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Surveillance report 2017 – Stroke and transient ischaemic attack in over 16s: diagnosis and initial management (2008) NICE guideline CG68

Surveillance report

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Contents

Surveillance decision

We will plan an update of the guideline on diagnosis and initial management of stroke and transient ischaemic attack (TIA). The update will focus on:

- referral for specialist assessment and subsequent imaging in people with suspected transient ischaemic attack
- use of pharmacological or mechanical methods for clearing blood clots
- early antihypertensive treatment in haemorrhagic stroke
- decompressive hemicraniectomy in people older than 60 years.

We will also amend the guideline to take account of updates to technology appraisals since it was published.

Reason for the decision

We found 349 new studies through surveillance of this guideline. New evidence that could affect recommendations was identified. Topic experts, including those who helped to develop the guideline, advised us about whether the following sections of the guideline should be updated:

Rapid recognition of symptoms and diagnosis

- How accurately do scoring systems predict which patients with suspected TIA need to be referred urgently for specialist assessment?

Topic experts advised that the current recommendations on using the ABCD² score to triage people with suspected TIA are no longer appropriate. At the time of developing the guideline, stroke service capacity was more limited than it is now and was an important consideration. Topic experts thought that stroke services have now developed sufficiently that assessing people with suspected TIA within 24 hours is achievable. Additionally, the ABCD² score does not help to decide who to refer for specialist assessment.

The topic experts were concerned about service capacity due to inappropriate referrals to the stroke clinic. However, this issue was thought to need to be addressed by local networks rather than the guideline.

Decision: This review question should be updated.

- After TIA, which modality (MRI or CT) should be used?

The NICE guideline on diagnosis and initial management of stroke and TIA and a Health Technology Assessment (Wardlaw et al. 2014) advise against routine imaging and recognise that specialist assessment is necessary to make decisions about imaging. However, topic experts indicated that imaging was performed routinely in some services, and sometimes involved both CT and MRI. This suggests that current recommendations are not being implemented appropriately.

The topic experts thought that routine CT imaging could waste resources and expose people to unnecessary radiation. Topic experts thought that current recommendations for specialist assessment with subsequent imaging only in people whose vascular territory or pathology is uncertain generally remained relevant. However, there may be a need to review the appropriate type of imaging and sequences to use.

Decision: This review question should be updated.

- In patients with a suspected minor stroke/TIA, does early versus late expert assessment reduce mortality or morbidity?

The topic experts thought that reviewing the use of the ABCD^2 score would have implications on the recommendations resulting from this review question because late assessment would no longer be necessary.

The topic experts also agreed that it was important to address early aspirin use. They thought that the conclusion of Rothwell et al. (2016) about self-administering aspirin had potential health implications if haemorrhage was the cause of stroke. In TIA and minor stroke, the topic experts thought that consideration should be given to who should give the initial advice for people to take aspirin: initial telephone triage services (NHS 111), paramedics, or the first treating physician.

Topic experts thought that the guideline should also consider the risks of people with continuing symptoms taking aspirin without full medical assessment.

Decision: This review question should be updated and address early aspirin use.

Pharmacological treatments for people with acute stroke

- Thrombolysis in people with acute ischaemic stroke.

Topic experts indicated that off-label uses of alteplase, particularly around its use in older patients should be addressed in the guideline.

The use of thrombectomy was also thought to need coverage in the guideline. Although these interventions are separate there is some overlap of populations: some people can have both treatments, some can have alteplase only, and some can have thrombectomy only.

Guidance on identifying patients who would benefit from thrombectomy and transporting patients to a centre that can perform thrombectomy was thought to be needed.

Decision: This review question should be updated to address off-label uses of thrombolysis and the place of mechanical thrombectomy in the care pathway.

Maintenance or restoration of homeostasis

- What is the safety and efficacy of measures to manipulate blood pressure versus treatment as usual in patients with acute stroke?

Evidence consistently shows no benefit of blood pressure lowering in ischaemic stroke so the topic experts thought no update was necessary for antihypertensives in ischaemic stroke. Current recommendations to lower blood pressure to enable alteplase administration or in hypertensive emergencies remain sufficient.

However, the topic experts indicated a need to assess blood pressure lowering in haemorrhagic stroke.

Decision: This review question should be updated.

Surgery for people with acute stroke

- Which patients should be referred for decompressive hemicraniectomy?

The topic experts agreed that this section needs to be updated. Clinicians may not want to do hemicraniectomy in patients older than 60 years because of poor functional outcome, but the topic experts thought that this approach would be paternalistic, and should not affect patients' choice.

Decision: This review question should be updated.

Other clinical areas

We also found new evidence that was not thought to have an effect on current recommendations. This evidence related to non-pharmacological treatments and interventions to prevent venous thromboembolism in people with acute stroke.

For any new evidence relating to published or ongoing NICE technology appraisals, the guideline surveillance review deferred to the technology appraisal decision.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all the new evidence and views of topic experts, we decided that a partial update is necessary for this guideline.

See how we made the decision for further information.

Commentary on selected new evidence

With advice from topic experts we selected 2 studies for further commentary.

Early mobilisation and optimum positioning of people with acute stroke – very early mobilisation

We selected the AVERT trial for a full commentary because it is a large trial that included sites in the UK and topic experts indicated that this study is of clinical interest.

What the guideline recommends

The NICE guideline on diagnosis and initial management of stroke and transient ischaemic attack (TIA) recommends that people with acute stroke should be mobilised as soon as possible (when their clinical condition permits) as part of an active management programme in a specialist stroke unit. Additionally, people with acute stroke should be helped to sit up as soon as possible (when their clinical condition permits).

Methods

The AVERT Trial Collaboration Group (2015) conducted a randomised controlled trial of very early mobilisation compared with usual care over 14 days. Very early mobilisation had 3 elements: starting within 24 hours of stroke onset; focus on out of bed activities such as standing, sitting and walking; and should have led to 3 more sessions out of bed than the usual care group. The 'dose' of out-of-bed activity was determined by a detailed protocol.

Eligible patients (n=2,104) were aged 18 years or older, had confirmed ischaemic or haemorrhagic stroke, and were admitted to a stroke unit within 24 hours of stroke onset. Treatment with recombinant tissue plasminogen activator was allowed. People who were too unwell to participate were excluded, for example, if they were admitted to the intensive care unit or had clinically significant disability before the stroke.

The primary outcome was a favourable outcome at 3 months (Rankin Scale score of 0–2). Secondary outcomes included change in Rankin Scale, walking unassisted for 50 metres, deaths and adverse events. Staff were trained to conceal the mobilisation protocol and group allocation so that patients remained unaware of their treatment allocation. Outcome assessors and data analysts were blind to treatment allocation.

Results

Overall, people in the very early mobilisation group were mobilised significantly earlier (median 18.5 hours after stroke, interquartile range 12.8 to 22.3 hours) than the usual care group (median 22.4 hours, interquartile range 16.5 to 29.3 hours, p<0.0001). The very early mobilisation group also had more mobilisation sessions (6.5 versus 3, p<0.0001), longer mobilisation (31 minutes versus 10 minutes per day, p<0.0001) and more mobilisation overall (201.5 minutes versus 70 minutes, p<0.0001). Outcomes were measured until discharge, or for 14 days, whichever came first. There was a significantly lower rate of favourable outcomes at 3 COmonths after stroke in the very early mobilisation group compared with usual care (adjusted odds ratio [OR] 0.73, 95% confidence interval [CI] 0.59 to 0.90, p<0.004). Adjusted analyses took into account baseline stroke severity and age. The unadjusted analysis was not significant but remained in the direction of very early mobilisation having worse outcomes.

There were no significant differences in the secondary outcomes of changes in Rankin Scale (adjusted OR 0.94, 95% [CI] 0.85 to 1.03) or walking unassisted for 50 metres (adjusted OR 1.04, 95% CI 0.94 to 1.15). Deaths (OR 1.34, 95% CI 0.93 to 1.93), non-fatal adverse events (incidence rate ratio [IRR] 0.88, 95% CI 0.72 to 1.07), serious immobility adverse events (IRR 0.92, 95% CI 0.62 to 1.35) and serious neurological adverse events (IRR 1.26, 95% CI 0.95 to 1.66) did not differ significantly between groups.

The authors noted that outcomes, particularly death, may have been worse in people with haemorrhagic stroke; however, a comparison of deaths was not reported and differences in favourable outcome between ischaemic stroke and haemorrhagic stroke were not significant (p>0.05).

A regression analysis of the AVERT trial assessed the relationship between the dose of mobilisation and response. This repeated the major primary and secondary analyses with dose characteristics (time from stroke onset to first out-of-bed mobilisation, frequency, daily amount and total amount) as independent variables. When time from stroke onset to first out-of-bed mobilisation and frequency were constant, each additional 5 minutes of out-of-bed activity per day reduced the odds of a favourable outcome. When time from stroke onset to first out-of-bed mobilisation and daily amount were kept constant, increasing the frequency of sessions improved the odds of favorable outcome by 13% (95% CI 9% to 18%, p=0.001) and improved the odds of walking 50 metres unassisted by 66% (95% CI 53% to 80%, p=0.001). People were more likely to have a favourable outcome if they were aged 76.3 years or younger, or had less severe stroke. A longer time to first mobilisation may be associated with less favourable outcome or likelihood of walking

50 metres unassisted, but the effect sizes were small (no more than 1%) and the statistical significance varied across analyses.

Strengths and limitations

Strengths

The study was a large trial of a complex intervention, so the use of a detailed protocol should have ensured that the intervention was applied consistently across sites. It included study sites in the UK, thus is directly relevant to stroke care in the UK. Additionally, reporting of mobilisation levels in both groups provides useful information that may have been missed if only outcome data were reported.

Limitations

Participating sites had discretion on their usual care policies, so there may have been clinically relevant differences in usual care between sites. Because both groups had fairly high levels of mobilisation, it is difficult to distinguish what factors contributed to the poorer outcomes in the intervention group. For example, they may have been mobilised too soon, or for too long, or a specific activity may be associated with poorer outcomes (sitting may have less effect on the patient than walking).

Impact on guideline

In this study, the usual care group had a better functional outcome, but they also had substantial levels of mobilisation early after stroke. Therefore, mobilisation guided by the patient's wishes or clinical condition may be a better strategy than enforcing a strict mobilisation protocol. Further analysis suggested that increased frequency of mobilisation may be beneficial, but increased duration of mobilisation may be harmful. There is no clear evidence that earlier time to first mobilisation is harmful. This finding is consistent with the recommendations in the guideline to help people to sit up and undertake mobilisation when their clinical condition permits.

Imaging in people who have had a suspected TIA or non-disabling stroke – cost-effectiveness of MRI

We selected a Health Technology Assessment by Wardlaw et al. (2014) for a full commentary because it was a large, UK-funded review with potential impact on NICE's guideline on diagnosis and initial management of stroke and TIA.

What the guideline recommends

The guideline recommends that people who have had a suspected TIA (that is, they have no neurological symptoms at the time of assessment [within 24 hours]) should be assessed as soon as possible for their risk of subsequent stroke using a validated scoring system, such as ABCD².

People with TIA or minor stroke assessed to be at high risk of stroke should have specialist assessment within 24 hours of onset of symptoms. People at lower risk of stroke should be assessed as soon as possible, but definitely undergo a specialist assessment within 1 week of onset of symptoms. All people with suspected TIA or confirmed ischaemic stroke should have aspirin 300 mg daily started immediately, and measures for secondary prevention as soon as the diagnosis is confirmed.

Additionally, people who have had a suspected TIA who need brain imaging (that is, those in whom vascular territory or pathology is uncertain) should undergo diffusion-weighted MRI except where contraindicated, in which case CT scanning should be used.

Examples where brain imaging is helpful in the management of TIA are: people being considered for carotid endarterectomy in whom it is uncertain whether the stroke is in the anterior or posterior circulation; people with TIA where haemorrhage needs to be excluded, for example long duration of symptoms or people on anticoagulants; if an alternative diagnosis (for example migraine, epilepsy or tumour) is being considered.

All people with suspected non-disabling stroke or TIA who after specialist assessment are considered as candidates for carotid endarterectomy should have carotid imaging within 1 week of onset of symptoms. People who present more than 1 week after their last symptom of TIA has resolved should be managed using the lower-risk pathway.

People with stable neurological symptoms from acute non-disabling stroke or TIA who have symptomatic carotid stenosis of 50–99% according to the NASCET (North American Symptomatic Carotid Endarterectomy Trial) criteria, or 70–99% according to the ECST (European Carotid Surgery Trialists' Collaborative Group) criteria, should:

- be assessed and referred for carotid endarterectomy within 1 week of onset of stroke or TIA symptoms
- undergo surgery within a maximum of 2 weeks of onset of stroke or TIA symptoms

- receive best medical treatment (control of blood pressure, antiplatelet agents, cholesterol lowering through diet and drugs, lifestyle advice).

Methods

Wardlaw et al. (2014) conducted a Health Technology Assessment (HTA) of the cost-effectiveness of MRI, including diffusion-weighted MRI in people with TIA and minor stroke. Systematic reviews, with meta-analysis if the data allowed, were conducted to assess:

- the overall risk of stroke after TIA
- usefulness of the ABCD^2 score to predict risk of stroke after TIA
- diagnosis of TIA, minor stroke and mimics
- assessment of diffusion-weighted imaging and adding imaging results to ABCD^2 scores.

Clinical and imaging services for stroke prevention after TIA were assessed by surveying stroke specialists and radiographers. Models for predicting stroke after TIA were evaluated by review and meta-analysis of citation search results and individual patient data from a UK cohort. Finally, cost-effectiveness of imaging in treating and preventing stroke was investigated by systematic review of published data and a new cost-effectiveness model.

The primary outcome measure of the HTA was the incremental cost-effectiveness of MRI compared with CT for the whole population. Secondary outcomes measures included the number of strokes prevented per strategy; costs; and quality-adjusted life years (QALYs).

Overall stroke risk after TIA

A systematic review and meta-analysis was conducted to estimate the overall risk of stroke after a person has a TIA.

Results

Systematic review of 53 studies showed pooled stroke risks after TIA of:

- 5.2% (95% CI 3.2% to 6.9%) within 7 days (28 studies, n=12,332)
- 6.7% (95% CI 5.2% to 8.7%) within 90 days (34 studies, n=19,769)
- 11.3% (95% CI 7.5% to 16.6%) after 90 days (9 studies, n=8,699).

Strengths and limitations

Strengths

The systematic review was well reported and included many studies that were not available when the guideline was developed.

Limitations

The evidence base consisted of multiple reports from the same population. Although the authors took steps to reduce double counting of people, it cannot be entirely ruled out. Around half of studies did not clearly report the time from TIA to assessment and diagnosis. The studies had highly significant heterogeneity, and although random-effects meta-analyses were conducted, possible causes of heterogeneity were not fully explored. For example, the time from TIA to assessment and diagnosis varied across studies. Additionally, the effect of the age of included studies was not investigated. The authors discussed the possibility that newer studies would show lower risk of recurrent stroke, but concluded that other factors were likely to cause the observed differences between trials. However, no sub-analysis by date of publication was done and the forest plots did not order the studies by date, so it is difficult to determine whether this conclusion was based on the evidence.

A citation of previous findings of a 4-week stroke risk of 20% was incorrectly attributed to the guideline. This figure was instead from The Department of Health's Implementing the National Stroke Strategy – an imaging guide.

Impact on guideline

The guideline reported stroke risks stratified by ABCD² score only; however, data used in the cost-effectiveness analysis showed a 7-day stroke risk of 5.5% and a 90-day stroke risk of 9.2%. The 7-day stroke risk was similar to that seen in the HTA (5.2%). The 90-day stroke risk after TIA may be lower (at 6.7%) than was estimated from the evidence available during development of the guideline (9.2%). No recommendations are directly affected by the new evidence.

ABCD² score and risk of stroke after TIA

A systematic review and meta-analysis was conducted to assess whether the ABCD² score usefully discriminates between people who are are high or low risk of subsequent stroke.

Results

Overall, about two-thirds of people with TIA had an ABCD² score of 4 or more and a approximately a third had an ABCD² less than 4. Systematic review of 26 studies (n=12,586) showed the following pooled stroke risks:

- At 7 days (16 studies, n=6,920)
  - 2.4% (95% CI 1.3% to 4.2%) for people with ABCD² score less than 4
  - 7.5% (95% CI 4.7% to 11.7%) for people with ABCD² score of 4 or more.
- At 90 days (19 studies, n=9,849)
  - 2.1% (95% CI 1.3% to 3.3%) for people with ABCD² score less than 4
  - 7.1% (95% CI 4.6% to 10.7%) for people with ABCD² score of 4 or more.
- At more than 90 days (3 studies, n=1,073)
  - 5.2% (95% CI 1.0% to 28.9%) for people with ABCD² score less than 4
  - 17.2% (95% CI 8.8% to 30.9%) for people with ABCD² score of 4 or more.

Sensitivity analysis addressed only studies that reported outcomes at both 7 days and 90 days and excluded 1 study that reported inconsistent results (lower subsequent stroke at 90 days than at 7 days). The pooled stroke risks were:

- At 7 days (9 studies, n=4,291)
  - 1.6% (95% CI 1.0% to 3.4%) for people with ABCD² score less than 4
  - 4.7% (95% CI 2.4% to 8.7%) for people with ABCD² score of 4 or more.
- At 90 days (9 studies, n=4,291)
  - 2.7% (95% CI 1.5% to 4.7%) for people with ABCD² score less than 4
  - 8.2% (95% CI 4.7% to 14.0%) for people with ABCD² score of 4 or more.

A narrative summary of associations between ABCD² score and carotid stenosis and other factors linked to high risk of stroke indicated that ABCD² did not predict presence or absence of carotid stenosis. Another narrative summary concluded that relying on the ABCD² score in the general

population (including stroke mimics) may miss true TIAs or minor strokes while a large proportion of stroke mimics would be assessed urgently.

Strengths and limitations

Strengths

Most of the studies included only cases confirmed by a neurologist or stroke specialist, although some studies relied on diagnosis by an emergency physician.

Limitations

Limitations of the evidence base included the time from TIA to assessment, which varied greatly from within 24 hours to 7 days, but many studies did not report this information clearly. About half of the included studies were retrospective. Studies had considerable heterogeneity and analyses had wide confidence intervals.

Conclusions about proportion of likely stroke mimics and an absence of association with carotid stenosis were based on narrative summaries of evidence. That evidence had not been collected systematically to answer questions about those conditions, but to answer the question of stratifying stroke risk by ABCD² score.

Impact on guideline

No pooled data on stroke risk by ABCD² score were available during development of the guideline; however a large study that informed the guideline showed broadly similar results to those found in the HTA. At 7 days, the risk of stroke was 1.2% for ABCD² score of less than 4; 5.9% for ABCD² score of 4 or 5; and 11.7% for ABCD² score of more than 5. At 90 days the risk of stroke was 3.1% for ABCD² score of less than 4; 9.8% for ABCD² score of 4 or 5; and 17.8% for ABCD² score of more than 5.

The HTA concluded: 'Current clinical guidelines recommend urgent treatment only for patients with high ABCD² scores, whereas patients with low scores should be triaged for further clinical assessment within 1 week. This would risk missing patients with carotid stenosis requiring endarterectomy.'

However, although the guideline uses the ABCD² score to triage the urgency of specialist assessment, all patients with suspected TIA who are considered to be candidates for carotid endarterectomy should have carotid imaging within 1 week of symptom onset.

The findings of subsequent stroke risk suggest that the risk of stroke after TIA may be lower than estimated during guideline development. The recommendation to triage by ABCD² score was made with consideration that stroke services could be overwhelmed if urgent specialist assessment was recommended for all people with suspected TIA or minor stroke. New advice from topic experts indicates that stroke services may be more able to assess all patients urgently than at the time of guideline development.

Models for predicting stroke after TIA

Models for predicting stroke after TIA were evaluated by review and meta-analysis of citation search results and individual patient data from a UK cohort. This section of the HTA investigated whether any other methods of risk assessment could replace the ABCD² score.

Results

Assessment of other clinical prediction models identified 18 studies that used CT to predict subsequent stroke, and 10 studies that used carotid imaging. Having a lesion identified on CT was not significantly associated with subsequent stroke (hazard ratio [HR] 1.74, 95% CI 0.82 to 3.70; 3 studies, n=4,499). Carotid stenosis was significantly associated with subsequent stroke (HR 3.02, 95% CI 1.18 to 7.75).

Multivariate survival analysis of individual patient data from the Lothian Stroke Register (n=2,011) found significant associations between stroke and both having a lesion on CT and carotid stenosis in multiple models. However, none of the 4 models predicted stroke within 7 days. In this cohort, 3 people had a subsequent non-fatal stroke, and 3 people died within 7 days. The carotid and CT imaging results for these patients were not reported.

The authors noted that models were better at predicting being alive and well at 90 days and fatal or non-fatal disabling stroke at 2 years; however, no statistical data were reported for these outcomes. The best performing prediction model was noted to include clinical variables plus carotid and brain imaging and correctly predicted 47% of outcomes at 2 years.

Strengths and limitations

Strengths

The authors clearly described the citation searching process they used to find relevant articles. Exclusion of articles published before 1990 means the results should be applicable to modern

clinical practice. The authors tried to avoid double-counting of data reported in several publications.

Limitations

The citation search process may not have identified all relevant studies. Included studies varied in many ways, such as whether the population had possible or definite TIA or follow up for 7 days, 30 days, or 90 days. CT scans were done from within 24 hours to within 1 month of symptom onset.

Additionally, the authors noted that the Lothian Stroke Register dataset was collated in the 1990s and imaging technology may detect more lesions by scanning in thinner slices. However, this problem would also apply to the studies used in the meta-analysis.

Impact on guideline

The guideline recommends that all people with TIA or minor stroke who are candidates for carotid endarterectomy should have carotid imaging within 1 week of symptom onset and if surgery is appropriate, it should be performed within 2 weeks of symptom onset. In finding a link between carotid stenosis and subsequent stroke, the new evidence supports current recommendations. However, there is no strong evidence to suggest that the timing of treatment of carotid stenosis 'within 2 weeks' needs to change.

Diffusion-weighted MRI

Results

Of 47 studies (n=9,078), 18 were prospective cohort studies, 17 were retrospective cohort studies, and 12 did not clearly report this information. About a third of people with TIA had a visible ischaemic lesion on diffusion-weighted MRI (summary estimate 34.3%, 95% CI 30.5% to 38.4%). About two-thirds (69%) of people with minor stroke had a visible ischaemic lesion (4 studies, n=627) but statistical analysis was not reported for this result.

A narrative summary of adding ABCD^2 score to imaging suggested improved prediction of recurrent stroke. The authors noted that in clinical practice, the rate of negative imaging would be higher because the population would include stroke mimics; they also questioned the need for routine use of ABCD^2 score or MRI.

Strengths and limitations

Strengths

The authors attempted to find reasons for heterogeneity such as whether participants had TIA or minor stroke or time to imaging, but no clear relationship was found.

Limitations

The initial aim was to compare CT with MRI in TIA and minor stroke; however, no comparisons were available in the published literature. Included studies varied in many criteria, including time between onset of symptoms and undergoing diffusion-weighted MRI.

Impact on guideline

The guideline recommends diffusion-weighted MRI for some people with TIA or minor stroke, that is, those in whom vascular territory or pathology is uncertain. In the pathway of care, specialist assessment would already have excluded most stroke mimics. Additionally, the guideline notes: 'Not all patients with TIA need brain scanning. The selection of patients for urgent scanning is dependent on clinical features; it is important that brain scanning does not delay the institution of optimum secondary prevention or the detection and treatment of significant carotid stenosis.' The finding that diffusion-weighted MRI is not valuable in all patients with TIA supports the current recommendations.

Diagnosis of TIA, minor stroke and mimics

Results

Data from 16 studies (n=14,542), plus unpublished clinic data and an audit from a UK region were identified. About a third of people assessed for possible TIA had a non-cardiovascular diagnosis (summary estimate 35%, 95% CI 28% to 42%). Results were broadly similar in analysis by setting:

- hospital or emergency department summary estimate 32% (95% CI 10% to 66%)
- TIA clinic summary estimate 34% (95% CI 24% to 46%)
- population-based studies summary estimate 40% (95% CI 23% to 60%).

The most common non-cardiovascular diagnoses were migraine (14.4%) syncope (6.6%), seizure or epilepsy (5.0%), psychiatric disorders (4.4%) and vertigo (4.0%). Other less common diagnoses were

peripheral nerve disorders, postural hypotension, transient global amnesia, toxins such as drugs, metabolic causes such as hypoglycaemia, and brain tumour.

Risk of stroke within 90 days was 0% for non-cardiovascular causes and up to 5.2% for TIA. Further analysis was impossible because of the 0 events in the non-cardiovascular group. People with TIA had significantly higher risk of stroke, myocardial infarction or vascular death combined at 90 days than those with non-cardiovascular causes of TIA symptoms (OR 1.59, 95% CI 1.40 to 1.81; 4 studies).

Strengths and limitations

Strengths

The systematic review was conducted using appropriate methods (Meta-analysis Of Observational Studies in Epidemiology; MOOSE).

Limitations

Although the authors used random-effects meta-analyses to account for the high heterogeneity between studies, there were large differences in study design such as setting, inclusion criteria and type of clinician leading on diagnosis. Accurate diagnosis of TIA, minor stroke and stroke mimics requires specialist clinicians and facilities, so the variability in study designs may lead to results that are not fully representative of specialist assessment.

Impact on guideline

Although no recommendations were made about diagnosis of stroke mimics, when developing the guideline, the committee noted that 'good clinical assessment is essential to detect stroke mimics and to establish the vascular territory involved where possible'. Diagnosis of stroke mimics was considered to be part of specialist assessment and the new evidence does not indicate any change to this view.

Clinical and imaging services for stroke prevention after TIA

Clinical and imaging services for stroke prevention after TIA were assessed by surveying stroke specialists and radiographers.

Results

Overall the response rate was 45%, with 114 surveys completed by stroke services and 146 imaging facilities. Specialist stroke prevention services were reported to be available at 97% of hospitals – 99% of those ran at least once a week, 47% ran every weekday, and 31% ran 7 days a week. In 86% of services 1–5 new patients attended each time. Less than half of services (43%) indicated that they had capacity to see more patients.

Half of centres had a rate of final diagnosis of TIA or minor stroke of 41–60%. Most people had been started on secondary prevention such as aspirin by their GP before they attended the stroke clinic. In most centres (71%), diagnosis was made by, or with input from, a consultant (usually stroke specialists, neurologists, or geriatricians).

Most patients were seen at the stroke service within a week of referral (35% by the next day, 25% within 2 and 3 days, 21% within 3 and 7 days, and 6% within 1 and 4 weeks). Urgency of assessment was stratified by with $ABCD^2$ score in 13% of services.

Carotid or brain imaging often happened on the same day or the next day, but 7% of centres indicated that no brain imaging was done. Two-thirds of services had results of imaging delivered on the same day, but 71% of services received positive scanning results immediately. Responses from radiology services were generally consistent with those from stroke services.

MRI was available in 99% of services and diffusion-weighted MRI was available in 96% of services. CT was used routinely in 84% of services, and MRI was used routinely in 51% of centres. The frequency of requesting MRI after CT varied widely, but was most frequently reported to happen in about 10% of cases. The type of MRI sequences used differed across departments.

Carotid imaging was done with Doppler ultrasound in 95% of services. Carotid endarterectomy was done within 1 week of deciding on this treatment in 59% of centres and within 1 month in 37% of centres.

Strengths and limitations

Strengths

The surveys were designed by a multidisciplinary group that had expertise in neurology, neuroradiology, medical physics, methodology and health economics. The questionnaires were tested in a pilot study. Both surveys had a fairly high response rate of 45%.

Limitations

There is a risk of bias from possible differences between stroke services with high response rates and services with low or no response. Some respondents may have used clinic data to fill out the survey, others may have relied on memory, resulting in potential inaccuracies and recall bias.

Impact on guideline

The results of the surveys suggest that not all stroke services are currently following the pathway of care recommended in the guideline. In particular, there was little use of ABCD^2 score to stratify people at high and low risk of recurrent stroke. Additionally, a large proportion of people with suspected TIA or minor stroke have routine imaging with CT or MRI, which contrasts with the guideline, which recommends MRI only in a subset of people (those in whom vascular territory or pathology is uncertain).

Topic experts advised that sending patients for routine imaging before specialist assessment, thereby conducting scans that might not be needed is a poor use of resources, and routine use of CT may expose people to unnecessary raditation.

Cost-effectiveness of imaging in treating and preventing stroke

The cost-effectiveness of imaging in treating and preventing stroke was determined by systematic review of published data and a new cost-effectiveness model. Results from the other chapters of the HTA also informed the model.

Results

A systematic review of 4 existing cost-effectiveness analyses was conducted and used to inform the economic model. No previous studies compared the cost-effectiveness of MRI with the cost effectiveness of CT for TIA and minor stroke. Doppler ultrasound was reported to be the most effective and least costly method for imaging carotid stenosis in 2 studies.

The cost-effectiveness model was populated with assumptions based on data obtained in the authors systematic reviews reported above, as well as calculations and estimates from other published and unpublished data. Some assumptions were also informed by professional opinion.

The base-case scenario was immediate MRI plus carotid ultrasound compared with immediate CT plus carotid ultrasound for all people presenting to stroke services within a few hours of symptom onset. The population modelled was men and women aged 70 years over a 20-year period. The

base case indicated that immediate MRI would result in an increased cost of £77 and QALY loss of 0.0005 because of lower sensitivity of haemorrhagic stroke within a few hours of symptoms. Benefits of increased sensitivity of MRI over CT were negated because all people had secondary prevention and carotid ultrasound.

- The base case was then modelled for people presenting 7 days and 21 days after symptom onset. MRI became more cost-effective because of loss of sensitivity of CT to detect haemorrhage over time.
- Additional analysis repeated this strategy but included secondary prevention only in people with a lesion detected on MRI. CT plus ultrasound remained the most cost-effective option because of the risk of recurrent stroke in the 66% of people with TIA who have negative MRI findings.

Additional strategies modelled were:

- Delayed MRI and ultrasound for people scoring with ABCD² score lower than 4 (with immediate imaging in those scoring 4 or more) compared with immediate CT and ultrasound in people presenting within a few hours of symptom onset.
    - In this model, the incremental cost of MRI was £126 with a QALY loss of 0.0191, attributed to the increased risk of recurrent stroke in people with ABCD² score lower than 4 who have carotid stenosis but have not had diagnosis and surgery.
- Immediate carotid ultrasound for all people presenting within a few hours of symptom onset with delayed MRI for ABCD² score lower than 4 and immediate MRI for scores of 4 or more compared with immediate CT plus ultrasound.
    - Immediate CT plus ultrasound remained the most cost-effective option because people with ABCD² score lower than 4 who do not have carotid stenosis still have a small risk of recurrent stroke.
    - This strategy was also modelled for people presenting 7 days after symptom onset. MRI was associated with minor gain in QALYs but the incremental cost-effectiveness ratio was £159,325, which is higher than the usual threshold of £20,000 to £30,000.
- Immediate MRI plus carotid ultrasound compared with immediate MRI plus carotid magnetic resonance angiography compared with immediate CT plus carotid ultrasound compared with immediate CT plus carotid CT angiography.

  - Immediate CT plus ultrasound remained the most cost-effective strategy because angiography techniques are more expensive but are not more sensitive than ultrasound.

- Secondary prevention started in all people but MRI and ultrasound delayed for people with for ABCD² score lower than 4.

  - Immediate CT plus ultrasound remained the most cost-effective strategy.

Strengths and limitations

Strengths

The cost-effectiveness model was comprehensive and evaluated several different strategies from a UK perspective. Many of the assumptions that were used to populate the model were based on the best available data.

Limitations

The authors noted that there are gaps in the evidence base relating to the diagnostic performance of MRI and CT in TIA. Additionally, stroke risk may be affected by patients' use of anticoagulants or other treatments known to reduce risk of stroke, which could reduce the effectiveness of diagnosis and treatment of TIA.

Impact on guideline

The findings of the economic analysis that routine MRI is not cost-effective is consistent with recommendations in the guideline that MRI should be used only in a subset of people (those in whom vascular territory or pathology is uncertain). However, topic experts expressed concern that the economic model may not have fully accounted for the costs of missing a rare stroke mimic such as a brain tumour.

The finding that CT is a cost-effective strategy for routine imaging is inconsistent with current NICE guidance that decisions on imaging should be made after specialist assessement. Topic experts indicated that performing CT without specialist assessment may be an unnecessary use of resources and expose patients to radiation when they may not need CT.

Overall strengths and limitations

Strengths

Systematic reviews and meta-analyses were performed in line with Cochrane review methods, and if this was not possible, the alternative methods were well described. Additionally, appropriate tools were used to assess quality of included studies.

Although there were limitations in the evidence base, the HTA clearly described the limitations and how they were managed in analysis. Random-effects meta-analysis was used to account for heterogeneity if necessary.

Limitations

The authors noted that all meta-analyses had substantial heterogeneity that could not always be explained.

In several places, the HTA cited information from The Department of Health's Implementing the National Stroke Strategy – an imaging guide, and attributed the information to the NICE guideline. Although there are many similarities between the recommendations in these publications, there are also substantial differences. Additionally, some of the pathway of care indicated in the NICE guideline appears to have been misunderstood.

Overall impact on guideline

The authors of the HTA noted that the third of people with stroke mimics with an $ABCD^2$ score of 4 or more would 'go down the fast-track route and undergo' MRI. However, the pathway of care recommended in the guideline is fast access to specialist assessment, which uses clinical expertise to identify stroke mimics. Furthermore, no imaging is recommended routinely – only to resolve diagnostic uncertainty.

The HTA concluded that resources should focus on identifying underlying risk factors for stroke, identifying the small proportion of people presenting with TIA who have haemorrhage, and diagnosing mimics, all of with were deemed to need specialist assessment, which is consistent with the guideline. A further conclusion that routine MRI is not cost-effective is also consistent with the guideline, which does not recommend routine imaging in TIA or minor stroke.

The HTA differentiates between the 'fast-track' (specialist assessment within 24 hours) and the 'slow stream' (specialist assessment within 7 days). Therefore, treatment according to the guideline

should differ by only 6 days. Carotid imaging is not dependent on ABCD² score – all people should have this imaging within 7 days of symptoms.

The usefulness of the ABCD² score in stratifying risk of subsequent stroke may be questionable because two-thirds of people will be designated as high risk. However, the survey of stroke services reported in the HTA indicated that less than half of people are seen within 24 hours, but 94% of people are seen within a week. Topic experts indicated that stroke clinics that currently run a weekly TIA clinic should be able to spread those assessments throughout the week.

The evidence suggested that the ABCD² score should no longer be used to stratify the speed of specialist assessment. Additionally, establishing the most appropriate imaging strategy is necessary.

How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 8 years after the publication of the NICE guideline on diagnosis and initial management of stroke and transient ischaemic attack.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Previous surveillance update decisions for the guideline are on our website.

New evidence

We found 166 new studies in a search for randomised controlled trials and systematic reviews published between 29 January 2014 and 1 December 2015. We also considered 3 additional studies identified by members of the guideline committee who originally worked on this guideline.

Evidence from 180 studies identified in previous surveillance 3 years and 6 years after publication of the guideline was also considered.

From all sources, 349 studies were considered to be relevant to the guideline.

We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A for summaries of evidence and references for all new studies considered.

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline. This included a meeting with experts to discuss potential areas for update.

Views of stakeholders

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because this was an 8-year surveillance review, and the decision was to update, we did not consult on the decision.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

NICE Surveillance programme project team

Sarah Willett
Associate Director

Philip Alderson
Consultant Clinical Adviser

Emma McFarlane
Technical Adviser

Lynne Kincaid
Technical Analyst

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