Cost-effectiveness of diagnostic strategies prior to carotid endarterectomy


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study compared different strategies for the diagnosis of severe carotid stenosis. The strategies compared were:

Doppler ultrasound (DUS) alone;

initial DUS imaging followed by contrast-enhanced magnetic resonance angiography (CEMRA) when DUS demonstrates 50% or higher stenosis;

initial DUS imaging followed by digital subtraction angiography (DSA) when DUS demonstrates 50% or higher stenosis;

"combination DUS and CEMRA" strategy in which both tests are performed, and if the results regarding severe stenosis are not in agreement an additional DSA is performed; and

"CEMRA and selective DUS review" strategy. In this strategy patients are treated medically if CEMRA shows 70% or lower stenosis. If both tests show a severe stenosis, patients proceed to surgery. An additional DSA test is performed only if CEMRA is positive and DUS is negative.

Positive patients were treated either medically or surgically by carotid endarterectomy (CEA). Details of the medical treatment used were not provided.

Type of intervention
Diagnosis.

Economic study type
Cost-utility analysis.

Study population
As this was a modelling study, the target population comprised a cohort of recently symptomatic patients with a transient ischaemic attack (TIA) or who had experienced a non-disabling stroke during the last 6 months.

Setting
A setting was not explicitly specified at the outset. The economic study was carried out in the UK.

Dates to which data relate
The data on diagnostic accuracy were derived from a prospective study conducted between 2000 and 2003 that was published in 2004. Further effectiveness data were derived from studies published between 1999 and 2003. The cost data were derived from studies published between 1999 and 2004. All costs were reported from the financial year 2002/2003.
Source of effectiveness data
The effectiveness data were derived from completed studies. In addition, transition probabilities were assigned after an analysis of individual patient data up to 10.8 years after the conduct of the European Carotid Surgery Trial. Details were provided in a separate study (Rothwell et al. 2003, see ‘Other Publications of Related Interest’ below for bibliographic details).

Modelling
The authors constructed a decision analytic model, using DATA software (version 4.0; Treeage Software, Williamstown), to estimate the cost-effectiveness of the five diagnostic strategies. The authors also constructed a Markov model to evaluate the long-term costs and quality-adjusted life-years (QALYs) for three groups of patients, or patients with occlusions who were treated appropriately or inappropriately. The three patients groups were patients with mild stenosis (0 - 49%), patients with moderate stenosis (50 - 69%) and patients with severe stenosis (70 - 99%). The health states included in the model were healthy, non-disabling stroke, disabling stroke, fatal stroke and deaths from other causes. The model estimated that 58% were essentially healthy at presentation with a TIA and that 42% presented with a non-disabling stroke. The patients were assumed to remain stable in the same health state, or to advance to a more severe health state but not to a less severe state. Transition probabilities were assigned to each health state. The Markov model included the risk of having a non-disabling stroke, disabling stroke, or fatal stroke for each stenosis category for medical or surgical therapy, after 30 days or 1, 3, 5 and 10 years after treatment. Risks of death from all causes were stratified according to severity of stenosis, but were assumed to be the same for medical and surgical treatment after the first month, owing to the fact that CEA does not impose extra long-term risks of dying from causes other than strokes. The model also assumed that patients suffering DSA-related strokes do not undergo surgery subsequently and remain on medical therapy. The length of the cycle was 1 month. The time horizon of the model was 10.8 years.

Outcomes assessed in the review
The input parameters used in the decision analytic model were:
the sensitivity and specificity of the diagnostic tests and diagnostic strategies;
the diagnostic misclassification rate, defined as the total percentage of false positives and false negatives;
the discordant rate in the case of combined diagnostic strategies; and
the risk of having a non-disabling stroke, disabling stroke, or fatal stroke after 30 days or 1, 3, 5 and 10 after treatment.
A further parameter in the Markov model was the monthly risk death from all causes, stratified according to stenosis severity.

Study designs and other criteria for inclusion in the review
The authors included a single-centre prospective study involving 167 patients. A large prospective series and a meta-analysis were also included in the review. The European Carotid Surgery Trial was also used as a source of outcomes. No other inclusion or exclusion criteria were reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.
Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Overall, the authors used 6 primary studies to provide effectiveness data.

Methods of combining primary studies
A narrative method was used to combine the studies.

Investigation of differences between primary studies
No differences between the primary studies were investigated.

Results of the review
For DUS alone, the sensitivity was 88.1% (95% confidence interval, CI: 80.3 - 95.8), the specificity was 60.7% (95% CI: 52.0 - 69.3) and the diagnostic misclassification rate was 29.6% (95% CI: 23.1 - 36.1).

For CEMRA, the sensitivity was 93.0% (95% CI: 87.0 - 98.9), the specificity was 80.6% (95% CI: 73.8 - 87.4) and the diagnostic misclassification rate was 15.0% (95% CI: 10.1 - 19.9).

For DSA, the sensitivity and specificity were both 100% and the diagnostic misclassification rate was 0%.

For "combination of DUS and CEMRA", the sensitivity was 96.6% (95% CI: 88.3 - 99.0), the specificity was 79.8% (95% CI: 71.1 - 88.4) and the diagnostic misclassification rate was 10.1% (95% CI: 5.8 - 14.3). The discordant rate between the two tests was 24.9% (95% CI: 18.7 - 31.0).

For "CEMRA and selective DUS review", the sensitivity was 91.9% (95% CI: 88.5 - 95.4), the specificity was 86.0% (95% CI: 79.6 - 92.3) and the diagnostic misclassification rate was 11.6% (95% CI: 7.1 - 16.2). The discordant rate between the two tests was 6.9% (95% CI: 3.3 - 10.5).

In all patients imaged with DSA, a proportion of 0.85% incurred a procedure-related stroke. Complications were weighted as non-disabling stroke (45%), disabling stroke (33%) and fatal stroke (22%).

The risk of non-disabling, disabling and fatal stroke for each stenosis category and according to each treatment module are too numerous to report here. The reader is referred to the original study (Table 2).

The risk of any stroke for patients with carotid occlusions was 5% for the first 3 years, and 2% for the subsequent years. There was a 46% risk for non-disabling stroke, 34% for disabling stroke, and 20% for fatal stroke. In case of inappropriate surgical treatment of an occlusion, there was an excess risk of stroke of 4.2% during the first month.

Measure of benefits used in the economic analysis
The authors used QALYs as the measure of benefit in the economic analysis. The utility values were derived from a published systematic review using time trade-off scores (Post et al. 2001, see 'Other Publications of Related Interest' below for bibliographic details). The health benefits were discounted at a rate of 3%.

Direct costs
The health care costs included in the analysis comprised the cost of DSA, CEMRA and CEA, the cost of acute hospital admission for a disabling and non-disabling stroke, and the monthly cost of community health care for non-disabling and disabling stroke survivors. The unit costs were reported only for the diagnostic tests, while summary costs were used in all other cases. The cost of DUS in the five diagnostic strategies evaluated was identical and, therefore, was excluded from the analysis. The costs of long-term medical therapy were omitted as they were assumed to be analogous.
in patients treated either medically or surgically. The authors reported that inpatient care for strokes was assigned proportions of 61, 69 and 91% of total acute stroke costs for non-disabling, disabling and fatal strokes, respectively. The costs of CEMRA and DSA examinations were derived from a concurrent activity-based cost analysis in 20 patients. Monthly costs were calculated from the Office of Population Censuses and Surveys. All costs were appropriately inflated to reflect 2002/2003 prices, based on the medical component of the Consumer Price Index rates. As the time horizon of the model was more than 2 years, all the costs were appropriately discounted.

**Statistical analysis of costs**
The costs were reported as mean values and the authors provided the standard deviation and the 95% CI, which were all derived from published sources.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($). The authors reported that they had used appropriate exchange rates for currency conversions, but the exchange rates used were not reported.

**Sensitivity analysis**
A one-way sensitivity analysis was carried out on critical parameters of the model to assess the robustness of the results to variability in the data. Such parameters included cost parameters, utilities, prevalence of severe stenosis in study population, risks of DSA and the discount rate. Ranges and 95% CIs were used in the sensitivity analysis. The discount rate (3% in base-case analysis) was varied from 0 to 6%.

**Estimated benefits used in the economic analysis**
The strategy "CEMRA and selective DUS review" resulted in 6.1590 QALYs over the 10-year period;

the CEMRA strategy resulted in 6.1585 QALYs;

the strategy "combination of DUS and CEMRA" yielded 6.1591 QALYs;

the DSA strategy yielded 6.1256 QALYs; and

the DUS alone strategy yielded 6.1572 QALYs.

**Cost results**
The total costs per patient were reported.

The "CEMRA and selective DUS review" yielded a total cost of $35,205 per patient;

the CEMRA strategy resulted in a total cost of $35,436 per patient;

the "combination DUS and CEMRA" strategy resulted in a total cost of $35,476 per patient; and

the total cost of the DSA strategy was $35,632 per patient; and

the total cost of the DUS alone strategy was $35,970 per patient.

**Synthesis of costs and benefits**
The costs and benefits were summarised in the form of an incremental cost-utility ratio (ICUR), by dividing the total costs by the number of QALYs saved.

The incremental analysis demonstrated that the CEMRA strategy, the DSA strategy and the DUS alone strategy were strictly dominated strategies. The "CEMRA and selective DUS review" strategy was the most cost-effective, yielding a cost of $5,716 per QALY. The "combination DUS and CEMRA" strategy was slightly more effective, but also more expensive than the "CEMRA and selective DUS review" strategy, resulting in an ICUR in excess of $4 million per QALY saved.

The one-way sensitivity analysis demonstrated the robustness of the results to variability in the input parameters.

In general, the probabilistic sensitivity analysis confirmed the robustness of the results of the base-case analysis. When choosing a threshold of $50,000/QALY saved, the probability that "CEMRA and selective DUS review" remained most cost-effective was 39.2% compared with 26.5% for the "combination DUS and CEMRA" strategy and 24.5% for CEMRA. The probability that "DUS alone" would become the most cost-effective strategy was only 8.7%, needing a specificity of DUS of 75% or higher.

Authors’ conclusions
The analysis demonstrated that the contrast-enhanced magnetic resonance angiography and confirmatory digital subtraction angiography ("CEMRA and selective DUS review") diagnostic strategy is the optimal strategy for screening recently symptomatic patients and detecting severe carotid stenosis.

CRD COMMENTARY - Selection of comparators
The choice of the comparators was explicitly justified. The DSA diagnostic technique is considered to be the 'gold' standard. However, the authors did not discuss the existence of newer and more advanced treatment options (e.g. aggressive lipid lowering therapy, folate supplements or targeted blood pressure reduction, or carotid angioplasty and stenting). Therefore, the analysis can be characterised as partial. You should decide if the technologies compared in the study represent widely used technologies in your own setting.

Validity of estimate of measure of effectiveness
It appears that the authors have not carried out a systematic review. Although this is common practice with models, it does not ensure that the best data available are used in the model. The authors did not fully describe their methodology, particularly the inclusion criteria and selection process. It appears that the available data have been used selectively. The parameters were not derived from a synthesis of the primary studies, and the authors based half of their estimates on the results from a single trial. The authors did not consider the impact of differences between the primary studies when estimating effectiveness. The estimates were investigated using sensitivity analysis, and the authors justified the ranges selected based on the literature.

Validity of estimate of measure of benefit
The measure of benefit was the QALYs, which were obtained from the decision analysis model. The estimation of utility weights was taken from a published systematic review and was based on the time trade-off approach. The authors explored a range of utility values in the sensitivity analysis. The benefits were appropriately discounted.

Validity of estimate of costs
The analysis of the costs was performed from the perspective of the health care provider. Although it appears that all the relevant categories of costs have been included in the analysis, some individual costs were omitted from the analysis, although their omission is unlikely to have affected the authors' conclusions. The costs and the quantities were not reported separately, which would not enable the analysis to be easily reworked for other settings. The costs were derived from published sources, and a sensitivity analysis was conducted to assess the robustness of the estimates used. The ranges used appear to have been appropriate. Discounting was appropriately conducted and prices from different

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years were appropriately inflated, although the exchange rates used for currency conversions were not reported. The price year was reported, which will aid any future reflation exercises.

Other issues
The authors compared their findings with those from other studies and found them generally to be in agreement. Any differences were adequately justified. The issue of generalisability of the results to other settings was not directly addressed. The authors only draw attention to the fact that MRA in their setting was performed by experienced personnel and that the expertise of personnel in different settings should be subjected to quality control. The authors do not appear to have presented their results selectively. The study enrolled recently symptomatic patients who were screened for severe stenosis and this was reflected in the authors' conclusions.

The authors reported a number of limitations to their study. First, the analysis was restricted to the detection of severe stenosis only, and was not expanded to moderate stenosis cases which might also benefit from CEA. The model was also restricted only to patients who were eligible for magnetic resonance imaging. Second, the authors did not perform a complex sensitivity analysis to analyse variations in monthly risk probabilities of stroke and deaths. Third, the patients were assumed to have had appropriate medical treatment if the initial DUS suggested 50% or lower stenosis; there might have been an element of verification bias because it would be unethical for such patients to be subjected to the risks of confirmatory DSA. Finally, it could be argued that the authors used underestimates of the specificity of DUS, mainly due to controversy lying in the literature.

Implications of the study
Although the authors did not make specific recommendations for changes in policy or practice, they suggested that further research should focus on the improvement of the quality (highest resolution) of CEMRA. This may also result in greater cost-effectiveness of the technique.

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Other publications of related interest


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