

New national guideline for stroke management: where do we go from here?

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The last few years have seen major changes in the way in which stroke care is delivered in the UK. The first three editions of the *National clinical guideline for stroke*, prepared by the Intercollegiate Stroke Working Party, have had a major influence on these developments. Stroke has changed from a condition for which there was thought to be little or no treatment, to one where we have a number of evidence-based treatments that can make a dramatic difference to patients' outcomes and the risk of recurrence. Moreover, the field is continuing to advance. Stroke physicians have a strong track record of collaborating in multi-centre national and international studies. These trials have led to major new developments in the evidence underlying stroke care since the last *National clinical guideline for stroke* was published in 2008. The recent publication of the 4th edition of the *National clinical guideline for stroke* is therefore timely, and updates and expands on the previous guideline.¹ The guideline contains over 300 specific recommendations covering almost every aspect of stroke management. It would be impossible to be familiar with all of these, but in the new edition the Intercollegiate Stroke Working Party has helpfully identified 28 key recommendations that they felt, if followed, would greatly enhance stroke care in the UK. The new edition has also introduced an 'Evidence to Recommendations' section, outlining in more detail why a particular recommendation has or has not been made.

The new edition of the *National clinical guideline for stroke* must be one of the most comprehensive guidelines ever published. Well over a hundred people worked on preparing this guideline and sifted through a massive amount of published data, meeting regularly to establish the facts. The Intercollegiate Stroke Working Party reflects the multidisciplinary nature of stroke care and, perhaps unusually for guidelines, less than a third of the members of the working party were stroke physicians. The other members of the group represented general practice, radiology, rehabilitation medicine, therapists, nurses, paramedics and patient associations. It is therefore perhaps not surprising that there are more pages of recommendations on the organisation of stroke services and rehabilitation treatment than there are on acute care and prevention. This reflects an increasing emphasis on research in stroke rehabilitation, which is bound to lead to further recommendations for evidence-based therapy in the future. There are also important new recommendations concerning nursing care. For example, one of these is the incorporation of evidence from the CLOTS trial, which showed that the

graduated compression stockings do not prevent deep vein thrombosis in stroke patients.² These were widely used on stroke wards, and as the guideline emphasises, stopping treatment when it is no longer beneficial will save the NHS considerable resources that can be better spent elsewhere.

One of the main treatments that has driven the substantial changes in services delivering acute stroke care has been the evidence that intravenous thrombolysis with tissue plasminogen activator (alteplase) improves outcome in suitable patients. In the 2008 guideline, alteplase was only recommended in patients seen within three hours of symptom onset. The new guideline incorporates the results of the 3rd European Cooperative Acute Stroke Study (ECASS-3)³ and the 3rd International Stroke Trial (IST-3)⁴ (only published in May this year) into two new recommendations. Firstly, suitable patients under the age of 80 years seen between three and four-and-a-half hours after known stroke symptom onset should be considered for treatment with alteplase. Secondly, all patients seen between three and six hours of symptom onset should be considered for treatment with alteplase on an individual basis. This latter recommendation reflects some uncertainty generated by the results of IST-3, which hopefully will be resolved by further analysis of the data from the trial in the future.

Many of the changes in the document reflect new evidence, but some also reflect the expectations of clinicians and patients rather than firm evidence. One example of this is that in 2008 the recommendation for patients without indications for immediate brain scanning – eg those not suitable for thrombolysis – was a brain scan within 24 hours of admission. This has been changed in the new guideline to a recommendation that scanning should occur as soon as possible and at most within 12 hours of admission. Of course, this time scale is a compromise and many hyperacute units have a policy of scanning all patients on arrival to the hospital. There is no doubt that an immediate scan aids decision-making about management, even if the patient is not eligible for thrombolysis. There are also advantages to combining computed tomography (CT) or magnetic resonance imaging (MRI) scans with CT angiography or magnetic resonance angiography (MRA) on admission. For example, the immediate identification of an arterial occlusion responsible for an ischaemic stroke or an aneurysm responsible for cerebral haemorrhage is an important aid to appropriate management.

Another aspect of stroke care where there has been a big change in management in the last few years is the provision of carotid endarterectomy. Although the evidence has been available for some years that the benefits of carotid endarterectomy are greatest in patients with recent symptoms, it is only recently

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that attention has been paid to the importance of investigating transient ischaemic attacks (TIAs) and minor strokes as soon as possible, and referring for carotid endarterectomy when required. The new guideline rightly recommends that any patient with a carotid territory TIA or stroke, suitable for carotid endarterectomy, should have carotid imaging performed urgently to estimate the degree of stenosis and, if this identifies a relevant stenosis, a second non-invasive imaging investigation should also be done urgently to confirm the degree of stenosis. The guideline then recommends that, in suitable patients, carotid endarterectomy should be performed as soon as possible and within one week of the onset of symptoms. This timescale is not strictly evidence-based, but reflects the increasing emphasis on treating stroke as an emergency. There is certainly good evidence that some patients will have had a recurrent stroke while waiting for surgery, but there is also good evidence that surgery has significantly higher risk when performed within 48 hours of onset of symptoms. The ideal time to perform surgery appears to be 3–14 days after the onset of symptoms.⁵ Some of the recommendations are inevitably based on research done over 20 years ago, which may well be out of date. For example, the guideline recommends that the final decisions regarding carotid endarterectomy should be supported by risk tables or the web-based risk calculator available from the Oxford University Stroke Prevention Research Unit. The problem with these risk tables is that they are based on the risk of stroke in patients with carotid stenosis recorded over 20 years ago, before the introduction of statins, newer antiplatelet agents or better treatment of hypertension. An ongoing trial, the 2nd European Carotid Surgery Trial (ECST2), is currently testing the accuracy of the risk predictor in the current context of optimised medical treatment (www.ecst2.com). The trial evidence concerning the treatment of asymptomatic stenosis is also out of date, and the guideline appropriately recommends that surgery or angioplasty/stenting should not routinely be performed unless it is carried out as part of a randomised trial. There are two such trials currently recruiting patients with asymptomatic stenosis in the UK: ECST2 and the 2nd Asymptomatic Carotid Surgery Trial.

Where do we go from here?

Implementing guidelines is always a challenge. The new guideline is thicker than ever before and it is doubtful if anybody, other than the editors of the guideline, will ever read it cover-to-cover. The guideline addresses several audiences, including commissioners involved in purchasing services for people with stroke, clinical managers, clinical staff, patients and their carers. It is likely to be mostly used by clinicians trying to develop their own local protocols for stroke care. The guideline provides a very useful reference and source to back up service development and business cases for local changes. Some clinicians might be concerned that the guideline negates an individual patient approach or that the recommendations will be overzealously applied for fear that the guideline will be used to bolster an

unjustified medicolegal case. However, the preface emphasises that the recommendations in the guideline are only likely to be applicable to around 80% of clinical situations, 80% of the time. This means that about one-third of clinical decisions are not covered by the guideline, leaving plenty of scope for individual decision-making.

The most important agency in implementing the guidelines is likely to come from commissioners. The National Stroke Strategy, published in 2007,⁶ sparked a revolution in the way in which stroke services have developed, particularly in the delivery of thrombolysis and high quality physiological monitoring to patients with acute stroke in line with the *National clinical guideline for stroke*. The most dramatic response to implementing the National Stroke Strategy has taken place in London, where successive National Sentinel Audits, also organised by the Intercollegiate Stroke Working Party, showed a huge variation in the quality of care and provision of stroke service at different hospitals – ranging from hospitals at the top of the league table to those at the bottom in terms of delivering treatment consistent with the guideline. Part of the problem was that the numbers of specialised staff and stroke unit beds were inadequate to deliver high quality care 24 hours a day, seven days a week, leading in particular to very low rates of thrombolysis. The response of Healthcare for London, supported by the PCTs, was to close half the London stroke units and enable chosen units to expand to a size sufficient to provide stroke unit care and rehabilitation for all those who needed it. Even more revolutionary, the decision was made to commission only eight hyperacute stroke units (HASUs). The London Ambulance Service now screens all suspected stroke patients with the FAST test and takes positive patients to one of the eight HASUs. These have now been fully operational for a year or so and each serves a population of around 1 million people, admitting around 2,000 patients per year. This model has been extremely successful and has allowed the development of protocols in line with the *National clinical guideline for stroke*, ensuring that all patients receive emergency brain scans, dramatically shortening door-to-needle times and, in some units, increasing the rates of thrombolysis up to a remarkable 15% of ischaemic stroke patients. Manchester is the only other city to have adopted this model of HASUs. Preliminary data suggest that the HASU model in London is not only effective at delivering thrombolysis, but reduces mortality and saves costs. In keeping with this, the new guideline recommends that all patients should be transferred directly to a specialised HASU for assessment for thrombolysis and other urgent interventions and states that ‘Commissioning of acute services requires the development of hub-and-spoke models of care (where a few hospitals in the region are dedicated to provide the hyperacute care for all patients)’.

Implementing the stroke guideline has been facilitated by the regional clinical cardiovascular and stroke networks. These networks link clinicians, therapists, nurses and managers, and facilitate shared stroke protocols and coordinated care. Until recently, the future of the stroke networks was uncertain; but fortunately the NHS Commissioning Board has announced that

the clinical stroke networks will continue to be supported within the cardiovascular networks as one of the first areas to be supported from 2013 in the new Strategic Clinical Networks.⁷ This should help to ensure that the new *National clinical guideline for stroke* is fully implemented throughout the country.

Another agency that has had a major influence on the delivery of the research underpinning the *National clinical guideline for stroke* has been the NIHR Stroke Research Network (SRN). This has been enormously successful in increasing the number of patients recruited to randomised clinical trials in the UK, mainly by supporting recruitment to trials in nearly every hospital in the country with stroke services, and providing research nurses and practitioners to assist in recruitment and data collection. The number of stroke patients recruited to randomised trials and other high quality studies in the UK since the introduction of the SRN has increased from just over 2000 per year in 2006–7 to over 12,000 per year in 2011–12, helping many struggling studies reach their planned sample size before funding ran out. Without this help from the SRN, many of the recommendations in the new guideline might never have appeared.

What of the future?

One major advance in hyperacute stroke treatment that has not yet reached the level of a specific mention in the guideline is the introduction of mechanical endovascular thrombus extraction for patients with ischaemic stroke secondary to major intracranial artery occlusion. This requires a trained interventional neuroradiologist to navigate a microcatheter intra-arterially from the groin to reach the site of intracranial obstruction and then extract the thrombus with a device. Currently, the most promising devices are stents that are deployed at the site of occlusion and then used to pull out the clot. Preliminary studies suggest that mechanical thrombus extraction is significantly more effective than intravenous or intra-arterial thrombolysis at recanalising blood vessels, and may well improve outcome.⁹ However, there is a significant risk of complications, including intracranial haemorrhage. There is therefore an urgent need for randomised trials to evaluate this new technology in comparison to conventional hyperacute stroke treatment. A number of such trials are in progress or are about to start, including a randomised trial about to start in the UK known as PISTE (Pragmatic Ischaemic Stroke Thrombectomy Evaluation). Because mechanical thrombus extraction requires an experienced neuroradiologist to deliver the treatment, its application is

currently limited to a small number of neuroscience centres: a recent survey by the British Association of Stroke Physicians reported that 24 NHS Trusts in the UK were delivering mechanical thrombectomy to occasional patients in 2011. If the trials confirm the expected benefit of mechanical thrombus extraction, there will then be the challenge of delivering the treatment to all eligible patients with stroke. This will require an expansion of current services and the development of rapid ambulance transfer protocols from HASUs without appropriate facilities to neuroscience centres. In rural areas this might, for example, require increasing use of air ambulances, since undoubtedly the time it takes to recanalise an occluded artery will be crucial in salvaging ischaemic brain. Hopefully, evidence from the randomised trials will be available to allow the next edition of the guideline to recommend mechanical thrombus extraction and the development of the service needed to deliver the treatment.

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