid interventions after mechanical thrombectomy, (iii) the optimal timing of carotid interventions in patients with unstable neurological symptoms, (iv) timing of carotid interventions after a disabling stroke and (v) managing the recently symptomatic patient with carotid 'subocclusion'.

Optimal timing of carotid interventions after intravenous thrombolysis

The US Food and Drug administration approved intravenous (iv) thrombolysis for the treatment of selected patients with acute ischaemic stroke in 1996. The 2019 American Heart Association (AHA) Guidelines recommend that iv recombinant tissue plasminogen activator (rtPA) be administered <4.5 hours of stroke onset, preferably within 3 hours. Evidence suggests that 50% will recanalyse their occluded vessels, with poorer outcomes in patients with acute ICA occlusion. For every 100 patients treated with iv rtPA, 33 will benefit, but 6 will suffer an intracranial haemorrhage (ICH).

The main concern about performing CEA (CAS) soon after iv thrombolysis is ICH. In a systematic review of 13 published series (361 patients), 30-day death/stroke rate was 3.6%, while the incidence of ICH was 2.5%. The ESVS guidelines advise that strict selection criteria for early CEA should be followed, including: (1) rapid neurological recovery of the patient after thrombolysis (modified Rankin Score 0-2); (2) the area of acute infarction should be less than one third of the middle cerebral artery (MCA) territory; (3) recanalisation of a previously occluded MCA mainstem should have been demonstrated; (4) there should be an underlying ipsilateral ICA stenosis 50-99% and (5) no evidence of parenchymal haemorrhage or significant brain oedema. Contraindications to early CEA after thrombolysis include: (1) severe persisting neurological deficit (modified Rankin score >3); (2) predicted high-surgical risk and (3) parenchymal haemorrhage on repeat imaging.
Accordingly, 24 hours after completion of lysis and with evidence of neurological recovery, ESVS advise that a carotid DUS should be performed to confirm the presence of a 50-99% stenosis, while a CTA should assess the status of the distal ICA (no residual thrombus), circle of Willis (ensure previously occluded MCA mainstem is now patent) and to exclude secondary parenchymal haemorrhage. CEA can then be considered <48 hours (Class Ila, Level C). However, it is also important to ensure that antiplatelet therapy is withheld for 24 hours after lysis (in order to reduce parenchymal haemorrhage), but restarted prior to CEA or CAS (Class I, Level C). In addition, patients undergoing early carotid interventions after thrombolysis should have post-interventional hypertension actively treated in order to reduce the risks of secondary parenchymal haemorrhage (Class I, Level C)\(^62\).

**Timing of carotid interventions after mechanical thrombectomy**

The 2019 AHA guidelines on acute stroke management endorse an active role for emergency mechanical thrombectomy (MT) in selected patients with acute ischaemic stroke\(^55\), based on a meta-analysis of five randomised trials which reported that MT was associated with a twofold improvement in functional outcome, compared with patients randomized to BMT alone\(^56\). A proportion of patients (perhaps 10%) undergoing emergency MV will have tandem lesions (ie embolic occlusion of the ipsilateral MCA and significant cervical ICA disease (thrombosis or >90% stenosis). The key issue is how the tandem cervical occlusion/stenosis should be treated.

There are four treatment options; (i) MT+CAS with antiplatelet therapy; (ii) MT+CAS without antiplatelet therapy; (iii) MT+carotid angioplasty with no stent deployed and no antiplatelet therapy and (iv) MT alone +/- deferred CEA/CAS. The debate largely revolves around the following issues. Firstly; MT+CAS will treat both pathologies, it will enhance intracranial clot lysis by increasing perfusion pressure within the circle of Willis (CoW), which should, therefore, confer better patency. However, CAS requires peri-procedural antiplatelet therapy (usually DAPT), which may increase the risk of ICH, especially if the patient has also received iv thrombolysis (which most will have done). CAS without antiplatelet therapy incurs a higher risk of instent thrombosis, while carotid angioplasty risks secondary embolisation of residual atherothrombotic debris.

No RCTs have been performed and there is little consensus in the world literature. A recent survey of stroke specialists observed that 59% would consider CAS at the time of MT, while 41% would not. Almost three quarters agreed there was uncertainty, but only 54% had sufficient equipoise to randomise patients in a multicentre trial\(^57\). Not surprisingly, no international guidelines of practice have made any definitive recommendation, other than advising that these patients should be considered for inclusion in a RCT.

The recently published TITAN registry has, however, refocused attention on the advantages/disadvantages of MT+CAS, versus MT alone\(^58\). This multicentre, observational registry (involving 482 patients undergoing MT), evaluated outcomes following each of the four treatment strategies detailed above. The main conclusions were that, after adjusting for confounding variables, CAS+MV+antiplatelet therapy was independently associated with significantly higher rates of recanalisation, with rates of symptomatic haemorrhage and mortality being similar across all four treatment strategies, including patients receiving peri-procedural antiplatelet therapy and/or iv thrombolysis\(^58\),\(^59\).

Clinical/imaging features mitigating towards considering MV+CAS might include; poor antegrade flow up the ICA after MT; poor collateralisation via the CoW after MT, patients with smaller volumes of infarction and lower bleeding risks. Features suggesting that CAS might not be necessary (or should be deferred) include; poor intracranial revascularisation after MV, good filling of the intracranial vessels via the vertebral arteries and contralateral ICA via the CoW after MV (indicating that an ipsilateral CAS is not necessary), large volume infarcts and patients at increased risk of bleeding.

The 2017 ESVS guidelines provide no advice on the role of synchronous CAS+MV, while the 2019 European Stroke Organisation simply advises that these patients be entered into an RCT\(^60\). Future guidelines will, no doubt, be better informed by the recently started TITAN RCT (ClinicalTrials.gov Identifier: NCT03978988).

**Interventions in neurologically unstable patients**

The term ‘neurologically unstable’ usually refers to two clinical scenarios; (i) crescendo TIAs and (ii) stroke-in-evolution. There is no formal definition for crescendo TIAs, but the 2017 ESVS guidelines suggested that three or more TIAs within a
seven-day period might be reasonable\textsuperscript{52}. Stroke in evolution (previously known as ‘stuttering hemiplegia’), refers to the situation where a patient suffers their neurological deficit which then starts to improve (but never back to normal), before subsequent events recur and the neurological condition progressively worsens. Not surprisingly, both conditions carry a high risk of stroke if left untreated, but interventions also carry a higher risk of death/stroke. A meta-analysis reported that 30-day stroke/death after urgent/emergency CEA was 20.2\% (95\%CI 12.0-28.4) in patients undergoing CEA for stroke-in-evolution and 11.4\% (95\%CI 6.1-16.7) in patients undergoing CEA for crescendo TIA\textsuperscript{61}. Notwithstanding these much higher procedural risks, the 2017 ESVS guidelines recommend that patients with 50-99\% stenoses who present with stroke-in-evolution or crescendo TIA\textsuperscript{s} should be considered for urgent carotid endarterectomy, preferably <24 hours (\textit{Class IIa, Level C})\textsuperscript{52}. Options for reducing embolisation prior to emergency surgery might include intravenous Dextran therapy, intravenous Tirofiban therapy or intravenous heparin in addition to antiplatelet therapy.

**Timing of carotid interventions in patients suffering a disabling stroke.**

A disabling stroke is defined as scoring 3-5 on the Modified Rankin score. Historically, there has been great hesitancy in intervening early in these patients, because of an increased risk of haemorrhagic transformation within the ischaemic infarct, which is associated with high rates of severe disability and death.

It is, however, important to be clear about the time frame. The 2017 ESVS carotid guidelines recommend that revascularisation be deferred in patients with 50-99\% stenoses who have suffered a disabling stroke (modified Rankin score >3), where the area of infarction exceeds one third of the ipsilateral middle cerebral artery territory, or who have altered consciousness/drowsiness (\textit{Class I, Level C}). This clinical scenario was typical of the type of patient who used to be referred some time after stroke onset, when the brain injury was irreversible. It does not, however, reflect the situation where a patient presents acutely with an ischaemic stroke and who is being considered for emergency mechanical thrombectomy (+/- CAS), as described earlier.

**Managing the recently symptomatic patient with carotid ‘subocclusion’**

An individual patient meta-analysis was undertaken in 6092 patients randomised within NASCET, ECST and SVACS (\textit{Table 2}). The benefit conferred by CEA increased with increasing stenosis severity, with the exclusion of ‘near-occlusion’. Patients with chronic near occlusion (defined as a 95-99\% stenosis with distal ICA collapse or a narrow calibre lumen with ‘trickle flow’) gained no obvious benefit from CEA\textsuperscript{16}. On the basis of this subgroup analysis, the 2017 ESVS guidelines recommended that CEA or CAS were not recommended in symptomatic patients with a chronic internal carotid near-occlusion, unless associated with recurrent ipsilateral symptoms (despite optimal medical therapy) and following multi-disciplinary team review (\textit{Class III, Level C})\textsuperscript{52}.

This recommendation has been challenged on the basis that the RCT data were nearly 30 years old, that only 269 near-occlusion patients were included (some of whom subsequently underwent CEA) and that more recent observational data suggest that the risk of late stroke (when treated medically) may be higher than anticipated\textsuperscript{62, 63}. The 2017 recommendation will be the subject of an updated review in the 2022 ESVS carotid guidelines.

**References**


10. European Carotid Surgery Triallists Collaborative Group. MRC European Carotid Surgery Trial: Interim results for symptomatic patients with severe (70-99%) or mild (0-29%) carotid stenosis. Lancet 1991;337:1235-1243


