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EFNS TASK FORCE/CME ARTICLE

EFNS guideline on neuroimaging in acute stroke. Report of an EFNS task force

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Neuroimaging techniques are necessary for the evaluation of stroke, one of the leading causes of death and neurological impairment in developed countries. The multiplicity of techniques available has increased the complexity of decision making for physicians. We performed a comprehensive review of the literature in English for the period 1965–2005 and critically assessed the relevant publications. The members of the panel reviewed and corrected an initial draft, until a consensus was reached on recommendations stratified according to the European Federation of Neurological Societies (EFNS) criteria. Non-contrast computed tomography (CT) scan is the established imaging procedure for the initial evaluation of stroke patients. However, magnetic resonance imaging (MRI) has a higher sensitivity than CT for the demonstration of infarcted or ischemic areas and depicts well acute and chronic intracerebral hemorrhage. Perfusion and diffusion MRI together with MR angiography (MRA) are very helpful for the acute evaluation of patients with ischemic stroke. MRI and MRA are the recommended techniques for screening cerebral aneurysms and for the diagnosis of cerebral venous thrombosis and arterial dissection. For the non-invasive study of extracranial vessels, MRA is less portable and more expensive than ultrasonography but it has higher sensitivity and specificity for carotid stenosis. Transcranial Doppler is very useful for monitoring arterial reperfusion after thrombolysis, for the diagnosis of intracranial stenosis and of right-to-left shunts, and for monitoring vasospasm after subarachnoid hemorrhage. Currently, single photon emission computed tomography and positron emission tomography have a more limited role in the evaluation of the acute stroke patient.

Objectives

The objective of the Task Force is to develop and publish an EFNS Guideline on the use of neuroimaging for the management of acute stroke. The Guideline is based on published scientific evidence as well as the consensus of experts. The resulting report is intended to provide updated and evidence-based recommendations regarding the use of diagnostic neuroimaging techniques, including cerebrovascular ultrasonography (US), in patients with stroke and thus guide neurologists, other healthcare professionals and healthcare providers in clinical decision making and in the elaboration of clinical protocols. It is not intended to have legally binding implications in individual situations.

This guideline evaluates neuroimaging in acute stroke. Neuroimaging is also very important in the management of cerebrovascular disease in a more elective setting, for instance for the performance of angioplasty or the placement of an arterial stent. These procedures will be covered in future guidelines.

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Background

Stroke is the second cause of death and one of the major determining factors of hospital admission and

permanent disability [1]. In the developed countries, the proportion of the population over the age of 65 years is growing and this trend is likely to increase stroke incidence in the next decades. Major advances in the understanding of the mechanisms of stroke and its management have been made thanks to the substantial progress in neuroimaging techniques. However, the multiplicity of neuroimaging techniques available for the evaluation of stroke patients has increased the complexity of decision making for physicians. Neurologists, who have been educated to manage acute stroke patients, should be trained in the use of neuroimaging, which allows for the development of a pathophysiologically oriented treatment.

Successful care of acute stroke patients requires a rapid and accurate diagnosis because the time window for treatment is narrow. In the case of intravenous thrombolysis for ischemic stroke, the treatment is safer and more effective the earlier it is given [2]. Current recommendations call for a 3-h time limit for intravenous thrombolysis [3] that can be extended to 6 h for intra-arterial thrombolysis [4]. Thus, the neuroimaging protocol designed to determine the cause of stroke should delay treatment as little as possible. Neuroimaging can not only separate ischemic from hemorrhagic stroke, but also provide information about the presence of ischemic but still viable and thus salvageable tissue (penumbra tissue) and vessel occlusion in the hyperacute phase of ischemic stroke. Therefore neuroimaging is critical for an improved selection of patients who could be treated with thrombolysis up to the 3-h limit and beyond [5]. Thus, neuroimaging criteria have been used for patient selection and outcome in the Desmoteplase in Acute Stroke trial, using thrombolysis between 3 and 9 h after stroke onset [6]. Determining stroke type using neuroimaging goes well beyond separating ischemic from hemorragic stroke. For instance, the depiction of multiple cortical infarcts may lead to a fuller work-up for cardiogenic emboli [7]. In arterial dissection, the characteristic semilunar high-intensity signal in the vessel wall on magnetic resonance imaging (MRI) alerts to the presence of this cause of stroke [8].

Search strategy

The Cochrane Library was consulted and no studies were found regarding the use of neuroimaging techniques in stroke. A comprehensive literature review using the MEDLINE database has been conducted by searching for the period 1965–2005. Relevant literature in English including existing guidelines, meta-analyses, systematic reviews, randomized controlled trials, and observational studies and have been critically assessed. Selected articles have been rated based on the quality of study design, and clinical practice recommendations have been developed and stratified to reflect the quality and the content of the evidence according to EFNS criteria [9] (Table 1).

Table 1 Evidence classification scheme for a diagnostic procedure [9]

Class I: A prospective study in a broad spectrum of persons with the suspected condition, using a 'gold standard' for case definition, where the test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy
Class II: A prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by 'gold standard') compared with a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy
Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where test is applied in a blinded evaluation
Class IV: Any design where test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls)
Rating of recommendations
Level A rating (established as useful/predictive or not useful/predictive) requires at least one convincing class I study or at least two consistent, convincing class II studies
Level B rating (established as probably useful/predictive or not useful/predictive) requires at least one convincing class II study or overwhelming class III evidence
Level C rating (established as possibly useful/predictive or not useful/predictive)
Good clinical practice point rating (GCPP, supported primarily by expert opinion

Method for reaching consensus

The author panel critically assessed the topic through analysis of the medical literature. A proposed guideline with specific recommendations was drafted for circulation to all panel members. Each panelist studied and commented in writing on each successive guideline draft, revised to progressively accommodate the panel consensus. After the approval of the panelists, two independent experts gave their opinion on the final version.

Results

Imaging of the brain

The primary objectives of brain imaging in acute stroke are to exclude a non-vascular lesion as the cause of the symptoms and to determine whether the stroke is caused by an ischemic infarction or a hemorrhage. It is not possible to exclude stroke mimics, such as a neoplasm, and distinguish between ischemic and hemorrhagic stroke based exclusively on the history and

physical examination [10]. Determining the nature of the lesion by brain imaging is necessary before starting any treatment, particularly thrombolysis and antithrombotic drugs (class I, level A).

Computed tomography (CT)

Conventional CT of the head is the examination most frequently used for the emergent evaluation of patients with acute stroke because of its wide availability and usefulness (class II, level B). It has been utilized as a screening tool in most of the major therapeutic trials conducted to date [2]. It is useful to distinguish between ischemic stroke and intracerebral or subarachnoid hemorrhage (SAH), and can also rule out other conditions that could mimic stroke such as brain tumors. Signs of early ischemia may be identified as early as 2 h from stroke onset, although they may appear much later [11]. Early infarct signs include the hyperdense middle cerebral artery (MCA) sign [12,13] (indicative of a thrombus or embolus in the M1 segment of the vessel), the MCA dot sign [14,15] (indicating thrombosis of M2 or M3 MCA branches), the loss of the gray-white differentiation in the cortical ribbon [16] or the lentiform nucleus [17], and sulcal effacement [18]. The presence of some of these signs has been associated with poor outcome [18]. In the European Cooperative Acute Stroke Study (ECASS) I trial those patients with signs of early infarction involving more than one-third of the territory of the MCA had an increased risk of hemorrhagic transformation following treatment with thrombolysis [19]. A secondary analysis of other thrombolytic trials with a 6-h time window (ECASS II and Multicentre Acute Stroke Trial – Europe (MAST-E) demonstrated that the presence of early CT changes was a risk factor for intracerebral hemorrhage (ICH) [20,21] and similar results have been observed in larger series of patients [22]. However, in the National Institute of Neurological Disease and Stroke (NINDS) trial and the Australian Streptokinase Trial there was no relation between intracranial hemorrhage and early CT changes [23,24], and has been argued that the poorer outcome in patients with CT changes may have more to do with delayed treatment than with the changes themselves, with additional damage of the potentially salvageable tissue in the larger, CT-visible infarcts [25]. Because ischemic changes are difficult to detect for clinicians without an adequate training in reading CT [26,27], scoring systems have been developed to quantify early CT changes, like the Alberta Stroke Programme Early CT Score (ASPECTS). More extensive early changes using ASPECTS correlate with high rates of intracranial hemorrhage and poor outcome at long term, and therefore might improve identification of ischemic stroke patients who particularly benefit from thrombolysis and those at risk of symptomatic hemorrhage [28,29]. However, given the conflicting evidence, the presence of decreased attenuation on early CT, even affecting more than one-third of the MCA territory, cannot be construed to be an absolute contraindication to the use of thrombolytic therapy in the first 3 h after stroke (class IV, level GCPP).

Conventional CT contrast enhancement is not indicated for the acute diagnosis of stroke, and seldom may be helpful to show the infarcted area in the subacute stage (2–3 weeks after stroke onset) when there may be obscuration of the infarction by the 'fogging effect' [30,31] (class IV, level C).

Computed tomography shows acute ICHs larger than 5 mm in diameter as areas of increased attenuation. Not depicted by CT are petechial hemorrhages and bleedings in patients with very low hemoglobin levels [32], because the high density of blood on CT is a function of hemoglobin concentration. CT demonstrates the size and topography of the hemorrhage and gives information about the presence of mass effect, hydrocephalus, and intraventricular extension of the bleeding. In addition, it may identify (although not as well as MRI) possible structural abnormalities (aneurysms, arteriovenous malformations or tumors) that caused the hemorrhage. The characteristic hyperdensity of ICH on CT disappears with time, becoming hypodense after approximately 8–10 days [33,34]. For this reason CT is not a useful technique to distinguish between old hemorrhage and infarction.

With newer CT helical units, SAH can be detected in 98–100% of patients in the first 12 h from the onset of symptoms [35,36] and in 93% of patients studied within the first 24 h [37,38]. CT is the imaging procedure of choice to diagnose SAH (class I, level A). Some experts recommend performing the study with thin cuts (3 mm in thickness) through the base of the brain, because small collections of blood may be missed with thicker cuts [39] (class IV, level GCPP). CT cannot identify SAH in patients with low hemoglobin levels, because blood may appear isodense, and in those scanned after 3 weeks of the bleeding, when blood has usually been metabolized [40].

Cerebral venous thrombosis (CVT) is an uncommon cause of stroke [41,42]. CT can show direct signs of venous thrombosis and other indirect non-specific signs, but in about one-third of cases CT is normal [43,44]. Direct signs on unenhanced CT are the cord sign, corresponding to thrombosed cortical veins, and the dense triangle sign, corresponding to a thrombus in the superior sagital sinus, and, on enhanced CT of the sagital sinus, the delta sign [45]. Indirect signs such as local hypodensities caused by edema or infarction,

hyperdensities secondary to hemorrhagic infarction, or brain swelling and small ventricles suggest the diagnosis of CVT. CT venography has emerged as a good procedure to detect CVT [46] (class III, level C).

Perfusion-CT (PCT) techniques, such as slow-infusion/whole-brain PCT and dynamic PCT, may help distinguish between reversible and irreversible areas of ischemia. Slow-infusion PCT is useful to evaluate the perfusion of the entire brain, but only provides qualitative information related to cerebral blood volume and therefore cannot be used to differentiate reversible from non-reversible ischemia [47,48]. Dynamic PCT involves dynamic acquisition of sequential CT slices during the intravenous administration of iodinated contrast media [49,50]. PCT allows the estimation of cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) in a limited volume of brain tissue, currently 20- to 48-mm in thickness, but faster CT equipment is becoming available to permit the study of larger regions of the brain. Areas with prolonged MTT are hemodynamically compromised. In these areas, the regions with increased CBV resulting from vasodilatation and collateral recruitment are considered to have preserved autoregulation and to represent 'tissue at risk,' whereas regions with decreased CBV correspond to the infarct core [49,51,52]. PCT overestimates brain hemodynamic values in pixels including large vessels [53]. PCT can be performed and analyzed in less than 15 min [52]. However there are no studies to date demonstrating that perfusion CT is useful for the selection of candidates to thrombolysis. Pregnancy, diabetes, renal failure, and allergy to contrast material are relative contraindications to perform a perfusion brain CT. Perfusion CT is particularly helpful for the study of stroke patients for whom MRI is contraindicated, such as those with pacemakers (class IV, level GCPP).

Magnetic resonance imaging

Magnetic resonance imaging has a higher sensitivity than conventional CT and results in lower inter-rater variability in the diagnosis of ischemic stroke within the first hours of stroke onset [54–59] (class I, level A). MRI is particularly useful to show lesions in the brain stem or cerebellum, identify lacunar infarcts, and document vessel occlusion and brain edema [55,57] (class I, level A). In addition, new MRI techniques can provide information about tissue viability. Diffusion-weighted (DWI) and perfusion-weighted (PWI) MRI studies may inform about the presence of reversibly and irreversibly damaged ischemic tissues in the hyperacute phase of stroke [60–66]. DWI may demonstrate deeply ischemic or infarcted brain tissue within minutes of onset of symptoms [67]. PWI requires the intravenous administration of gadolinium and provides information about brain tissue perfusion at a given time. The most widely used indicator of brain perfusion is the *time-to-peak*, being the time until the intravenous gadolinium bolus reaches brain tissue. This model-independent measure allows an estimation of the severity of ischemia in comparison with the non-affected hemisphere in an objective manner [68]. The absolute volume difference or ratio of the PWI area and the DWI area (diffusion–perfusion mismatch) is a useful method to estimate the presence of ischemic penumbra tissue [69,70]. Not only the volume of abnormal perfusion but also its degree predicts the extent of ischemic brain damage [71]. PWI/DWI-mismatch has been evaluated in several studies as a selection tool for thromboyltic therapy beyond 3 h [72] and in a recent phase II trial it was used as a selection tool and surrogate parameter for thrombolysis within 3–9 h [6]. However, the extent of DWI/PWI mismatch did not predict outcome after thrombolysis in an earlier open label study [72].

Magnetic resonance imaging can help identify occluded intracranial arteries by the loss of the normal intravascular flow voids [55]. Some sequences, as T2*-weighted MRI or fluid-attenuated inversion recovery (FLAIR; hyperintense artery sign), may demonstrate acute MCA thromboembolism with a higher sensitivity than CT, but the type of arterial change on MRI does not predict recanalization, clinical outcome or ICH after intravenous thrombolysis [73,74].

Intracranial hemorrhage with acute stroke is easily detectable on MRI using T2*-weighted images [75–77]. MRI can identify intraparenchymal hemorrhage within the first 6 h after symptom onset as accurately as CT [77,78]. Susceptibility-weighted T2*-sequences (gradient echo) can also detect clinically silent parenchymal microbleeds, not visible on CT, which may leave enough local hemosiderin to remain detectable for months or years after the bleeding. Although microbleeds are associated with a history of ICH and prospectively have been shown to pose a 3% risk of ICH [79], the risk of bleeding after thrombolysis in patients with microbleeds has not been established. Whilst some retrospective studies reported an increased risk of symptomatic hemorrhage after thrombolysis [80,81], a more recent publication from one of the same groups failed to document it [82]. MRI is also useful to date the hemorrhagic event accurately and to detect lesions (as tumors, vascular malformations or aneurysms) that may underlie the ICH [83]. To detect these lesions, repeated studies may be needed after some of the swelling and vasospasm have subsided.

Subarachnoid hemorrhage can be detected using T2* [84] and FLAIR [85,86] MR sequences, but at present

CT remains the imaging method of choice for this diagnosis (class I, level A).

Arterial dissection is a leading cause of stroke in young persons [42]. MRI is the initial procedure of choice [57,87,88], replacing conventional angiography as the gold standard (class II, level B), because MRI can show the mural hematoma of the dissected vessel on the axial images [89] (high signal in the wall). Visualization of these changes in the vertebral artery is more difficult than for the larger carotid artery, making diagnosis of vertebral dissection less reliable. The study can be completed with MR angiography (MRA) to visualize occlusion of the artery, pseudoaneurysms or a long stenotic segment with tapered ends [90,91]. Other techniques, including US [92,93] or CT angiography [90,91], may be useful for the non-invasive diagnosis of arterial dissection.

Cerebral venous thrombosis. Magnetic resonance combined with MRA is the method of choice for the diagnosis and follow-up of CVT [44,94,95]. MR is more sensitive than CT to show parechymal abnormalities and the presence of thrombosed veins.

In summary, MRI is very helpful in the clinical setting for the management of acute stroke and to guide decisions regarding thrombolysis [5] (class I, level A). It is particularly helpful for the study of stroke patients for whom perfusion CT may be dangerous, such as those with renal failure or diabetes. However, MRI in the acute phase of stroke is not widely available at European hospitals [96]. Other limitations and contraindications for the use of MRI are: claustrophobia, agitation, morbid obesity, the presence of intracranial ferromagnetic elements, an aneurysm recently clipped or coiled, otic or cochlear implants, some old prosthetic heart valves, pacemakers, and some, not all, neurostimulators.

SPECT and PET

Single photon emission computed tomography (SPECT) and positron emission tomography (PET) are functional neuroimaging techniques based on the principles of tracer technology using radiolabeled substances as systemically administered tracers. In the setting of stroke SPECT has been used for the evaluation of cerebral perfusion. Earlier perfusion SPECT studies failed to show any advantage of SPECT over the structured clinical evaluation (NIH, Canadian, Scandinavian stroke scales) in the prediction of the evolution of acute stroke [97]. However, using ethyl cysteinate dimer (ECD) SPECT in the first 6 h after stroke, Barthel *et al*. [98] were able to determine which patients would develop massive MCA-territory necrosis, with hemispheric herniation. These patients have a high risk of hemorrhage following thrombolysis and could potentially be helped by early decompressive hemicraniectomy [99]. Complete MCA infarctions were predicted with significantly higher accuracy with early SPECT compared with early CT and clinical parameters. The predictive value increased when the findings on CT, clinical examination and SPECT were considered [98]. Other studies have found SPECT to add predictive value to the clinical score on admission [100–102]. Those studies suggest that a patient with a normal SPECT study performed within 3 h of stroke onset, will most likely recover spontaneously and therefore may not benefit from thrombolysis. A patient with a dense deficit in the entire MCA distribution has a high risk of hemorrhage with thrombolysis, and, depending on age and other factors, should be considered for decompressive hemicraniectomy. The patients most likely to benefit from thrombolysis are the ones with less massive lesions [98,100]. Thus, SPECT is helpful in the evaluation of acute stroke (class III, level C). Unfortunately, the need to perform either CT or MRI in acute stroke renders the performance of SPECT difficult within the time frame allotted for the evaluation of these patients. SPECT is also helpful in the evaluation of cerebral perfusion in non-acute cerebrovascular disease, for instance in the days after a SAH [103] (class III, level C).

Positron emission tomography allows to measure a large variety of physiological variables including the cerebral blood flow, the cerebral blood volume, the cerebral glucose metabolism as well as neurotransmitters and neuroreceptors, such as benzodiazepine receptors with flumazenil, an accurate marker of neuronal loss [104]. As PET has been considered the gold standard for these kinds of measurements in humans, it is also extremely well suited to help identify the degree of ischemic damage in the brain. However, it does not allow for the reliable identification of lesions in the vessels or non-vascular lesions giving rise to the stroke syndrome. This, coupled with the cost and current lack of availability of this technique, renders it less useful than MRI and CT for most practicing neurologists.

Imaging of the extracranial vessels

Imaging of the extracranial and intracranial vessels will help identify the underlying mechanism of the stroke (atherothrombotic, embolic, dissection or other). Non-invasive imaging methods are increasingly accepted as replacements of digital substraction angiography (DSA) in carotid stenosis evaluation prior to endarterectomy, in order to avoid the risks of DSA [105] (class IV, GCPP). US, comprising Doppler sonography and color-coded duplex sonography, is probably the

most common non-invasive imaging examination performed to aid in the diagnosis of carotid disease. The peak systolic velocity and the presence of plaque on grayscale and/or color Doppler/Duplex US images are the main parameters that should be used when diagnosing and grading internal carotid artery (ICA) stenosis [106]. The examination may be limited by the presence of extensive plaque calcifications, vessel tortuosity and in patients with tandem lesions. In addition, Doppler US is both technician- and equipment-dependent and all sonographers should be able to demonstrate that they have validated their testing procedures.

Magnetic resonance angiography using time-of-flight angiography (TOF) and contrast-enhanced MRA (CEMRA) are powerful means to assess vascular pathology. Either technique provides specific information: whilst TOF visualizes changes of flow in the arteries or veins depending on imaging parameters, CEMRA visualizes the vascular lumen. MRA and US have yielded comparable findings. Two meta-analysis [107,108] and several reviews [109,110] have compared the diagnostic value of Doppler US, MRA, and conventional DSA for the diagnosis of carotid artery stenosis. The meta-analysis published by Blakeley *et al.* [107] in 1995 concluded that Doppler US and MRA had similar diagnostic performance in predicting carotid artery occlusion and $>70\%$ stenosis. In the systematic review performed by Nederkoorn *et al.* [109] for the diagnosis of 70–99% stenosis, MRA had a pooled sensitivity of 95% and a pooled specificity of 90%, and US 86% and 87%, respectively. For recognizing occlusion, MRA had a sensitivity of 98% and a specificity of 100%, and DUS had a sensitivity of 96% and a specificity of 100%. Thus, CEMRA is slightly more precise than US and appears to achieve a higher sensitivity for the detection of stenosis, and to allow improved differentiation of tight stenosis from occlusion. However, the difference is small and other factors such as availability and quality of US performance may render one procedure more useful than the other (class II, level B).

Computed tomography angiography, a contrast-dependent technique, has been compared with DSA for the detection and quantification of carotid stenosis and occlusions [111–116]. A recent systematic review concludes that this technique has demonstrated a good sensitivity and specificity for occlusion (97%), but the pooled sensitivity and specificity for detection of a 70–99% stenosis by CTA were 85% and 93% respectively [115] (class II, level B).

Digital substraction angiography is the reference method to determine the degree of carotid stenosis because endarterectomy trials for symptomatic [117–119] and asymptomatic [120] patients were performed using this method. However angiography carries the risk of stroke and death [105,121] and many centers are not using DSA prior to carotid endarterectomy [106,122], particularly when non-invasive methods are concordant (class IV, GCPP). When non-invasive methods are inconclusive or there is a discrepancy between them, DSA is necessary.

Imaging of the intracranial vessels

Transcranial Doppler (TCD) is a non-invasive ultrasonographic procedure that measures local blood flow velocity and direction in the proximal portions of large intracranial arteries [123,124]. It is useful for screening for intracranial stenosis [125,126] and occlusion [127] in patients with cerebrovascular disease (class II, level B). In children with sickle cell disease, detection of asymptomatic intracerebral stenoses using TCD allows selection of a group at high risk of future stroke, who benefit from exchange transfusion [128] (class I, level A). It is also useful for the detection and monitoring of intracranial artery vasospasm after SAH, particularly in the MCA [129] (class I, level A). TCD can be used to monitor recanalization during thrombolysis in acute MCA occlusions [130] (class II, level B). There is increasing interest in its therapeutic use. *In vitro* studies demonstrate it has an additive effect on clot lysis when used with recombinant tissue plasminogen activator (rtPA), and clinical studies have suggested that continuous TCD monitoring in patients with acute MCA occlusion treated with intravenous thrombolysis may improve both early recanalization and clinical outcome [131,132]. TCD allows for the documentation of a right-to-left shunt in patients with ischemic stroke (class II, level A). TCD discloses a shower of air bubbles in the MCA after the intravenous injection of saline mixed with air bubbles [133–135].

Even in asymptomatic patients, TCD is the only imaging technique that allows detection of circulating emboli (class II, level A). These appear as short duration high-intensity signals, because they reflect and backscatter more ultrasound than the surrounding red blood cells. Studies have shown that asymptomatic embolization is common in acute stroke, particularly in patients with carotid artery disease [136,137]. In this group the presence of embolic signals has been shown to predict the combined stroke and transient ischemic attack (TIA) risk [138–142] and more recently the risk of stroke alone [143] (class II, level A). Embolic signals have been also used as surrogate markers to evaluate antiplatelet agents in both single-center studies [144] and recently in the multicenter international Clopidogrel and Aspirin for Reduction of Emboli in

Symptomatic Carotid Stenosis trial [145]. Embolic signal monitoring is used to monitor embolization following carotid endarterectomy; the presence of frequent embolic signals in this setting predicts early postoperative stroke [146] and can be reduced by more aggressive antiplatelet treatment, including dextran [147] and clopidogrel [148]. TCD can also be used to determine cerebrovascular reserve by determining the extent to which MCA flow velocity can increase in response to the vasodilator carbon dioxide or acetazolamide. Reserve is reduced in a proportion of patients with carotid occlusion and tight stenosis, and impaired reserve predicts recurrent TIA and stroke risk particularly in the group with carotid occlusion [149,150] (class III, level B).

Transcranial Doppler examination cannot be performed in about 10–15% of patients, particularly older women, because they lack a transtemporal window due to the thickness of the skull [151]. The use of intravenous echo contrast agents may improve detection of flow velocities in patients with limited transtemporal window [152]. TCD velocities may be altered in patients with cardiac pump failure (low velocities) or anemia (increased velocities).

Magnetic resonance angiography can identify intracranial steno-occlusive lesions mainly in the proximal segments. Compared with DSA, the diagnostic accuracy of MRA for the identification of the proximal intracranial arterial stenosis has a high sensitivity and specificity (superior to 80%) [153–155] (class II, level B). CT angiography is another useful technique but with less sensitivity and specificity than MRI, because it does not allow for assessment of stenosis in the cavernous portion of the internal carotid or in arteries with circumferential wall calcification [154,156].

Magnetic resonance and CT angiography can be used to show large aneurysms (class II, level B), but these techniques fail to identify aneurysm of less than 5 mm in diameter, those located in the intracranial carotid artery, and cannot clearly establish the critical relationship of the neck of the aneurysm(s) with arterial branches [157–159]. DSA is needed to demonstrate small aneurysms and before surgery or endovascular treatment (class I, level A). MR and CT angiography have been used for screening individuals with a history of intracranial aneurysm or SAH in first-degree relatives [59,160]. Despite relatively limited sensitivity, CT angiography is indicated for suspected or confirmed aneurysms that demand further verification of their presence, geometry, or relationship to parent artery branches and osseous anatomic landmarks. Low-volume high-density contrast media have substantially increased the ability of CT angiography to depict small aneurysms, small branches, and collateral vessels [161].

Recommendations

Imaging of the brain

Non-contrast CT scan is the established imaging procedure for the initial evaluation of patients with stroke to document or exclude ICH and SAH (class II, level C). However, CT use has been consecrated more by availability than by randomized studies comparing its effectiveness with MRI. Either CT or MRI should be used for the definition of stroke type and treatment of stroke (class I, level A).

Given the controversial nature of data on early CT infarct signs involving more than one-third of the territory of the MCA as predictors of the outcome of IV rtPA treatment, the presence of such signs cannot be construed as an absolute contraindication to thrombolysis in the first 3 h after stroke (class IV, level GCPP). Perfusion CT is helpful when MRI is not available and for the study of stroke patients for whom MRI is contraindicated (class IV, level GCPP). MRI has a higher sensitivity than conventional CT for the documentation of infarction within the first hours of stroke onset, lesions in the posterior fossa, identification of small lesions, and documentation of vessel occlusion and brain edema (class I, level A). In conjunction with MRI and MRA, perfusion and diffusion MR are very helpful for the evaluation of patients with acute ischemic stroke (class I, level A). Perfusion and diffusion MR are helpful to select patients for intravenous thrombolysis beyond 3 h (class II, level B). MRI with MRA is the method recommended for the diagnosis and follow-up of arterial dissection (class II, level B).

Single photon emission computed tomography is helpful to predict the malignant course of brain swelling with large hemispheric infarctions (class III, level C). SPECT is also helpful in the evaluation of cerebral perfusion in non-acute cerebrovascular disease, for instance in the days after a SAH (class III, level C).

Detection of hemorrhagic stroke

In stroke, MRI can detect acute and chronic ICH (class I, level A). Although the detection of SAH is possible with MRI, currently CT scan is the diagnostic procedure of choice (class I, level A).

Imaging of extracranial vessels

Ultrasonography is the non-invasive *screening* technique indicated for the study of vessels involved in causing symptoms of carotid stenosis (class IV, GCPP). MR angiography has slightly higher sensitivity and specificity than US to determine carotid stenosis and

occlusion, but other factors, such as availability, may render one procedure more useful than the other (class II, level B). CTA has a sensitivity and specificity similar to MR for carotid occlusion and similar to US for the detection of severe stenosis (class II, level B). DSA is generally recommended for grading carotid stenosis prior to endarterectomy (class I, level A), but when there is concordance of non-invasive methods cerebral arteriography may not be necessary (class IV, level GCPP).

Imaging of intracraneal vessels

Transcranial Doppler is very useful for assessing stroke risk of children aged 2–16 years with sickle cell disease (class I, level A), detection and monitoring of vasospasm after SAH (class I, level A), diagnosis of intracranial steno-occlusive disease (class II, level B), diagnosis of right-to-left shunts (class II, level A), and for monitoring arterial reperfusion after thrombolysis of acute MCA occlusions (class II, level B). TCD can detect cerebral emboli and impaired cerebral hemodynamics. The presence of embolic signals with carotid stenosis predicts early recurrent stroke risk (class II, level A). The detection of impaired cerebral hemodynamics in carotid occlusion may identify a group at high risk of recurrent stroke (class III, level B).

Magnetic resonance angiography and CT angiography are very useful for the diagnosis of intracranial stenosis and cerebral aneurysms >5 mm (class II, level B). MRA is the recommended technique for screening cerebral aneurysms in individuals with a history of aneurysms or SAH in a first-degree relative (class II, level B). DSA is the recommended technique for the diagnosis of cerebral aneurysm as the cause of SAH (class I, level A). MRI with MRA is recommended for the diagnosis and follow-up of CVT (class II, level B). Alternatively, CT venography is accurate and can be used for the same purpose (class III, level C).

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Statement of the likely time when the guideline will need to be updated

This guideline should be reviewed and if necessary revised not later than 2008.

Conflicts of interest

None of the authors has a conflict of interest with regard to the contents of this manuscript.

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