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Are We Detecting and Operating on High Risk Patients in The Asymptomatic Carotid Surgery Trial?

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Objective: *This study aims to determine whether asymptomatic carotid surgery trial (ACST) centres have entered and can identify high risk patients using duplex.*
Design: *Retrospective study.*
Materials and methods: *Eighty-six vascular laboratories collaborating in ACST were studied. Equipment, operator experience, methodology and interpretation criteria were assessed. The ACST randomisation data were examined to determine whether patients believed to be at higher risk of stroke because of tight stenosis, contralateral occlusion or echolucent plaque were randomised.*
Results: *Laboratories (92%) had colour duplex and 62% of all operators had >3 years experience in carotid evaluation. The Doppler angle used to obtain peak velocity was 30–60° in 65%, 60° in 28% and 60–80° in 6% of laboratories. Sixty-two per cent reported diameter reduction, 27% area reduction, and 11% used both methods.*
One-third of 1657 randomised patients were reported to have ipsilateral echolucent plaque. Median ipsilateral stenosis was 80%, 8% had contralateral occlusion and 8.5% had bilateral >80% stenosis.
Conclusions: *Centres in ACST use experienced operators, high quality equipment and conscientious data recording. Variations in methods of determining carotid stenosis exist, but can be smoothed by simple data collection. Patients at higher perceived risk of stroke are being entered and with continued recruitment it should be possible to determine whether surgery improves disabling stroke-free survival.*

Key Words: Carotid endarterectomy; Asymptomatic carotid disease; Duplex; Risk factors.

Introduction

The Asymptomatic carotid surgery trial (ACST) has randomised over 1660 patients to determine the benefit of carotid endarterectomy (CEA) in patients with asymptomatic carotid stenosis.[1] The aim is to determine whether CEA and best medical treatment (BMT) improve stroke free survival when compared with best medical treatment alone. The trial will also try to identify patients in whom the benefit of surgery or of BMT might be greatest. It is an international multicentre trial involving 127 participating centres from 25 countries (Fig. 1). Patients with asymptomatic carotid stenosis are randomised when clinicians feel they are at risk of stroke but are unsure as to whether medical or surgical treatment is best. Unlike previous trials of CEA, a preoperative angiogram is not mandatory for randomisation. In this trial, carotid duplex ultrasound (CDU) is used for assessment of patients at randomisation and for follow-up.

Both angiographic and duplex criteria have been refined to give clinically relevant cut-off points to select patients for surgery based on the outcome of recent trials.[2] However different methods of measuring stenosis were used in previous trials, NASCET, ACAS and ECST. There is no accepted standard for the quantification of the primary carotid stenosis.[3,4] Further potential differences may arise from the increasing use of CDU without angiography when assessing patients who might be suitable for surgery. None of the present duplex criteria directly measure percentage stenosis directly. Most have been validated against angiography although some authors have validated duplex criteria against the residual lumen diameter from en bloc surgical specimens.[5] Presently there is no European consensus on the practice of CDU.[3] Examinations may be performed by vascular surgeons, technologists and radiologists using different methods.[6] Several different validated duplex criteria are currently in use.[4] More information is needed for standardisation of the

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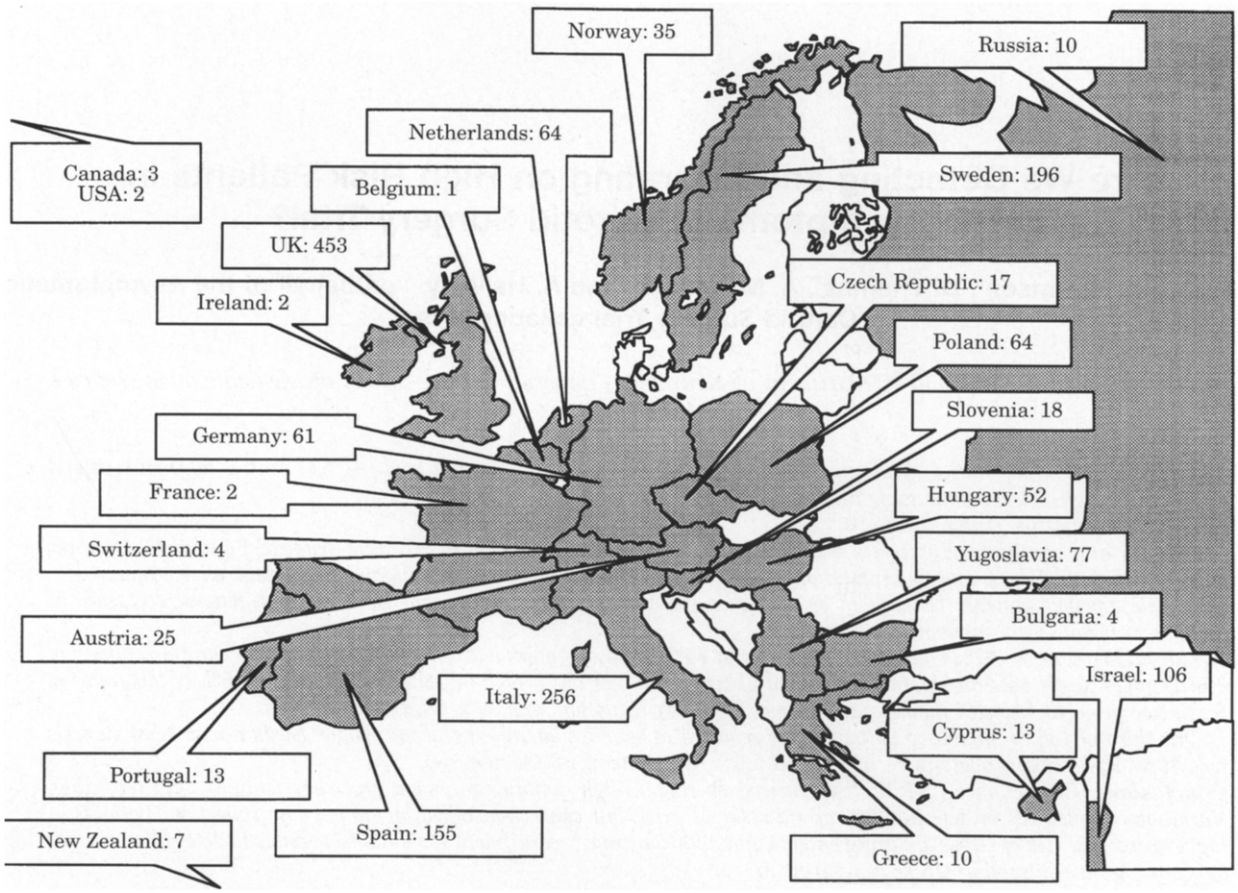

Fig. 1. Number of patients entered from each country collaborating in the ACST.

performance of carotid duplex, in order to ensure reproducible results in future clinical trials.

In ACST, patients may be perceived to be at higher risk of stroke because they have ipsilateral tight carotid stenosis, contralateral tight stenosis or occlusion or ispilateral echolucent plaque. The aim of this study is two-fold. First, to determine whether collaborating centres in the ACST are able to detect patients at higher perceived risk of stroke and, second, to determine whether collaborating centres in ACST are selecting patients at higher perceived risk of stroke.

Methods

Information on the current practice of vascular laboratories in the ACST was obtained by questionnaire. This included type and age of duplex equipment, number and experience of operators, documentation, methodology, stenosis evaluation and interpretation criteria. Information on patients' duplex risk factors suggesting higher stroke risk was obtained from the randomisation database.

Results

Questionnaires were sent to all 86 vascular laboratories participating in the trial. Seventy-one vascular laboratories responded (83%). Most centres had colour Doppler equipment (92%), the mean equipment age being 4.5 years (1–13 years). The largest single group of operators was vascular technologists (37%) followed by vascular surgeons (23%), radiologists (21%) and clinical physiologists (19%). Two-thirds of all operators (67%) had more than 3 years experience with carotid duplex. All centres had at least one person having more than 3 years experience. Most laboratories performed a large number of carotid scans per month. There were 31 centres (36%) performing over 100 scans per month, 30 centres (35%) performing between 50–100 scans per

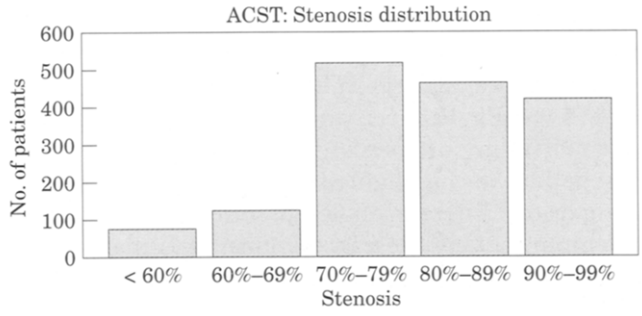

Fig. 2. Stenosis distribution. Graph shows number of patients against increasing severity of stenosis. Stenosis is expressed as percentage diameter stenosis with reference to the carotid bulb (i.e. ECST method).

month and 25 centres (29%) performing fewer than 50 scans per month.

Hard copy documentation was retained by 97% of labs. This was usually kept as video printout (66%) or on reporting forms (55%). All laboratories routinely used multiple sampling sites along the common and internal carotid artery. The use of a standard angle of insonation when determining peak systolic velocities was not consistent between centres in the study. The majority (67%) used an angle between 30 to 60 degrees, 27% were using 60 degrees consistently and six per cent were using an angle greater than 60 degrees.

The majority (64%) of respondents were measuring carotid stenosis by diameter reduction. There were 23% measuring carotid stenosis by area reduction and 13% were using both methods.

Using the randomisation database of 1650 patients, data on the risk factors evaluated by duplex was obtained. Median ipsilateral stenosis was 80% and the distribution of carotid stenosis is shown in Fig. 2. Fifty-six per cent of patients had ipsilateral stenosis greater or equal to 80%. Eight per cent had contralateral carotid occlusion, and in this group the median randomised stenosis was 78%. There were 138 patients (8.5%) with bilateral carotid stenosis of greater than 80%. Another 409 patients (25.2%) had already undergone contralateral carotid endarterectomy and in this group 66% had presented with contralateral symptomatic stenosis.

Information was available from 1024 patients (62%) on the presence of ipsilateral echolucent plaque. Of these, 510 patients (31%) had evidence of ipsilateral echolucent plaque on duplex. Combining these risk factors, 71% of patients had at least one or more of the following risk factors; stenosis $\geq 80\%$, bilateral stenosis $\geq 80\%$, contralateral occlusion or ipsilateral echolucent plaque.

Discussion

Since 1991, results of randomised trials have established widely accepted guidelines on patient selection for carotid endarterectomy. Many more CEAs are now performed because results reported in the NASCET, ECST and Asymptomatic Carotid Atherosclerosis Trial (ACAS) favoured surgical treatment.[7–9] There is now considerable interest in CEA for prophylactic management of asymptomatic carotid stenosis (ACS). At present about 40% of all CEAs performed in the U.S. and approximately 20% in Europe are done for ACS.[10] Results of ACAS, the only trial significantly endorsing operation, showed reduction in expected ipsilateral stroke rate from 2% per annum to 1% per annum in the surgical group.[9] Subgroup analysis to identify higher risk groups was not possible and the results leave many questions unanswered. If surgery is beneficial, the ongoing ACST is much needed to identify groups at higher stroke risk.

Patients in the ACST undergo initial carotid assessment and are followed up by duplex. CDU is now an accepted non-invasive method of assessing carotid disease, providing information on haemodynamically significant stenosis and plaque morphology. It has virtually no morbidity and is cheaper than angiography. Based on the outcome of ECST and NASCET, both angiographic and duplex criteria have been refined to give clinically relevant cut-off points to select patients for surgery. However the angiographic methods used in trials to measure carotid stenoses differ considerably.[4]

Will duplex become the new "gold standard"?

Sensitivity and specificity of carotid duplex has been measured against angiography in the past and some studies have shown good correlation.[11–13] There are ongoing studies measuring the correlation between duplex and magnetic resonance angiography, spiral CT and intravenous digital subtraction angiography.[14,15] Attempts are also being made to correlate carotid duplex with residual lumen diameter of en bloc carotid endarterectomy specimens and preoperative angiography.[5,16]

In the ACST, a duplex result for carotid stenosis is used instead of angiography for two reasons. First, the risk of stroke from angiography is high. This was demonstrated in ACAS where the stroke rate from angiography (1.2%) was almost as high as the stroke rate from surgery (1.8%). Second, while carotid duplex is the first common investigation, the use and

type of angiography differs between centres. An ongoing study within ACST on use of angiography has revealed increasingly selective use of both intra-arterial DSA (75%) and magnetic resonance angiography (5%) whilst a proportion were using intravenous DSA (20%). Only 41% of responding trialists were using carotid duplex and angiography regularly.[17] Many collaborating centres (55%) were selective users of angiography and some patients were referred for operation on the basis of carotid duplex alone. However, few centres (4%) had completely abandoned angiography.

The Ad Hoc Committee on Carotid Endarterectomy for the Society of Vascular Surgery has stated that CEA can now be performed on the basis of a duplex scan alone if, "the duplex scan is performed in a laboratory whose reliability has been well documented with prior correlation of their results and angiographic findings."[18] This may become difficult as fewer angiograms are performed in the future, and as duplex equipment becomes more sophisticated. Presently there is no European consensus on performance of carotid duplex or on an accepted method of laboratory validation.[3] From previous studies, many CEAs are now performed on the basis of duplex alone.[19]

The ACST is collecting information on the practice of carotid duplex throughout Europe. This is a unique opportunity to identify areas of common practice as well as areas that require standardisation. The present study demonstrates a high standard of operator experience and equipment in participating centres of the ACST. Almost all centres now have colour Doppler capability unlike ACAS in which centres sometimes used continuous wave Doppler. All ACST centres have an experienced sonographer of at least 3 years experience, and 61 centres (71%) performed more than 50 carotid scans per month. Two aspects of CDU examination differed widely. These were Doppler angle of insonation and reporting in either diameter or area reduction.

Doppler angle of insonation

Doppler measurements are taken at an angle of insonation (θ) between the direction of the ultrasound beam and the axis of the visualised artery. The velocity of blood flow is then obtained using the Doppler equation as

$$V = \frac{C \times f}{2 F \cos \theta}$$

where V = blood velocity, C = speed of ultrasound in tissue, f = Doppler frequency measured by the ultrasound device, F = transmitted ultrasound frequency and θ = angle between artery axis and ultrasound beam. The importance of using a standard angle of insonation was highlighted by Hoskins *et al.* in a study comparing different angles of insonation in a flow phantom model.[20] Results demonstrated that varying angle of insonation produced different velocities from the Doppler equation, leading to different grades of stenosis being reported.

Early duplex criteria produced by the University of Washington team in 1981 was validated using a standard angle of insonation at 60 degrees.[21,22] The use of a standard angle of insonation was advocated by the authors to obtain reproducible results between operators and centres. The angle of insonation at 60 degrees was chosen because it is anatomically convenient. If this could not be achieved then they recommended the angle used should be recorded for future scans.

After results of NASCET, ACAS and ECST were available, duplex criteria were retrospectively refined to provide precise cut-off points to identify patients who might now benefit from CEA.[23,24] The new criteria involved ratios, such as the ratio of peak systolic velocity in the internal carotid artery (ICA) to end diastolic velocity in the common carotid artery (CCA) to determine percentage stenosis. However these ratios also required the angle of insonation to be standardised when obtaining velocities in both the ICA and CCA.

In this study, many laboratories (67%) used a variable range of insonation between 30–60 degrees to obtain peak systolic and end diastolic velocities. These groups could be underestimating percentage stenosis when compared to that obtained at 60 degrees of insonation. Only 27% insonated at a consistent angle of 60 degrees. A small number (6%) used an angle between 60–80 degrees and might for the same reason be obtaining higher velocities in the same stenosis. Use of, or conversion to, a standard angle of insonation in this large international multicentre trial is important to accurately identify severity of carotid stenosis and also for follow-up. If patients were followed up over a mean period of 5 years, each patient would have then had six carotid scans. The first prior to randomisation, the second scan 4 months after and then annually. These scans should preferably be performed with the same angle of insonation.

Virtually all centres have conscientiously kept hard copy documentation on video printout or reporting form. The Doppler waveform showing peak systolic and end diastolic velocities can be obtained retrospectively and prospectively recorded together with

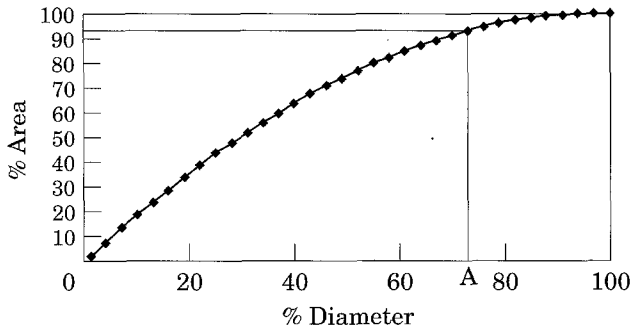

Fig. 3. Relationship between diameter and area reduction. Point A represents cut-off point for considering carotid endarterectomy in symptomatic patients according to ECST. Seventy per cent diameter reduction being equivalent to 92% area reduction.

the angle of insonation. Velocities can then be converted to a standard angle of 60 degrees using the Doppler equation. Data is now being collected as part of a separate study within the trial. ACST may in future be able to provide information correlating haemodynamically significant stenosis with stroke risk.

Area vs. diameter reduction

In this study one-quarter of laboratories reported carotid stenosis as area reduction. This is calculated by measuring the carotid lumen in transverse section at the point of maximum stenosis with digital callipers using colour Doppler and B-mode ultrasound. There are two potential areas for error, the effect of "colour spillage" making the lumen seem larger, and difficulty in selecting a transverse ultrasonic plane at the point of maximum stenosis. Three studies have validated this method against angiography and produced sensitivities of 85–97% and 87–89% when compared to angiography[25-27] Interobserver correlation was high ($r=0.83$).

To obtain comparable results between centres using velocity and B-mode criteria to measure stenosis, hard copy data is being obtained to determine if the velocity waveform has been obtained in conjunction with the B-mode measurement. It will then be possible to identify those reporting solely in area reduction on B-mode. The relationship between area and diameter reduction is shown Fig. 3.

Risk factors from duplex

From previous trials, the best established risk factor for stroke is degree of carotid stenosis. Other risk factors which may be studied by duplex include bilateral stenosis, contralateral occlusion and plaque echolucency. This study shows that most patients randomised in the ACST have a tight stenosis i.e. a diameter reduction greater than 70 per cent in relation to the carotid bulb. Patient populations in previous trials on ACS have had a similar proportion of patients with contralateral occlusion (8–12%) and history of contralateral CEA (20–27%).[9,10] Information on plaque echolucency is unique to the ACST. Echolucent plaque was found on duplex in 31% of patients. A combination of duplex risk factors may provide information to identify subgroups at higher risk of stroke, or if surgery is beneficial, to determine which patients may benefit most. In ACST, 71% of patients have one or more of the above duplex risk factors, and we hope that more patients will be randomised to strengthen the information obtained.

Conclusion

The ACST is an ongoing trial which is now larger than any other asymptomatic CEA trial. At its conclusion, it may be possible to derive important information from duplex assessment percentage stenosis, presence of contralateral occlusion, bilateral tight stenosis and ipsilateral plaque echolucency, to try to identify subgroups at higher risk of stroke.

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