NEUROLOGÍA

REVIEW ARTICLE

Diagnosis of delayed cerebral ischaemia and cerebral vasospasm in subarachnoid haemorrhage

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Abstract

Objective: A review of current foundations for the medical diagnosis of vasospasm and delayed cerebral ischaemia due to spontaneous subarachnoid haemorrhage.

Development: A review of available tests for the investigation of vasospasm (transcranial Doppler, angiographic methods) and delayed cerebral ischaemia (clinical exam, computerised tomography by X rays, magnetic resonance, emission computerised tomography, electroencephalography, microdialysis) based on type and quality of information, advantages and limitations. Grading and trends for application were also considered for differential diagnosis.

Conclusions: In current clinical practice the most advisable guideline for screening and diagnosis monitoring of vasospasm and delayed cerebral ischaemia is, in the first place, based on clinical examination and transcranial Doppler. Electroencephalographic monitoring, computerised tomography techniques and multi-modal magnetic resonance are justified in specific situations. Digital subtraction angiography is the current gold standard for diagnosis of cerebral vasospasm. There is a need for more and higher quality articles about the utility of diagnostic tests in this context.

Diagnóstico de la isquemia cerebral tardía y el vasospasmo cerebral en la hemorragia subaracnoidea

Resumen

Objetivo: Revisar los fundamentos actuales para el diagnóstico, en la práctica médica, del vasospasmo y la isquemia cerebral tardía por hemorragia subaracnoidea espontánea.

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Ictus agudo;
Isquemia cerebral;
Vasospasmo cerebral

Desarrollo: Se revisan las pruebas disponibles para investigar el vasospasmo (Doppler transcraneal, métodos angiográficos) y la isquemia cerebral tardía (examen clínico, tomografía computarizada convencional, resonancia magnética, tomografía computarizada de emisión, electroencefalografía, microdiálisis) en cuanto al tipo y calidad de la información que brindan, además de sus ventajas y limitaciones. Se aborda el diagnóstico diferencial, graduación y pautas de aplicación.

Conclusiones: En la práctica clínica actual la pauta más recomendable para el diagnóstico y la monitorización del vasospasmo y la isquemia cerebral tardía consiste, en primer lugar, en el examen clínico y por Doppler transcraneal. La monitorización electroencefalográfica, las técnicas de tomografía computarizada y resonancia magnética multimodal son apropiadas en situaciones específicas. La angiografía por sustracción digital es el estándar para el diagnóstico del vasospasmo cerebral. Se insiste en la necesidad de mejorar la calidad de los futuros artículos sobre la utilidad de las pruebas diagnósticas señaladas.

Introduction

Delayed cerebral ischemia (DCI) is a major cause of morbidity and mortality for patients suffering from subarachnoid haemorrhage (SAH).[1] The entity encourages current scientific interest due to the complexity of its pathogenesis, classically attributed to cerebral vasospasm, and to the uncertainty or controversy in several areas of diagnostic management because of the existence of inaccurate or equivocal information.[2-5]

A key aspect in the management of patients with SAH lies in the diagnosis of DCI and vasospasm because timely initiation of treatment can prevent cerebral stroke. Furthermore, early and accurate recognition of both disorders makes it possible to assess the effects of therapeutic interventions (fig. 1). In this article, we review the current bases for diagnosis of cerebral vasospasm and DCI in medical practice.

Articles were identified through the PubMed and IMBIOMED services, consistent with search terms in English (cerebral vasospasm, delayed cerebral ischemia, subarachnoid haemorrhage) or their equivalents in Spanish, respectively. We selected original investigations, meta-analyses and reviews from the past 10 years, with accessible full-texts, which specifically assessed diagnostic tests of interest. General reviews of diagnostic tests dealt with, although they met most of the criteria expressed, were chosen from the links provided in previously-identified articles.

Clinical manifestations

The clinical manifestations of DCI are mainly neurological. They consist of decreased consciousness or focal neurological deficit (new symptoms or worsening of previously detected manifestations). Disorders of the anterior cerebral artery (ACA) (apathy, akinetic mutism and occasional paraparesis) and internal carotid artery (ICA) or middle cerebral artery (MCA) (hemiparesis or hemiplegia, which may be associated with sensory deficit, hemianopsia and aphasia) are very distinctive.[1,6-8] Faciobrachial paresis and dysarthria may be caused by spasms of the upper and middle thirds of the basilar trunk with paramedian pontine stroke.[9] However, in vertebrobasilar circulation, clinical signs are less frequent and may be subtle, diffuse and unspecific.[10] Haemodynamic and respiratory disorders occur with brainstem ischemia. Spasms of the perforating arteries irrigating the ascending reticular activating system have been associated with peduncular hallucinosis (vivid visual hallucinations, abnormal sleep rhythms, waking or insomnia). Upper quadrantanopsia is related to posterior circulation disorders.[11]

Symptoms of DCI are related to systemic manifestations (clinical and analytical) that should not be considered as indicative for a diagnosis. The appearance of vomiting, increased headache intensity and neck stiffness coincides temporarily with vasospasm, but is best explained by continued irritation of the meninges and intracranial hypertension. Fever, increased pulse rate and leukocytosis indicate, firstly, an infection. In addition, hyponatraemia,
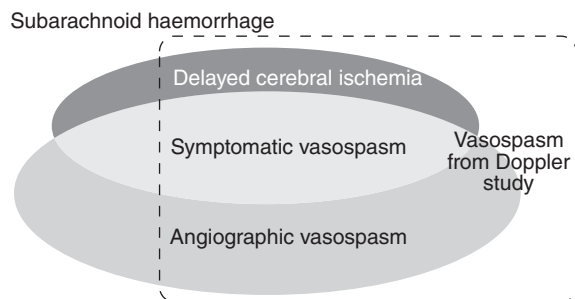

Subarachnoid haemorrhage

Delayed cerebral ischemia

Symptomatic vasospasm

Vasospasm from Doppler study

Angiographic vasospasm

Figure 1 Drawing reflecting the list and clinical significance of the main definitions related to cerebral vasospasm. Delayed cerebral ischemia (DCI) includes symptomatic vasospasm and/or cerebral stroke secondary to vasospasm. There may be patients with angiographic vasospasm, vasospasm from sonographic study or with subarachnoid haemorrhage without DCI.

Table 1 Differential diagnosis of cerebral vasospasm and delayed cerebral ischemia

Neurological disorders

Parenchymal, intraventricular, subdural and epidural cerebral haemorrhage

Progression of cerebral oedema and intracranial pressure

Hydrocephalus, subarachnoid rebleeding, diffuse cerebral ischemia

Clinical and subclinical epileptic crises, post-stroke state

Hyperaemia

Postpartum reversible cerebral vasoconstriction and by vasoactive substances

Vasospasm accompanied by migraine and spontaneous vasospasm

Atheromatous stenosis, hypoplasia, other pre-existing abnormalities of the Willis circle, variations of the angiographic technique

Angiography complications (cerebral stroke, arterial dissection)

Surgical retraction and temporary arterial occlusion

Vascular occlusion by clip

Direct compression by the aneurysm

Embolism of endovascular devices

Side effect of sedative drugs

Non-neurological disorders

Hypernatraemia, hyponatraemia, hypovolaemia, hypotension, hypoxia, cardiac arrhythmias, heart failure

Infections (especially of the lung and bladder) and fever

hypovolaemia, arterial hypotension, cardiac disorders and hypoxia are also involved as predisposing factors.[7,12,13]

The severity of neurological dysfunction depends on the degree, location and extent of arterial disease, the compensatory state of collateral circulation and cerebral perfusion pressure and on the severity of the brain injury. Focal deficit may fluctuate in intensity or come and go. In patients of a more severe clinical degree or under the influence of sedatives, it is difficult to diagnose neurological deterioration because of limitations in performing the clinical examination. Asymptomatic cerebral stroke can occur in patients with impaired consciousness and constitutes about 25% of DCI cases.[1,14-16] Another factor involved in clinical detection is the neurological training of medical staff and the implementation of evaluations with appropriate frequency and depth.

Delayed cerebral ischemia occurs with clinical manifestations, sudden or insidious, usually within 7-10 days of bleeding. When a neurological deficit appears in the first 3 days after the occurrence of SAH or after 12 days, it is important to reassess the date and raise the possibility of unnoticed bleeding. Acute neurological deficit can be explained by other factors (table 1). These causal or concurrent factors are usually determined through the clinical characteristics, laboratory data and structural neuroimaging.[5-7,12,13,17,18] However, several of these factors may be combined.

Cerebral angiography by digital subtraction

Cerebral digital subtraction angiography (DSA) is the gold standard for diagnosing cerebral vasospasm.[5-7,16,19,20] Radiographic evidence for vasospasm consists in the abatement of calibre and/or poor artery visualisation, with prolonged circulation time compared to a previous angiogram or standard values. Calibre narrowing can be mild (1-25%), moderate (25-50%), severe (50-75%) and very severe (>75%) (fig. 2).

"Symptomatic vasospasm" is defined by the clinical neurological manifestations of DCI that correspond to the radiological vasospasm location (usually, the arterial lumen is=1mm). "Angiographic vasospasm" is developed in 30-75% of patients with SAH, but only half of them show clinical DCI symptoms (fig. 1). Arterial spasm is usually evident within 3-5 days after SAH, reaches its maximum at up to 5-14 days later and is gradually resolved in 2-4 weeks. The disorder is
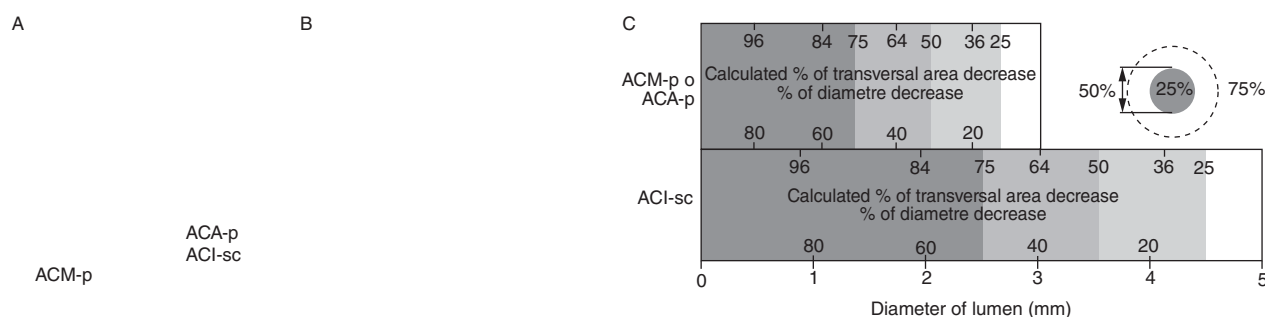

Figure 2 Representation of the method for grading vasospasm on carotid system arteriography. A: diagram of the location of the main branches of the internal carotid artery in an anteroposterior view. ACA-p: proximal segment of the anterior cerebral artery; ACM-p: proximal segment of the middle cerebral artery; ICA-sp: supraclinoid segment of the internal carotid artery. B: different degrees of vasospasm. C: practical method to estimate the percentage of stenosis according to the diameter of arterial lumen. A 50% reduction in diameter is estimated equivalent to a 75% decrease in cross-sectional area. Percent of stenosis = [1 —((D stenosis 1 × D stenosis 2) / (D normal 1 × D normal 2))] × 100; where D stenosis 1 and D stenosis 2 = diameter of the stenotic segment in two planes, and D normal 1 and D normal 2 = normal artery diameters in two planes. In practice, this requires image magnification to clearly delineate the edges of the arteries and appreciate differences of 0.1 mm.

Table 2 Abbreviated classification for severity of vasospasm and delayed cerebral ischemia[6,12,20,36,37]

Severity	Neurological clinical examination	Angiography	TCD		SPECT (hypoperfusion)	Cerebral perfusion CT
			MCA	BA		
I. Mild	Subclinical or asymptomatic	Localized with less than 50% in stenosis of arterial lumen	AFR 80-120 cm/s with ratio MCA/ICA < 3	AFR > 70 cm/s with BA/VA 2-2.5	70-85% of baseline value	Increment of ATT and rCBV (hypoperfusion without ischemia)
II. Moderate	Partial focal deficit or deterioration of consciousness without coma	Multisegmented with less than 50% stenosis of arterial lumen	AFR 120-179 (or 199) cm/s with ratio MCA/ICA 3-6	AFR > 85 cm/s with BA/VA 2.5-3	50-70% of baseline value	Increment of ATT in relation with decrease of rCBF and normal or increased rCBV (reversible ischemia)
III. Severe	Complete focal deficit or coma	Multisegmented with more than 50% stenosis of arterial lumen	AFR > 180 (or 200) cm/s with ratio MCA/ICA > 6	AFR >85 cm/s with BA/VA >3	20-50% of baseline value	Increment of ATT, decrease of rCBF and rCBV (stroke)

AFR: average flow rate; ATT: average transit time; BA: basilar artery; CT: computed tomography; ICA: internal carotid artery; MCA: middle cerebral artery; rCBV: relative cerebral blood volume; rCBF: regional cerebral blood flow; SPECT: Sngle-photon emission computed tomography; TCD: transcranial Doppler; VA: vertebral artery.

preferably located in the proximal arteries, located at the base of the brain and close to the intracranial aneurysm; it may then spread to other sites or deteriorate the reactivity of more distal arteries with further reduction of cerebral blood flow (CBF). Its location is correlated with the region affected by cerebral infarction in 25-80% of cases.[1,6,7,12,20-25].

The variability of angiographic diagnosis of vasospasm is explained by: a) lack of uniformity in the samples and in the values used for its identification and ranking (table 2); b) insufficient differentiation of the time when angiography is performed; c) poor angiographic technique, and d) low correlation with other diagnostic techniques or with an early initial angiogram.[10] Some authors define a specific reduction in the arterial lumen as significant (for example, 25, 30 or 50%), others accept any level of narrowing, and in some cases the calibre is not measured due to practical difficulties or is not communicated.[17,19-23].

The grading of vasospasms by transcranial Doppler (TCD) is difficult because of technical limitations and the heterogeneity of the values used. Diagnosis requires a second study to be compared with the baseline obtained within the first 72 hours of onset of subarachnoid haemorrhage.

Currently, performing an angiography daily or systematically for the sole purpose of determining whether there is vasospasm is not advisable due to: a) the occasional risk of complications (such as induction of vasospasm, cerebral stroke, arterial dissection and cardiac abnormalities); b) the amount of time and resources required for the procedure; c) the ease with which the disorder is recognised by less invasive, modern neurovascular diagnostic tests; d) the demonstration of arterial narrowing does not prove that clinical deterioration was caused by ischemia; and e) angiography does not allow vasospasm to be monitored. With reasonable use of non-invasive neurovascular tests, it is therefore possible to restrict the indication of DSA for patients who do not respond to medical vasospasm treatment and are candidates for endovascular therapy (fig. 3).

Transcranial Doppler

Transcranial Doppler (TCD) enables blood velocities to be measured in the proximal portions of large cerebral arteries and thus infer that increases in the average flow rate (AFR) are caused by a reduction of the vessel lumen. Compared with conventional TCD, the transcranial colour echo-Doppler device is more sensitive, making it possible to visualise intracranial vascular structures in real time. The main advantages of TCD are that it is non-invasive, requires no special means (contrast agents, gases or drugs), has a minimal risk of side effects, its cost is relatively low and it can be carried out serially in bedridden patients, in the room and during the intraoperative period.[24,26-32]

Detected AFR may be particularly informative for diagnosing vasospasm. Generally, very low or very high (<120 or >200 cm/s) MCA AFRs are useful for predicting angiographic vasospasm negatively or positively, while intermediate speeds have a low predictive value.[6,12,26,33] In contrast, Scherle et al[23] obtained a low positive predictive
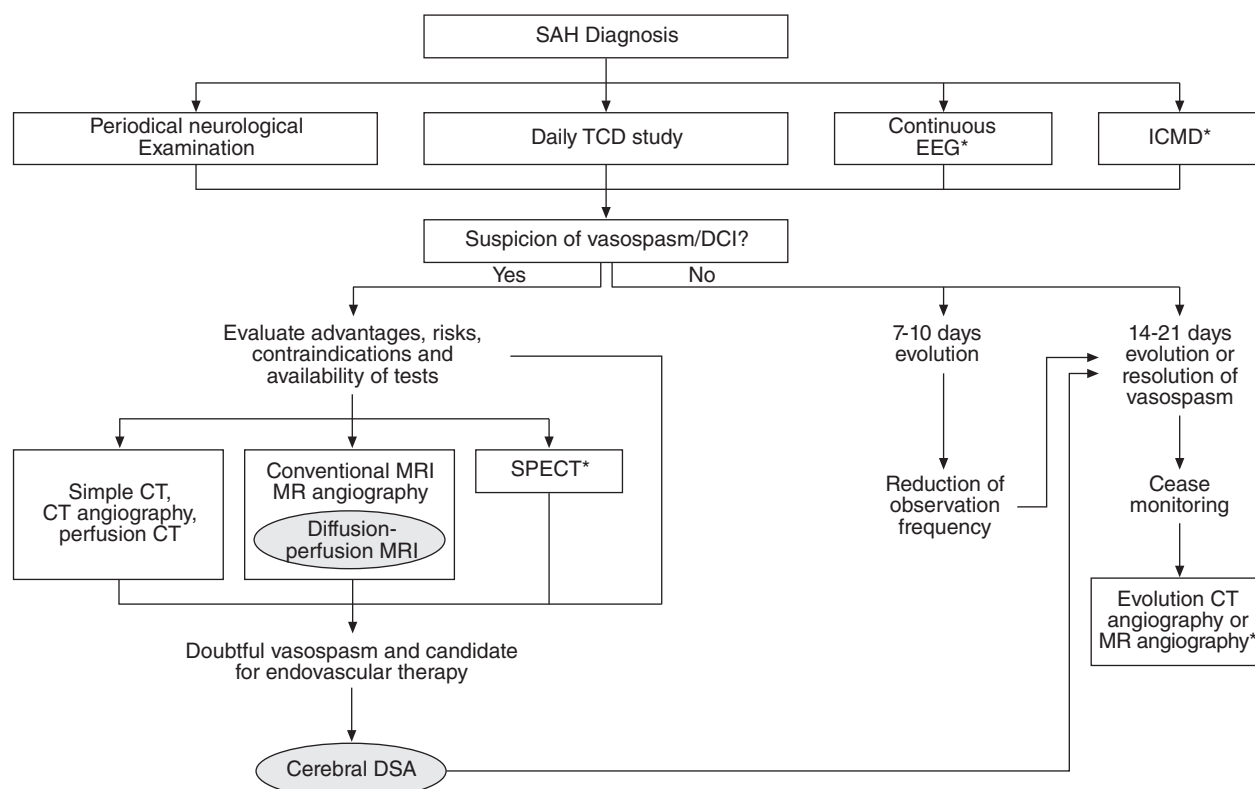
Figure 3 Diagnostic algorithm of cerebral vasospasm and delayed cerebral ischemia (DCI). The most recommended conventional patterns and alternatives applicable in specific situations are identified (*). DSA: digital subtraction angiography, EEG, electroencephalography; ICMD: intracerebral microdialysis; MRI: magnetic resonance imaging; SAH: subarachnoid haemorrhage; TC: Computerized tomography scan; TCD: transcranial Doppler.

value (42%) and good negative predictive value (87%) when correlating angiographic vasospasm taking the AFR of 120 cm/s as the cut-off point. The recommended AFR cut-off criteria for vasospasm varies in the remaining brain arteries: 130 cm/s (ACA), 110 cm/s (posterior cerebral artery), 80 cm/s (vertebral artery) and 95 cm/s (basilar artery).[33]

An increase in AFR is also the result of hyperaemia, alone or in combination with proximal vasospasm in the same vessel; it is usually associated with hypertension- haemodilution- hypovolaemia therapy. Lindegaard index values (ratio of the AFR in the cerebral vessel of the chosen carotid system to the AFR in the homolateral extracranial ICA) and the ratio of the basilar artery AFR to the average AFR of the vertebral arteries (total sum of the AFR on both sides / 2) are helpful in order to calculate these states (table 2).[27-34]

In the meta-analysis performed by Lysakowski et al,[19] it was concluded that TCD can be used with certainty to identify patients with MCA spasm (high positive predictive value), that there is no certainty of normality when the technique does not indicate spasm of this artery and that the evidence of accuracy or usefulness is scarce for the remaining situations and arteries. Most research on the subject has low methodological quality, patient samples are small and with low risk for the phenomenon, prejudice can not be excluded in the absence of blinded observers, and the reporting of the original data frequently cannot be assessed. Classically, we must rely on the definitions of

vasospasm issued arbitrarily, which do not necessarily correlate with DCI and other important data. Therefore, correlation coefficients compared with 2?2 tables based on arbitrary cut-off criteria would probably be more informative.

Generally, TCD methods have several important limitations: *a*) they do not offer the same structural detail as angiographic methods; *b*) they do not diagnose cerebral ischemia; *c*) they study only the proximal segments of large intracranial vessels; *d*) the results can have considerable variability and uncertainty among observers because the procedure depends on the operator and on the definition of critical thresholds and quality control at each institution; *e*) the acoustic window may be inadequate; and *f*) AFR increases may be related to several individual factors (blood pressure, blood volume, haematocrit, intracranial pressure, age, time of evolution) or to impaired autoregulation during haemodynamic manipulation.[19,31-33]

Given the TCD limitations, AFR values of the cerebral arteries should not be used in isolation when starting intensive treatment. It is also necessary to evaluate initial and evolution clinical data, and the results of other diagnostic tests applied. To assess the treatment intended for vasospasm, applying DSA should be considered when:

- TCD is normal during the risk period of vasospasm and clinical neurological deterioration occurs, with no other

obvious explanation, or there is clinical and sonographic discrepancy.

- There are normal AFR values for the ACA and MCA in patients with aneurysms of the anterior communicating artery.

Cranial computerized tomography

Faced with a delayed ischemic neurological deficit, images from simple cranial computed tomography (CT) show cerebral stroke caused by vasospasm in 20-40% of cases.[35,36] By means of this test, Rabinstein et al[35] described two common distribution patterns of cerebral stroke after SAH: a) single cortical, typically near the ruptured aneurysm, and b) multiple diffuse lesions, including those with subcortical location, and often unrelated to the site of rupture of the aneurysm. Most lesions detected were cortical with territorial or limiting distribution. Deep strokes tended to be clinically asymptomatic in the acute phase. Focal or diffuse distribution of vasospasm by TCD or angiogram was not useful in reliably predicting the subsequent stroke pattern. Haemorrhagic stroke from vasospasm is rare and occurs especially in patients undergoing induced hypertensive therapy.

Conventional cranial CT is less accurate than magnetic resonance imaging (MRI) and single-photon emission CT (SPECT), but it is widely available and its images are easier to obtain and interpret. With the development of technologies that have expanded the use of CT, namely CT angiogrphy and CT perfusion imaging, it is possible to integrate information on the spasm location with quantitative CBF measurement. All this can be done in a relatively short period and without moving the patient.[20-22,35]

Contrast CT perfusion is increasingly being used in emergency situations to assess DCI. Average transit time (ATT) maps are very sensitive in the screening of patients with acute cerebral ischemia, while relative cerebral blood flow (rCBF) and relative cerebral blood volume (rCBV) maps are more specific for stroke diagnosis. Angiographic vasospasm occurs with decreased rCBF, particularly when it is severe. There are three distinct patterns among the perfusion abnormalities possibly related to vasospasm (table 2). The technique is non-invasive, provides direct anatomic correlation and reports the haemodynamic state with a relatively high, quantitative and reproducible resolution.[20-22,36]

The determination of rCBF by xenon-enhanced CT perfusion scanning has been proposed to guide the medical management of vasospasm and to differentiate DCI from other processes in patients with SAH. The main disadvantages of this technique are: a) high sensitivity to motion artefacts associated with an acquisition time lasting several minutes; b) exposure to relatively high levels of radiation; c) contraindications for cases with severe respiratory disease or mechanical ventilation with a volume of less than 250 ml; d) doubts about precise parameter quantification; and e) possible side effects of xenon (nausea, dizziness and sedation), which make it difficult to steady the head. These reasons make xenon CT an experimental study that is an alternative to the other perfusion tests.[36]

Therefore, conventional cranial CT combined with contrasted CT perfusion scanning and CT angiography represents an accurate and advantageous diagnostic technique in patients with suspected vasospasm secondary to SAH. The multimodal CT protocol is particularly useful for unconscious patients, in whom clinical examination is uninformative.

Angiography by computerized tomography

CT angiography has emerged as a fast, accurate and minimally invasive method for precise anatomical description of intracranial vessels, diagnosis of intracranial aneurysms and diagnosis and monitoring of vasospasm. In small series, it is reported that the technique is perfect for detecting severe proximal spasm, and is very sensitive and accurate in the diagnosis of normal vessels. Sensitivity and accuracy are significantly reduced for slight-moderate proximal vasospasm. The concordance is excellent when comparing the severity of vasospasm determined by multi-section CT angiography and conventional angiography in proximal and distal arterial segments.[20,22,23]

A conventional cranial CT study is often indicated upon suspicion of vasospasm. This can be immediately followed by CT angiography and CT perfusion scanning. These possibilities make CT angiography a useful technique in emergency situations where accurate and early therapeutic action is needed. The angiographic method overcomes the limitations of DSA and MR angiography, especially in neurocritical or uncooperative patients. This is because it is quicker, requires fewer resources, does not hinder patient care, has fewer contraindications, has less frequent motion artefacts, carries no serious neurological risks and requires only minimal sedation in case of psychomotor agitation.[20,22,26]

Its disadvantages include: a) the need to bring the patient to the equipment; b) exposure to radiation; c) the administration of intravenous contrast and its potential adverse effects; d) lower resolution of images with respect to DSA; e) the difficulty of assessing the images with artefacts caused by metallic objects (e.g., clip artefacts); f) opacification of venous structures that hinders assessing intracavernous ICA and of the sylvian segment of the MCA; g) higher time demand for selecting useful images and post-processing, and h) the variability between observers in preparing and interpreting the images. For these reasons, CT angiography is recommended as a control angiography study for diagnosis when vasospasm is suspected and DSA is not available or does not involve endovascular treatment.[20,22]

Cranial magnetic resonance

Multimodal MRI studies consist of sequences of standard MRI images, echo-planar diffusion MRI images, Time-of-Flight MR angiography and dynamic gadolinium-enhanced perfusion MRI, and may include spectroscopic imaging. This protocol has allowed the following findings to be described:

- Ischemic lesions are visible on diffusion MRI at a very early stage after arterial occlusion and before

abnormalities appear on T2-weighted images. The lesions in both studies may be concomitant and reveal reductions in the apparent diffusion coefficient in the territory corresponding to the arterial spasm with no concomitant abnormalities on diffusion MRI.

- Perfusion abnormalities are more marked than diffusion abnormalities (mismatch, perfusion/diffusion). Small and sometimes multiple focal ischemic lesions are usually described in the diffusion MRI, surrounded by a larger area of decreased rCBF and increased ATT in all patients with symptomatic vasospasm. The most useful indicator in perfusion MRI is the ATT measurement, while CBV is usually normal or slightly decreased.
- Lactate, oedema and increased rCBV occur in the same area and are correlated with each other and with clinical neurological deficit.[36-39]

Despite the limitations of the technique (patient transport, cost, duration, test environment), diffusion-perfusion MRI can be safely applied in selected SAH patients and provides more detailed information than other neuroimaging techniques.[36-39]

Magnetic resonance angiography

Concordance of MR angiography with DSA is substantial. When considering each vessel separately, the specificity is excellent for all locations, as is the sensitivity for the ACA, although it is lower than sensitivity for the ICA and the MCA.[40] Among its advantages are the absence of exposure to ionizing radiation, non-requirement for intravenous contrast administration, and the possibility of serial studies.

The practical application of the technique by time of flight for the diagnosis of vasospasm has the following problems:

- The signal increased by methaemoglobin in the SAH adjacent to the arteries can cause false negative results of vasospasm in the subacute phase. The most severe affectation by vasospasm occurs precisely in those arteries.
- Endovascular coils or compatible aneurysm clips often make it difficult to visualise adjacent arteries, and their artefacts can increase false negatives of significant stenosis.
- The presence of non-compatible metal devices, such as aneurysm clips, and less advanced equipment for monitoring of neurocritical patients prevent its indication.
- The full study requires a long acquisition time and patient cooperation. The limitation as to acquisition time is higher in critically ill patients, frequently undergoing mechanical ventilation. Examination time can be reduced by limiting the observable arterial area to the anterior circulation, but this is a source of errors.
- Diffuse vasospasm results in a poorly defined MR angiography that is often difficult to interpret and should not be confused with artefacts or technical problems.

MR angiography is not an alternative to DSA and CT angiography in accurately assessing cerebral vasospasm,

but it does have a potential application as a non-invasive diagnostic technique in selected patients.[26,40,41]

Emission tomographies

SPECT and positron emission tomography (PET) can be useful in patients with poor clinical state, and offer a higher sensitivity than simple cranial CT for diagnosing cerebral strokes and their extension. SPECT is a comfortable technique for the patient, provides multiplanar images and cerebral arteriography can be ignored when faced with a negative cerebral ischemia study.[5,42]

Applying SPECT and PET systematically in DCI detection is limited due to: a) technical factors; b) reduced availability; c) economic cost; d) the possibility of errors in the analysis; e) the need to correlate the results with the structural neuroimage; and f) lack of clinical trials confirming its usefulness. In addition, PET is not feasible in emergency situations and its diagnostic accuracy is unknown.[36,42,43]

Electroencephalography

Electroencephalographic monitoring of SAH provides constant information about brain function and may allow the detection of reversible DCI. In the acute phase of stroke, electroencephalography (EEG) may show a polymorphous delta activity and the attenuation of fast activity. In addition, a high correlation between angiographic vasospasm and focal slowing of the EEG have been found.[14,15]

Digital EEG charts can be used to monitor the effects of sedatives and anticonvulsants, for early detection of epileptic seizures and cerebral dysfunction secondary to vasospasm. These charts can also be used to indicate the need for additional neurodiagnostic testing or therapeutic changes. Quantitative EEG changes tend to precede by 2-3 days the DCI manifestations detectable by clinical examination or other continuous monitoring techniques. A decrease in the alpha/delta ratio after stimulation (alpha power/delta power) greater than 50% in a single measurement is a parameter with high sensitivity and specificity for detecting DCI in patients suffering stupor or coma. The alpha/delta ratio can supplement the clinical exam in patients with SAH for the diagnosis of dysfunction from DCI. A decrease in relative variability of the alpha rhythm (6-14/1-20 Hz) has also been observed in this disorder.[14,15]

Continuous EEG is not included in usual neurointensive monitoring due to scepticism about the alleged vulnerability to artefacts, the equipment cost and dependence on neurophysiologically-trained personnel.[44] Despite this, continuous electroencephalographic monitoring may be recommended in patients at high risk of vasospasm and impaired consciousness.

Intracerebral microdialysis

Neurochemical monitoring by intracerebral microdialysis (ICMD) in the 7-10 days following intracranial aneurysm surgery has been proposed as a useful tool to characterise

the patterns of markers of energy metabolism (glucose, pyruvate and lactate), excitotoxins (glutamate and aspartate) and derivatives of neuronal damage (glycerol) in SAH. Compared with TCD and angiography, ICMD has a high specificity but low sensitivity as a tool for the diagnosis of delayed ischemic neurological deficit. The cerebral ischemic pattern (increase of lactate/glucose and lactate/pyruvate ratios greater than 20%, followed by an increase of 20% in glycerol concentration) precedes DCI manifestation by an average interval of 11 h. It was found that transient CBF reductions were correlated with extracellular elevation of glutamate and glycerol, while the lactate/pyruvate ratio was only noticeable after prolonged hypoperfusion. [43,44]

Although encouraging results have been described, ICMD has several limitations that invalidate its recommendation as a systematic neurointensive method: a) the need to place the catheter in the precise spot that may suffer ischemia; b) it does not allow evaluation of more than one brain region; c) measurements made in a restricted brain volume are difficult to extrapolate; d) the benefits as an early or more sensitive DCI indicator are uncertain compared with other detection methods; e) basal neurochemical values vary among individuals; f) there is a wide range of values from subclinical ischemia to severe ischemia; g) the scarce accuracy of the neurochemical processes that take place in DCI; h) reduced accuracy of the measurements for the development of reactive gliosis around the catheter tip; i) tissue trauma secondary to the invasive procedure,; and j) it is expensive, time consuming and requires experience in neurosurgery and analysis. [5,43,44]

Conclusions

Clinical reasoning and analysis of the design of the investigations carried out are key aspects in the indication of tests for the diagnosis of vasospasm and DCI in spontaneous SAH. The use of multiple and imprecise medical terms to describe vasospasm may make it more difficult to assess and manage patients. A grading method according to the diagnostic test proposed could serve to standardise the main research on the subject.

In current clinical practice, the most highly recommended and available pattern for the diagnosis and monitoring of vasospasm and DCI is the rational use of evidence addressed. The algorithm shown emphasises, in the first place, clinical and TCD examination, and outlines EEG monitoring in cases at high risk for vasospasm and impaired consciousness. We conclude that multimodal CT and MRI techniques are appropriate in specific situations for the early, adequate identification of parenchymal and/or cerebral artery disease. Digital subtraction angiography is the gold standard for diagnosis of cerebral vasospasm and is recommended when there is no response to medical treatment and the patient is a candidate for endovascular therapy. However, further research is needed to perfect the application patterns of the tests formulated.

Conflict of interests

The authors declare no conflict of interests.

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