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CAROTID MASTERCLASS

Prediction and Prevention of Stroke in Patients with Symptomatic Carotid Stenosis: The High-risk Period and the High-risk Patient

P.M. Rothwell*

University Department of Clinical Neurology, University of Oxford, Oxford, United Kingdom

Carotid bifurcation stenosis is an important cause of ischaemic stroke, particularly in patients with recent transient ischaemic attack or minor stroke. Large randomised trials of endarterectomy have shown that surgery reduces the risk of stroke in patients with ≥50% recently symptomatic carotid stenosis, but more recent research has shown that the effectiveness of surgery is highly dependent on timing and on patient selection. Early surgery has been shown to be essential to reduce the high risk of stroke in the first few weeks after a TIA or minor stroke, and targeting treatment on the basis of timing and individual risk modelling has been shown to be useful in selecting patients with most to gain from endarterectomy for symptomatic stenosis. This article reviews current understanding of the high-risk period after TIA and minor stroke and recent developments in the identification of the high-risk patient – both in the acute phase and in the long-term.

Keywords: *Carotid stenosis; Endarterectomy; Risk prediction; Stroke prevention.*

Introduction

Ipsilateral ≥50% carotid stenosis is found in about 10–15% of carotid territory TIAs and ischaemic strokes, and is associated with a particularly high risk of recurrent stroke both in the acute phase and the long-term. However, the majority of patients with symptomatic carotid stenosis will not have a subsequent ipsilateral ischaemic stroke. This review will consider three separate questions related to prediction and prevention of stroke in patients with recently symptomatic carotid stenosis. Firstly, what is the high-risk period after TIA and minor stroke and what are the implications for medical and surgical intervention? Secondly, which individual patients are at highest risk of major stroke in the days after a TIA or minor stroke and therefore require urgent carotid imaging and treatment? Thirdly, which patients with recently symptomatic stenosis are at highest long-term risk of stroke and will therefore be most likely to benefit from endarterectomy in the longer-term?

*Corresponding author.
E-mail address: peter.rothwell@clneuro.ox.ac.uk

The High-risk Period

About 15–20% of stroke patients report a preceding TIA,[1–3] and a similar proportion have a preceding minor stroke. The time-window for prevention is short, with over 40% of TIAs occurring during the week prior to the stroke.[3] The consequences of non-urgent assessment of TIA were illustrated by an audit of 210 consecutive patients with suspected TIA referred to a standard weekly specialist clinic in the UK, in which all patients who did not attend the clinic appointment were traced to ensure inclusion of all follow-up strokes.[4] Although the median delay from referral to the clinic appointment (9 days) was less than the UK average, 11 (5.3%) patients had a stroke after referral but prior to their scheduled appointment, nine of which were disabling.

Early prospective studies of prognosis underestimated the immediate risk of stroke after a TIA and minor stroke,[5] but recent hospital-based and population based cohort studies have reported risks of up to 10% at 7 days and 15% at 30 days (Fig. 1).[1,2,6] A recent systematic review of all published studies of the early risk of stroke after TIA showed that the observed risk was dependent on the methods and setting of the study, with the highest risks in population-based studies with high rates of

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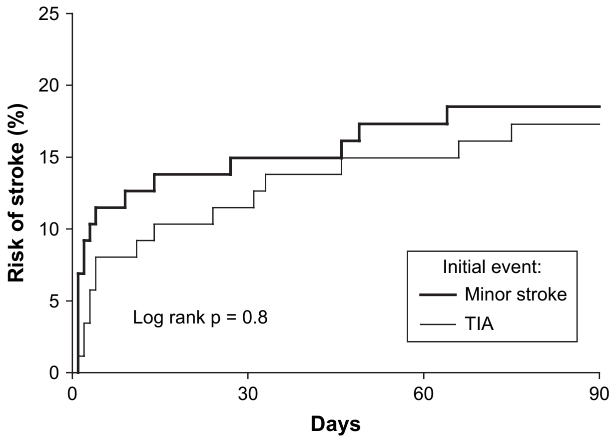

Fig. 1. Cumulative risk of stroke following a TIA or minor stroke in the Oxford Vascular Study.[2]

ascertainment and face-to-face follow-up but without urgent treatment, and the lowest risks reported in studies that involved urgent assessment and treatment.[7]

The underlying aetiology of TIA and minor stroke that is associated with the highest early risk of stroke is large artery atherosclerosis (usually carotid bifurcation stenosis). In a meta-analysis of data from 1709 patients in four population-based studies, large artery disease was present in only 14% of patients but this group had 37% of early recurrent strokes.[8] A population-based study of prognosis of patents with TIA or minor stroke and ≥50% symptomatic carotid stenosis reported risks of stroke in the region of 20% during the first two weeks (Fig. 2),[9] and other studies have

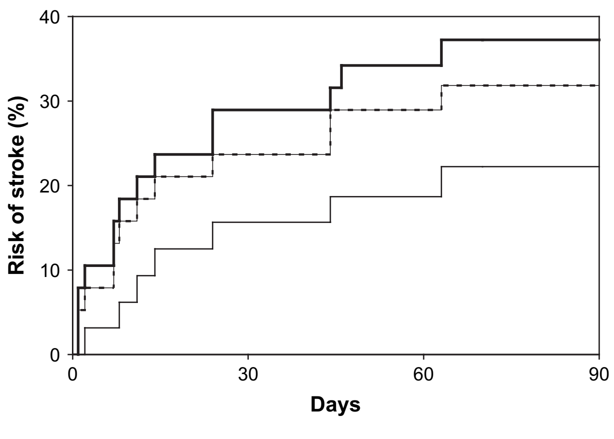

Fig. 2. The risk of recurrent stroke in all patients with TIA or non-disabling ischaemic stroke in the Oxford Vascular Study population who were found to have ≥50% symptomatic carotid stenosis censored prior to any endarterectomy (thick line).[9] The dotted line shows this same risk excluding strokes that occurred prior to the patient seeking medical attention after the initial TIA or minor stroke. The thin line shows this latter risk excluding cases in whom carotid imaging was performed after the recurrence and showed a complete occlusion at that time.

highlighted the high risk of stroke if endarterectomy is delayed.[10] Fig. 2 shows that the high-risk period after a TIA or stroke appears also to last longer in patients with symptomatic carotid stenosis than in patients with other aetiologies of TIA and stroke (Fig. 1), which increases the potential for prevention.

The high risk of stroke after a TIA means that reliable diagnosis is crucial − the risk of ipsilateral ischaemic stroke distal to a ≥50% symptomatic carotid stenosis during the first 30 days after a TIA or minor stroke is about 100 times greater than that during a 30 day period in a patient with a similar degree of asymptomatic stenosis. Clinical assessment by a neurologist or stroke physician is therefore very important in determining whether urgent endarterectomy is necessary.

Medical treatment in the high-risk period

Given the very high early risk of stroke after TIA or minor stroke, urgent medical treatment is indicated. The benefits of urgent treatment were demonstrated recently in the EXPRESS (Early Use of Existing Preventive Strategies for Stroke) Study[11] and the SOS-TIA Study.[12]

The EXPRESS Study was a prospective population-based sequential comparison study of the effect on process of care and outcome of more urgent assessment and immediate treatment in clinic, rather than subsequent initiation in primary care, in all patients with TIA or minor stroke. The study was nested within a rigorous population-based TIA and stroke incidence study, such that case ascertainment, investigation, and follow-up were complete and identical in both periods. The standard treatment protocol was: aspirin (300 mg loading, 75 mg daily), or clopidogrel if aspirin was contraindicated; simvastatin (40 mg daily); blood pressure lowering (increase existing medication if required, or start perindopril 4 mg daily ± indapamide 1.25 mg daily); and carotid endarterectomy and anticoagulation as required. In patients seen within 48 h of their event or those seen within 7 days who were thought to be at particularly high early risk, clopidogrel (75 mg daily to be stopped after 30 days) was recommended in addition to aspirin. Brain imaging was required prior to starting combination antiplatelet treatment or anticoagulation after a minor stroke.

The primary outcome in the EXPRESS study was the risk of stroke during the 90 days after first seeking medical attention, with independent blinded (to study period) audit of all events. Of all 620 patients with TIA or minor stroke in the study population who presented to medical attention and were referred for outpatient assessment, 95% (591/620) were sent to the EXPRESS study clinic. Median (IQR) delay to assessment in the study clinic fell from 3 (2−5) days in phase-1 (2002−2004) to less than 1 (0−3) day in phase-2 (2004−2007, $p < 0.0001$), and the median delay to first prescription of treatment fell from 20 (8−53) days to 1 day (0−3) ($p < 0.0001$). The 90-day risk of recurrent stroke in the patients referred to the study clinic was 10.3% (32/310) in phase-1 versus 2.1% (6/281) in phase-2 ($p = 0.0001$, Fig. 3).

The EXPRESS Study showed that early initiation of existing treatments after TIA or minor stroke is safe and is associated with an 80% reduction in the risk of early recurrent stroke compared with initiation of treatment in primary care. The good prognosis associated with urgent and intensive treatment was also highlighted by the results of the SOS-TIA Study.[12] In 2003, an emergency TIA clinic was set up in an administrative region of Paris (11 million inhabitants). The SOS-TIA service was accessible 24-hour a day, 7 days a week, and initiated medical treatment and appropriate investigation immediately. In the first report of all 629 consecutive patients with definite TIA seen from January 2003 to December 2005, there were 12 strokes during three months follow-up and only two strokes within 7 days, giving risks of 1.9% and 0.3% respectively.[12]

Immediate antiplatelet treatment, usually with aspirin, is indicated in virtually all patients with TIA and minor ischaemic stroke, but there is increasing evidence that the combination of aspirin plus clopidogrel (as used in high-risk patients in the EXPRESS Study) will be more effective in the acute phase. In the MATCH trial,[13] patients randomized within the first week after the qualifying TIA or stroke showed a trend towards benefit from aspirin plus clopidogrel versus clopidogrel alone. In the CARESS trial,[14] 107 patients with recently symptomatic ≥50% carotid stenosis and micro-embolic signals (MES) detected on transcranial doppler were randomized to either aspirin alone (75 mg once a day) or the combination of aspirin and clopidogrel (300 mg loading then 75 mg once a day). The primary end-point (MES positivity at seven days after randomization) was significantly reduced on dual therapy versus monotherapy (43.8% vs 72.7%, $P = 0.005$) and there were fewer recurrent strokes in the dual therapy group although this was not statistically significant. Most recently, the FASTER Trial (Fast Assessment of Stroke and Transient Ischemic Attack to prevent Early Recurrence) also reported a trend towards a reduced early risk of stroke with aspirin plus clopidogrel (300 mg load followed by 75 mg/day) versus aspirin alone in patients who have had a TIA or minor ischaemic stroke within the previous 24 h.[15]

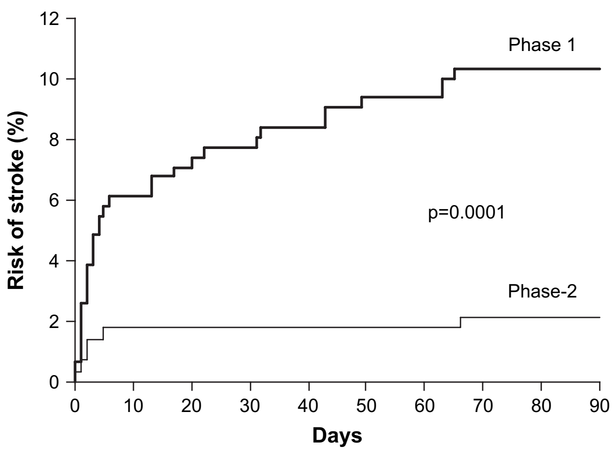

Fig. 3. The 90-day risk of recurrent stroke after first seeking medical attention in all patients with TIA or stroke referred to the EXPRESS Study Clinic in phase-1 (standard management) and in phase-2 (urgent treatment).[11]

These studies suggest that combination antiplatelet treatment is likely to reduce the risk of early recurrent stroke prior to endarterectomy in patients with symptomatic carotid stenosis. Although some surgeons do not like to operate on patients taking both aspirin and clopidogrel due to increased operative bleeding, there is no evidence of an increase in major bleeding and there may be a beneficial effect on the risk of perioperative ischaemic complications.[16,17] In one randomised trial, 100 patients with symptomatic carotid stenosis on aspirin therapy (150 mg) were randomized to 75 mg clopidogrel or placebo the night before surgery. In comparison with placebo, clopidogrel resulted in a 10-fold reduction in the number of patients having >20 emboli in the postoperative period detected by transcranial Doppler ($P = 0.01$).[16] Although the time from flow restoration to skin closure (an indirect marker of hemostasis) was significantly increased with clopidogrel, there was no increase in major bleeding complications or blood transfusions. The effectiveness of the combination of aspirin and dipyridamole has not been studied specifically in patients with carotid stenosis or in the acute phase after TIA or minor stroke.

Blood pressure lowering has been shown to be effective for secondary prevention of stroke, but many physicians are cautious about lowering blood pressure in patients with severe carotid stenosis because of the frequent loss of the normal autoregulatory capacity of the cerebral circulation in such patients, such that cerebral blood flow is directly dependent on perfusion pressure. Some reassurence is available from an analysis of the risk of stroke in relation to systolic blood pressure (SBP) stratified according to the presence or absence of flow-limiting (≥70%) carotid stenosis in patients randomised to medical treatment in the large RCTs of endarterectomy for symptomatic carotid stenosis.[18] Major increases in stroke risk were seen in association with bilateral ≥70% stenosis in patients with low systolic blood pressure (systolic < 130 mmHg), but not in patients with unilateral stenosis. It was concluded that aggressive blood pressure lowering prior to endarterectomy might well be harmful in patients with bilateral severe carotid stenosis or severe symptomatic stenosis with contralateral occlusion, but gradual blood pressure lowering is likely to be safe and beneficial in patients with only unilateral severe stenosis.

Endarterectomy in the high-risk period

Given that the risk of stroke on medical treatment after a TIA or minor stroke is highest during the first few days and weeks, particularly in patients with carotid stenosis, and that the risk then falls rapidly over the subsequent year,[19] early endarterectomy or stenting would seem sensible. However, there has been concern that the operative risk may be increased if surgery is performed too early. Although this is certainly true for patients with major cerebral infarction or stroke-in-evolution, there was no evidence of any increase in operative risk in patients operated within two weeks of their last event in either of the two large randomised trials (Table 1).[20,21] The findings were much the same in patients operated after TIA only or a non-disabling stroke with full recovery.[21] Further subdivision of the pooled trial data by time to surgery did not reveal any significant difference ($p = 0.52$) between the operative risk of stroke and death in patients operated within 1 week of the event (10/122, 8.2%, 95% CI = 4.0–14.6) and those operated one to two weeks after the event (15/238, 6.3%, 95% CI = 3.6–10.2), although the number operated within one week of a hemispheric stroke with incomplete recovery was too small to allow reliable estimation of risk.[21]

In a systematic review of all surgical case series reporting operative risk of endarterectomy by time since the presenting event, there was also no evidence that early surgery (within 2–4 weeks) was associated with a worse outcome than delayed surgery,[22,23] although emergency surgery for stroke-in-evolution or crescendo TIA was associated with high operative risk (19.2%, 95%CI 10.7–27.8, 13 studies).

The pooled analysis of data from the randomised trials showed that benefit from endarterectomy was greatest in patients randomised within two weeks of their last event,[20] particularly in patients with 50–69% stenosis, where the reduction in the 5-year risk of stroke with surgery was considerable in those who were randomized within 2 weeks of their last event (14.8%, 95% CI = 6.2–23.4), but minimal in patients randomized later (Fig. 4). Interestingly, the decline in benefit from endarterectomy with time since last event was more pronounced in women than men, highlighting the particular need for urgent surgery in women.[21]

Effective prevention of stroke with endarterectomy is undermined in many healthcare systems by delays in investigation and intervention. For example, in a study of all patients undergoing carotid imaging for TIA or stroke in Oxfordshire, UK, during 2003–2004, 85 patients were found to have 50–99% symptomatic stenosis, of whom 49 had endarterectomy, but in only 3 (6%) patients was surgery performed within two weeks of their presenting event and only 21 (43%) had surgery within 12 weeks.[9] However, performance can be improved. In a follow-up audit in Oxfordshire, UK, in 2005–2007, as part of Phase-2 of the EXPRESS Study, 40% of patients were operated within 7 days and 67% within one month of their presenting event.[11]

Table 1. The operative risk (95% CI) due to trial surgery in relation to the time between the last symptomatic ischaemic event and surgery in the European Carotid Surgery Trial (ECST) and the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[21]

	Time between last symptomatic ischaemic event and surgery								*P*
	<2 Weeks		2–4 Weeks		4–12 Weeks		>12 Weeks		
Any stroke or death within 30 days after trial surgery									
ECST	5/77	6.5%(1.0–12.0)	16/249	6.4%(3.4–9.5)	56/756	7.4%(5.5–9.3)	53/660	8.0%(5.9–10.0)	0.86
NASCET	20/283	7.1%(4.1–10.1)	14/281	5.0%(2.4–7.5)	36/555	6.5%(4.4–8.4)	22/296	7.4%(4.4–10.4)	0.64
Total	25/360	6.9%(4.5–10.1)	30/530	5.7%(3.9–8.0)	92/1311	7.0%(5.7–8.5)	75/956	7.8%(6.2–9.7)	0.48
Disabling operative stroke or death within 30 days after trial surgery									
ECST	2/77	2.6%(0.3–9.1)	6/249	2.4%(0.9–5.2)	31/756	4.1%(2.8–5.8)	23/660	3.5%(2.2–5.2)	0.61
NASCET	9/283	3.2%(1.5–6.0)	7/281	2.5%(1.0–5.1)	9/555	1.6%(0.7–3.1)	3/296	1.0%(0.2–2.9)	0.23
Total	11/360	3.1%(1.5–5.4)	13/530	2.5%(1.3–4.2)	40/1311	3.1%(2.2–4.1)	26/956	2.7%(1.8–4.0)	0.89

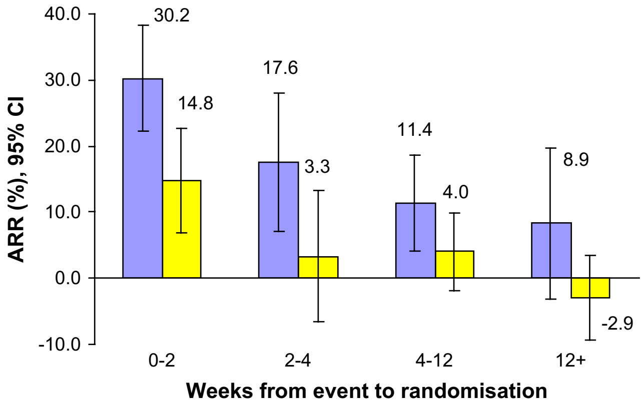

Fig. 4. The absolute reduction with surgery in the five year risk of stroke and operative death in patients with 50–69% stenosis (yellow bar) and ≥70% stenosis without near-occlusion (blue bar) stratified by the time from last symptomatic event to randomisation in a pooled analysis of data from randomised trials of endarterectomy for recently symptomatic carotid stenosis.[20] The numbers above the bars indicate the actual absolute risk reduction.

The High-risk Patient: Acute Phase

Validated models are now available to predict the early risk of stroke after a TIA,[4,24] such that front-line physicians can identify which patients with suspected TIA should be referred-on for emergency assessment. The six point ABCD score was derived from the model shown in Table 2: [Age ≥ 60 years = 1, Blood pressure (systolic > 140 mmHg and/or diastolic ≥ 90 mmHg = 1), Clinical features (unilateral weakness = 2, speech disturbance without weakness = 1, other = 0) and Duration of symptoms in minutes (≥60 = 2, 10–59 = 1, <10 = 0]). The score is a useful predictor of the 7-day risk of stroke after TIA. For example, in the original validation cohort, 95% of early strokes occurred in 27% of the patients with a score ≥5, with a 7-day risk of 12.1% patients with a score of 5 and 31.4% in those a score of 6.[4] Subsequent independent validations of the ABCD score have shown similar predictive power,[24] and the score has been refined by the addition of a point for diabetes (ABCD² score). Fig. 5 shows the validation of the score in six independent cohorts.[24]

Table 2. Prognostic model for the 7-day risk of stroke after a transient ischaemic attack (TIA) derived from two population-based studies of TIA in Oxfordshire, UK[4]

Risk factor	Hazard ratio (95% CI)	*P*
Age ≥60 years	2.57 (0.75–8.81)	0.133
Systolic BP > 140 mmHg or Diastolic BP ≥ 90 mmHg	9.67 (2.23–41.94)	0.002
Clinical features		
Unilateral weakness	6.61 (1.53–28.50)	0.016
Speech disturbance without weakness	2.59 (0.50–13.56)	
Other	1	
Duration of symptoms		
≥60 min	6.17 (1.43–26.62)	0.019
10–59 min	3.08 (0.64–14.77)	
<10 min	1	
Diabetes mellitus	4.39 (1.36–14.22)	0.014

Only one study has so far reported data on the prevalence of carotid stenosis by ABCD score.[25] Patients with low scores were just as likely to have symptomatic carotid stenosis as those with high scores, but the early risk of stroke was confined to patients with high ABCD scores.[25] Thus, although the score doesn't identify which patients have carotid stenosis it does seem to identify those patients with carotid stenosis who require urgent treatment. The ABCD system is therefore probably a useful tool for triaging access to carotid imaging and surgery in healthcare systems where delays are common.

The High-risk Patient: Long-term

Based on the pooled analysis of data from the three largest RCTs of surgery for symptomatic carotid stenosis,[26] and using the method of measurement of angiographic degree of stenosis used in the North American Symptomatic Carotid Endarterectomy Trial (NASCET),[27] endarterectomy reduced the 5-year absolute risk of any stroke or death by 15% in patients with 70–99% stenosis without near-occlusion, and by 7.8% in patients with 50–69% stenosis. However,

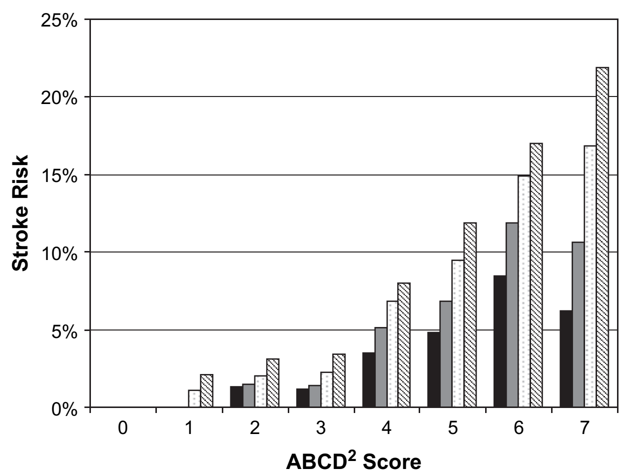

Fig. 5. The early risk of stroke by ABCD² score in pooled data from six independent cohorts of patients with TIA (4799 patients).[24] Stroke risks are shown at 2 days (black), 7 days (gray), 30 days (stippled), and 90 days (hashed).

although endarterectomy is of overall benefit, the majority of patients who were operated in the trials would not have had a stroke if they had had medical treatment alone. The overall absolute risk of stroke in the medical treatment groups in the ECST and NASCET was about 20% at three years, given that relatively few patients were randomized in the acute phase. Endarterectomy could have been of no value in the other 80% of patients who, despite having a symptomatic stenosis, were destined to remain stroke free without surgery and could only be harmed. It would, therefore, be useful to be able to identify in advance, and operate on, only those patients with a high risk of stroke on medical treatment alone.

Although the degree of carotid stenosis is a major determinant of benefit from endarterectomy, there are several other clinical and angiographic characteristics that influence the risks and benefits of surgery. Subgroup analyses of the pooled data from the large trials identified several clinically important interactions.[20] Sex ($p = 0.003$), age ($p = 0.03$), and time from the last symptomatic event to randomisation ($p = 0.009$) each modified the effectiveness of surgery (Fig. 6). Benefit from surgery was greatest in men, patients aged ≥75 years, and patients randomised within two weeks after their last ischaemic event. For patients with ≥50% stenosis, the number of patients needed to undergo surgery (NNT) to prevent one ipsilateral stroke in 5 years was 9 for men versus 36 for women, 5 for age ≥75 versus 18 for age <65 years, and 5 for patients randomised within 2 weeks after their last ischaemic event versus 125 for patients randomised >12 weeks.[20] These observations were consistent across the 50–69% and ≥70% stenosis groups and similar trends were present in both ECST and NASCET.[20] Benefit from surgery was also greatest in patients with stroke, intermediate in those with cerebral TIA and lowest in those with retinal events. There was also a trend in the randomised

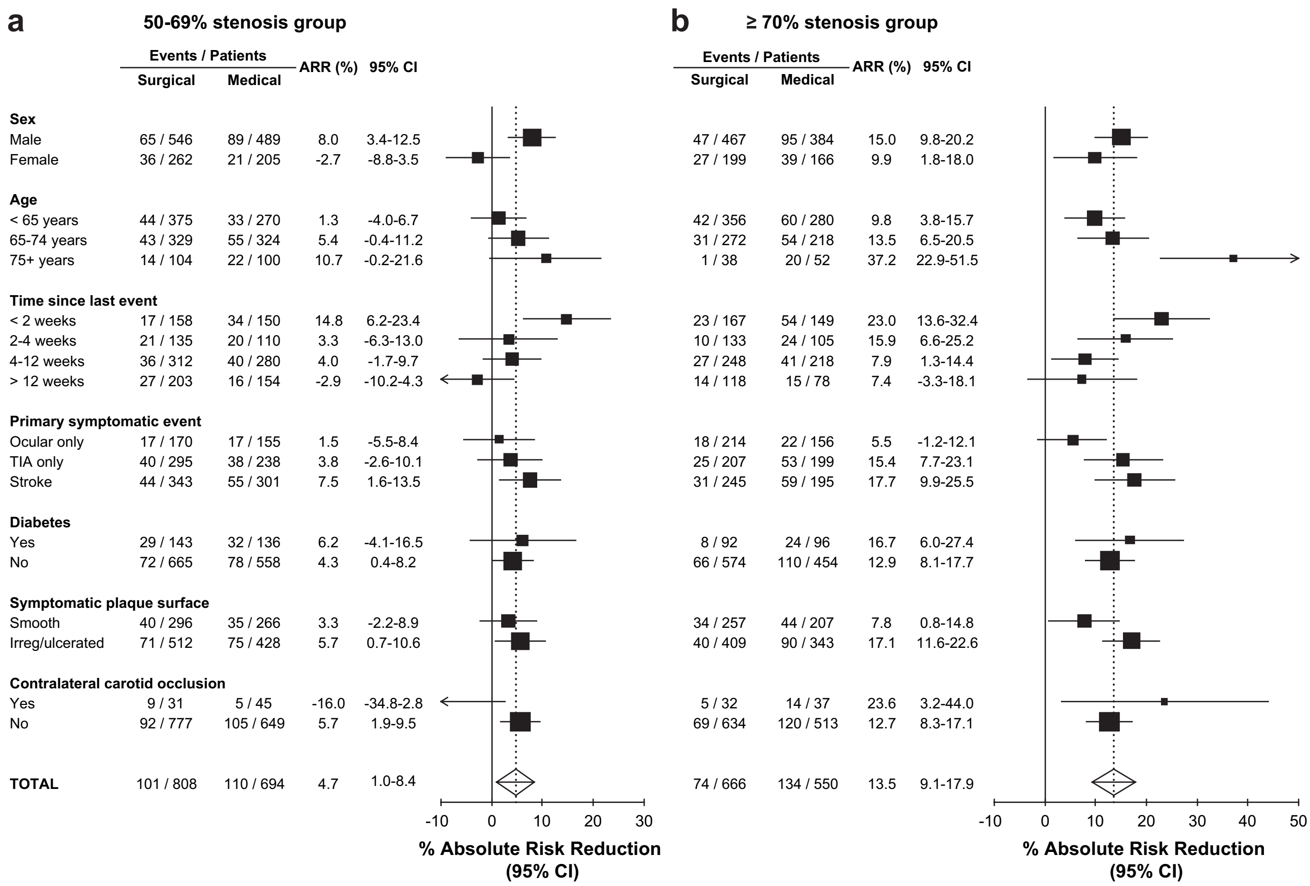

Fig. 6. Absolute reduction (ARR) with surgery in the 5-year risk of ipsilateral carotid territory ischaemic stroke and any stroke or death within 30 days after trial surgery according to predefined subgroup variables in an analysis of pooled data from the two largest randomised controlled trials of surgery for recently symptomatic carotid stenosis: (a) patients with 50–69% stenosis; (b) patients with ≥70% stenosis.[26]

trials towards greater benefit in patients with irregular plaque than a smooth plaque.[20]

These various subgroup observations are of some help in clinical practice, but individual patients frequently have several important risk factors, each of which interact in a way that cannot be described using univariate subgroup analysis alone. For example, what would be the likely benefit from surgery in a 78 year old (increased benefit) female (reduced benefit) with 70% stenosis who presented within two weeks (increased benefit) of an ocular ischaemic event (reduced benefit) and was found to have an ulcerated carotid plaque (increased benefit)?

One way in which clinicians can weigh the often-conflicting effects of the important characteristics of an individual patient on the likely benefit from treatment is to base decisions on the predicted absolute risks of a poor outcome with each treatment option using prognostic models. A model for prediction of the risk of stroke on medical treatment in patients with recently symptomatic carotid stenosis was derived from the ECST.[28,29] The model (available at www.stroke.ox.ac.uk), which takes into account the delay since the presenting event as well as the other major risk factors for stroke, was validated using data from NASCET and showed very good agreement between predicted and observed medical risk ($p < 0.0001$),[29] reliably distinguishing between individuals with a 10% risk of ipsilateral ischaemic stroke after five years follow-up and individuals with a risk of over 40% (Fig. 7). Importantly, Fig. 7 also shows that the operative risk of stroke and death in patients who were randomised to surgery in NASCET was unrelated to the medical risk ($p = 0.32$). Thus, when the operative risk and the small additional residual risk of stroke following successful endarterectomy were taken into account, benefit from endarterectomy at 5 years varied significantly across the quintiles ($p = 0.001$),[29] with no benefit in patients in the lower three quintiles of predicted medical risk (ARR = 0−2%), moderate benefit in the fourth quintile (ARR = 10.8%, 95% CI = 1.0−20.6), and substantial benefit in the highest quintile (ARR = 32.0%, 95% CI = 21.9−42.1).

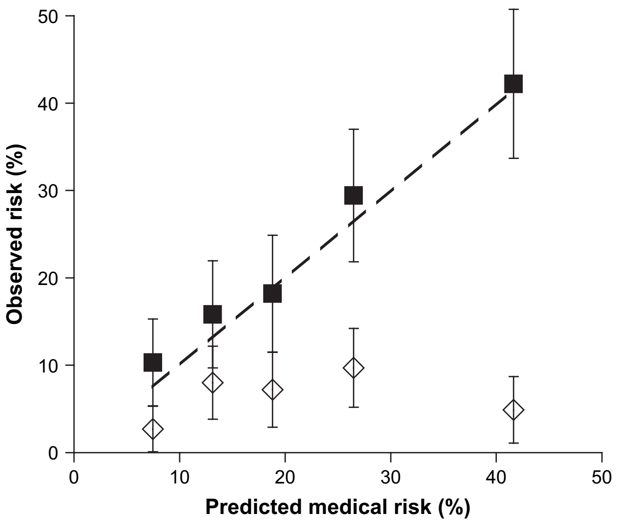

Fig. 7. Validation in North American Symptomatic Carotid Endarterectomy Trial (NASCET) patients with 50−99% stenosis of the European Carotid Surgery Trial (ECST) model for the 5-year risk of ipsilateral ischaemic stroke on medical treatment. Predicted medical risk is plotted against observed risk of stroke in patients randomised to medial treatment in NASCET (squares) and against the observed operative risk of stroke and death in patients randomised to surgical treatment (diamonds).[29] Groups are quintiles of predicted risk. Error bars represent 95% confidence intervals.

Fig. 8 shows the risk table for the five-year risk of ipsilateral ischaemic stroke in patients with recently symptomatic carotid stenosis on medical treatment derived from the ECST model. The table is based on the five variables that were both significant predictors of risk in the ECST model and yielded clinically important subgroup-treatment effect interactions in the analysis of pooled data from the relevant trials (sex, age, time since last symptomatic event, type of presenting event(s) and carotid plaque surface morphology).

One potential problem with the ECST risk model is that it might over-estimate risk in current patients because of improvements in medical treatment, such as the increased use of statins. However, such improvements in treatment pose more problems for interpretation of the overall trial results than for the risk modelling approach. For example, it would take only a relatively modest improvement in the effectiveness of medical treatment to erode the overall benefit of endarterectomy in patients with 50−69% stenosis. In contrast, very major improvements in medical treatment would be required in order to significantly reduce the benefit from surgery in patients in the high predicted-risk quintile in Fig. 7.

There are also other ways in which high-risk individuals might be identified, although no method has yet been shown to predict the risk of stroke over and above the ECST risk model. However, possible options are the detection of micro-embolic signals with transcranial Doppler ultrasound imaging, identification of individuals with particularly poor cerebral perfusion, and detection of unstable carotid plaques using various techniques of high-resolution non-invasive imaging. Further research is necessary before any of these techniques can be used routinely in clinical practice.

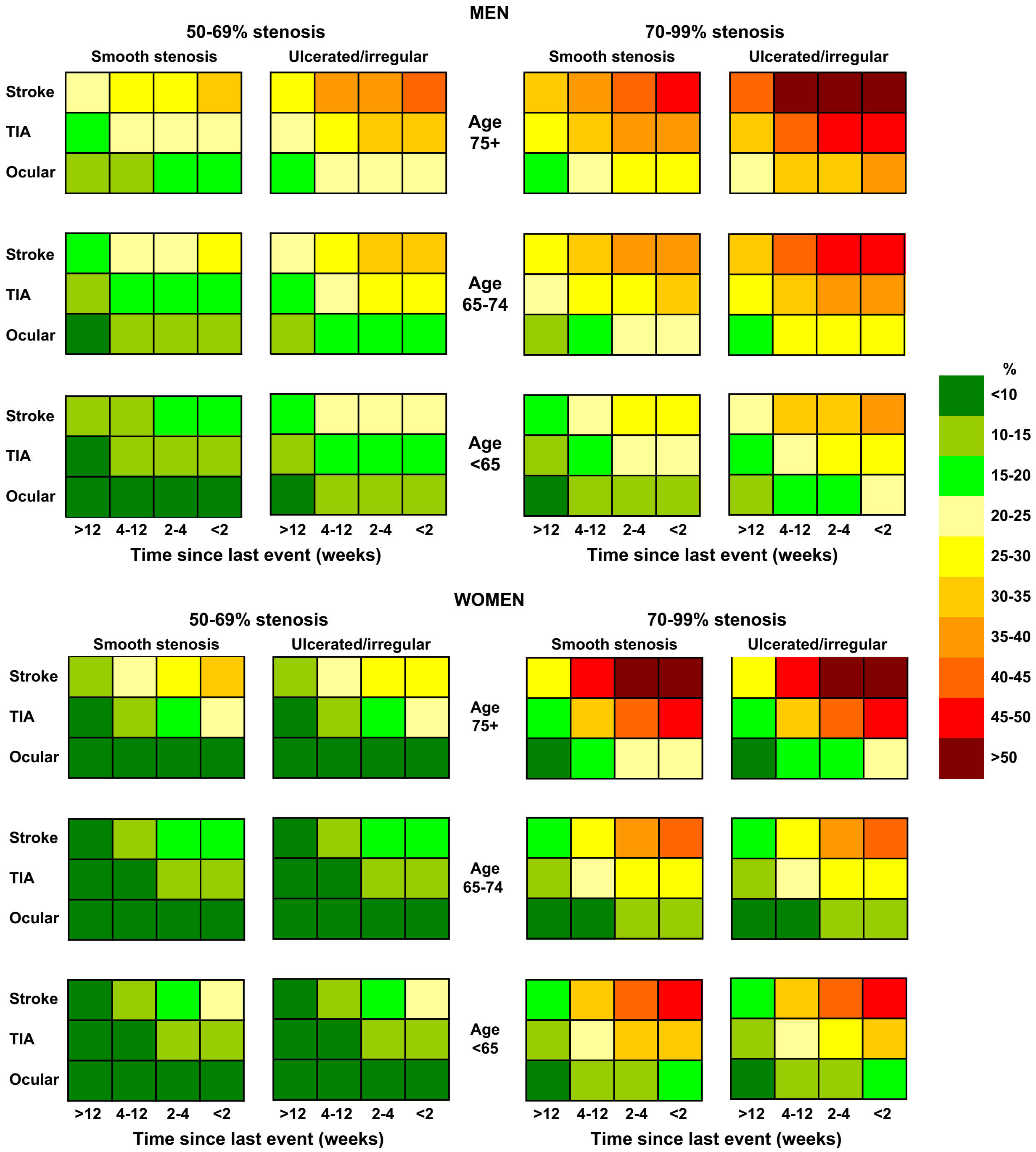

Fig. 8. A table of the predicted absolute risk of ipsilateral ischaemic stroke on medical treatment in ECST patients with recently symptomatic carotid stenosis derived from a Cox model based on six clinically important patient characteristics.[29]

Conclusion

Recent research has gone some way to identifying which patients are likely to benefit most from carotid endarterectomy and when intervention is most effective in patients with symptomatic stenosis. Individual risk modelling is useful in selecting patients for endarterectomy for symptomatic stenosis, although timely surgery and optimal medical treatment are of at least equal importance.

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