Color Doppler of the extracranial and intracranial arteries in the acute phase of cerebral ischemia

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Abstract Vascular imaging greatly improves the possibility of locating the site of vascular occlusion in patients with acute cerebrovascular disease. Different occlusive patterns may underlie the same clinical presentation, with different prognosis and different treatment: for this reason, a diagnostic tool able to identify quickly the status of the extra- and intracranial vessels is needed. Color Doppler ultrasound of the extracranial arteries is a reliable and accurate method able to localize and quantify the carotid artery stenosis. The ultrasound quantification of the degree of stenosis is based on both morphological and velocimetric criteria: B-mode, color or power Doppler and spectral analysis are used for this purpose. Also the analysis of the plaque is an integral part of the ultrasound examination: the B mode plaque characterization (structure and surface) plays an important role in the evaluation of risk of stroke. So color Doppler ultrasound is able to select patients who may require medical therapy, carotid endarterectomy or angioplasty and stenting. Transcranial color Doppler is an inexpensive, reliable, fast, non-invasive, bedside tool: in the acute phase of stroke, it is able to evaluate quickly the intracranial arteries and monitor the possible recanalization of occluded vessel ensuring the follow-up of dynamic lesions, such as the intracranial stenosis and occlusions.

Keywords Atherosclerosis · Carotid and vertebral arteries · Stroke · Ultrasound

Riassunto L'imaging dei vasi extra e intracranici, nei pazienti con insufficienza cerebrovascolare acuta, migliora

notevolmente la possibilità di localizzare la sede dell'eventuale occlusione vascolare. Infatti, differenti patterns occlusivi possono comportare una medesima presentazione clinica dello stroke, ma con diversa prognosi e diverso trattamento: per questo motivo è necessario uno strumento diagnostico in grado di identificare rapidamente lo stato dei vasi extra e intracranici. L'eco-color-Doppler delle arterie extracraniche è un metodo affidabile e preciso in grado di localizzare e quantificare la stenosi carotidea. La quantificazione ecografica del grado di stenosi è basata su criteri morfologici e velocimetrici: per questo scopo sono utilizzati il B mode, il color/power Doppler e l'analisi spettrale. Anche l'analisi della placca è parte integrante dell'esame ecografico: la caratterizzazione ultrasonografica della placca (struttura e superficie) svolge, infatti, un ruolo importante nella valutazione del rischio di stroke. In questo modo lo studio ultrasonografico delle arterie extracraniche è in grado di selezionare i pazienti che necessitano di terapia medica, di endoarteriectomia carotidea o di angioplastica/stenting. Il transcranial-color-Doppler è uno strumento affidabile, non invasivo, ripetibile, eseguibile al letto del paziente: nella fase acuta dello stroke è in grado di valutare rapidamente le arterie intracraniche e monitorare l'eventuale ricanalizzazione del vaso occluso garantendo il follow-up di lesioni dinamiche quali le stenosi e ostruzioni intracraniche.

Introduction

In all patients with symptoms and signs suggestive of acute cerebrovascular disease (CVD), other diagnoses should be excluded and the diagnosis of CVD should be confirmed with identification of stroke subtype: in fact, an etiological

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classification is fundamental for diagnostic, prognostic and therapeutic implications.

In the acute phase of cerebral ischemia, the imaging of the extra- and intracranial arteries is essential to establish as soon as possible the mechanism of cerebral ischemia; vascular imaging greatly improves the localization of the site of vascular occlusion [1].

Color Doppler Ultrasound of the extracranial arteries (CDU) and transcranial color Doppler (TCCD) are noninvasive imaging tests to explore the extra- and intracranial vessels and are useful to identify if there is a blockage and to localize any stenosis/occlusion in extracranial or intracranial vessels.

In particular, CDU is performed to have information about the degree of stenosis, the composition/surface of the carotid plaque, to determine the pathology and to select patients who may require medical therapy, carotid endarterectomy (CEA) or angioplasty and stenting [2, 3].

TCCD is able to detect, in real time, the site of the intracranial stenosis/occlusion and may be crucial to establish the type of acute therapy [4, 5].

Color Doppler ultrasound of the extracranial vessels in patients with acute cerebrovascular disease

Patients with acute CVD are candidates for urgent CDU evaluation and immediate initiation of appropriate medical or surgical treatment.

In the acute phase of cerebral ischemia, CDU is performed to localize the possible stenosis/occlusion, to have information about the degree of stenosis and the composition/surface of the plaque.

Ultrasounds (US) in acute phase also allow the diagnosis (or suspicion) of uncommon causes of stroke, so US imaging will help to identify the underlying mechanism of the stroke (atherothrombotic, embolic, dissection or other).

In this paper, we will discuss the US role in the most common and important diseases: atherosclerotic and dissection pathologies.

CDU and atherosclerotic pathology

Emergency CDU is needed to recognize the unstable plaque with a high-grade stenosis or with morphologic features of high risk for intracranial embolization, in fact CEA or angioplasty and stenting may be indicated when US or emergency angiographic examinations show the presence of a critical stenosis, an acute thrombosis or a thrombus/atheroma floating in the lumen [6, 7].

In particular, US studies have demonstrated an association between symptoms and echolucent plaques, surface ulceration, and degree of stenosis [8].

Anechogenic plaques (lipid rich, with intraplaque hemorrhage and low calcium content), heterogeneous plaques or plaques presenting an irregular surface are unstable with the potential for embolic accidents, in symptomatic patients, these plaques have been shown to herald an increased risk of subsequent development of transitory ischemic attack (TIA) or stroke (Figs. 1, 2, 3).

The degree of stenosis is the most correlated clinical event: the greater is the stenosis, the greater is the risk of TIA/stroke and the benefit of surgery [9]. So particular care should be taken to evaluate the percentage of stenosis.

Fig. 1 Stable plaque: homogenous, non-hemodynamic plaque with echogenic cap

Fig. 2 Unstable plaque: heterogeneous plaque with surface irregularity and high degree of luminal stenosis

Fig. 3 Unstable plaque: high degree of luminal stenosis with flow acceleration (peak systolic velocity = 219 cm/s) in the region of the stenosis

Although, CDU cannot precisely define the stenosis diameter percentage, a range of stenosis diameters may be estimated. The main parameters that should be used in diagnosing and grading internal carotid artery (ICA) stenosis are the peak systolic velocity (PSV) and the presence of plaque on grayscale and/or color Doppler/duplex US images.

The most significant sonographic features of a severe ICA stenosis include: a $\geq 50\%$ lumen diameter reduction of visible plaque at gray-scale imaging and a PSV greater than 230 cm/s, spectral broadening, color aliasing and post stenosis turbulence at color Doppler and pulsed wave Doppler imaging [10].

In symptomatic patients, the distinction between near occlusion and total, inveterate, ICA occlusion requires particular attention. This distinction may be difficult but it is clinically very important: patients with near occlusion may be surgical candidates, while patients with total occlusion are not [11].

In case of near occlusion, the velocity parameters may not apply, since velocity may be high, low, or undetectable: this diagnosis is established primarily by demonstrating a markedly narrowed lumen in color or power Doppler US and the presence of a Doppler signal orthograde downstream of the ICA “occluded” and in the siphon.

Total occlusion findings are direct visualization of a thrombus at gray-scale imaging, absent flow at color Doppler imaging, and damped resistive flow in the common carotid artery (CCA) at pulsed wave Doppler imaging.

If clinically appropriate, neuroradiological test may be used for confirmation in this setting.

The distinction between recent and inveterate ICA occlusion is equally important. In fact, while patients with recent occlusion may be surgical candidates, patients with inveterate occlusion are not at low risk of embolic phenomena.

Fig. 4 Inveterate ICA occlusion: ICA of small caliber and thrombus with a large hyperechoic component

Fig. 5 Recent ICA occlusion: ICA with preserved caliber and thrombus with large hypoechoic component

The CDU characteristics of recent ICA occlusion are, more frequently, thrombus with large hypoechoic component and ICA with preserved caliber, whereas the US features of inveterate ICA occlusion are thrombus with a large hyperechoic component and ICA of small caliber (Figs. 4, 5).

In patients who have an ischemic event, CDU is also capable of giving other valuable complementary, but very important, indirect informations such as about hemodynamic stenosis, or occlusion, of the ICA intracranial segment (in this case, in the explorable extra cranial district, is present high-resistance flow) and indirect information about heart rate and heart valves.

CDU and cervical-artery dissection

CDU is an excellent tool in screening for cervical-artery dissection (CAD) defined as the splitting of the arterial wall of the carotid or vertebral artery.

CAD, a major cause of cerebral ischemia in young adults, can lead to various clinical symptoms, some of which are benign (headache, neck pain, Horner's

syndrome, and cranial nerve palsy) but most patients have a stroke or TIA. The typical clinical manifestation of CAD is pain on one side of the head, face or neck, accompanied by a partial Horner's syndrome, and followed hours or days later by cerebral or retinal ischemia.

CAD dissection is associated with hematoma in the wall of carotid or vertebral artery, secondary either to an intimal tear or to direct bleeding within the arterial wall caused by ruptured vasa vasorum. The intramural hematoma can expand toward the intima (resulting in a stenosis of the artery), or the adventitia (resulting in an aneurismal dilatation of the artery) [12].

The treatment of CAD is still debated. Symptomatic CAD requires mainly medical management: although there are no randomized trials evaluating antithrombotic treatment, the conventional treatment for CAD, to prevent thromboembolic complications, is anticoagulation (heparin followed by oral warfarin) unless there are contraindications such as intracranial dissection or intracranial extension of the dissection.

Recent data have shown that thrombolysis in CAD appears safe (but more data on efficacy is required), and that endovascular therapy should be considered when medical management is insufficient [13, 14].

In the ICA dissection, the main US findings are [15, 16]:

- an arterial luminal flap or false lumen (the most specific sign) (Fig. 6);
- bulbar and/or proximal ICA hematoma or low-reflective thrombus with or without narrowed true lumen (Fig. 7);
- bulb and origin of ICA with high-resistance flow pattern to a stenotic hematoma in the cervical ICA segment not explored directly with the US ("indirect" sign) (Fig. 8). This non-specific feature is the most frequent sign and is also present in atherosclerotic or cardio embolic occlusion of the distal ICA segment. It should indicate the possibility of a dissection in an appropriate clinical setting (young patient with unilateral headache or partial Horner's syndrome and followed by cerebral or retinal ischemia).

In the vertebral artery (VA) dissection, ultrasonographic specific signs (segmental dilation of the vessel, eccentric channel) are detectable in only 20 % of patients, while non-specific signs (low-reflective thrombus, high-resistance spectral waveform, or absence of flow with no spectral Doppler waveform) are detectable in 92 % of patients [17, 18].

In conclusion, emergency CDU is very useful in the initial assessment of patients who are thought to have a CAD (unilateral headache without focal neurology): although the CDU most frequent signs are indirect and not

Fig. 6 Type 1 ("direct" sign 1): intimal flap with proximal ICA division into two compartments

Fig. 7 Type 2 ("direct" sign 2): bulbar hematoma (low-reflective thrombus)

Fig. 8 Type 3 (indirect signs): absence of atherosclerotic plaques (patency of the bulb and the first part of the ICA) and high-resistance flow pattern to the presence of hematoma in the ICA distal segment

Fig. 9 Narrowing of the middle cerebral artery lumen

specific, an abnormal pattern of flow is identified in more than 90 % of patients.

CAD is a dynamic process: morphological and clinical findings may change within days or hours. So US technique is the diagnostic investigation of choice for control of progressive morphological and hemodynamic changes [19].

Transcranial color Doppler in patients with acute cerebrovascular disease

In the acute phase of cerebral ischemia, patients may show similar clinical presentation but the occlusive patterns of the intracranial arteries and the severity of perfusion deficit may be dramatically different.

TCCD is one of the tools to explore the intracranial vessels, to identify if there is a blockage and to localize any stenosis/occlusion. In particular TCCD, in the acute phase of stroke, is very useful to monitor recanalization during therapy [20].

In case of focal hemodynamic intracranial stenosis (IS) the TCCD features are, in the region of the stenosis, a local flow acceleration, a disturbed flow with spectral broadening and retrograde flow components due to the increase in low frequency (Figs. 9, 10). Distal to the hemodynamic stenosis is present reduced maximum and mean flow velocities.

In case of a very severe stenosis, or a long (>1 cm) intracranial segment stenosis, or multiple stenoses in a single artery, a combination of low mean flow velocity and high-pulsatility index is possible [21, 22].

In presence of intracranial artery occlusion the TCCD features are the absence of color or power flow signal in the artery occluded, with no or minimal flow at the

Fig. 10 Narrowing of the middle cerebral artery lumen with local flow acceleration, disturbed flow with spectral broadening in the region of the stenosis due to the increase in low frequency and retrograde flow components

Fig. 11 Absence of power flow signal in the middle cerebral artery occluded and presence of normal appearance of other intracranial arteries

corresponding Doppler spectrum and presence of normal appearance of other ipsilateral intracranial arteries (Fig. 11).

TCCD, in acute stroke patients, is useful for: a) diagnostic; b) prognostic; c) therapeutic value.

- TCCD is able to detect, in real time, the site and to record the flow of the intracranial artery with steno/occlusion (US flow-grade classification): grade 0 = absent flow signal; grade 1 = minimal flow signal; grade 2 = blunted flow signal; grade 3 = dampened flow signal; grade 4 = stenotic flow signal; grade 5 = normal flow signal [23].
- TCCD is useful for prognostic value. Patients with distal middle cerebral artery (MCA) occlusion are twice as likely to have a good long-term outcome as patients with proximal MCA occlusion and patients with terminal ICA occlusions are least likely to show early or long-

term response. Also, the 5 degrees of the US flow-grade classification correlate with initial stroke severity, clinical recovery, and mortality in intravenous thrombolysis treated stroke patients [24, 25].

- c) As clinical response to thrombolysis is influenced by the site of occlusion, TCCD may be crucial to determine the type of acute therapy to institute. In fact, intravenous thrombolysis is more efficacious for distal thrombus whereas intra-arterial thrombolysis or mechanical thrombectomy may be more efficacious for treatment of a proximal large-vessel occlusion.

Also, TCCD is particularly useful in the monitoring of the reperfusion and the effectiveness of therapy. In acute phase, the intracranial stenosis/occlusions have a dynamic course and the speed of clot lysis is the strongest predictor of good outcome: unlike sudden and stepwise TCCD patterns, slow recanalization is associated with poorer short and long-term outcomes [26].

In absence of early recanalization during intravenous thrombolysis, there is clinical benefit to proceed to intra-arterial therapy [27]. In this case early TCCD patterns may help in making the choice of the modality of thrombolysis.

Finally TCCD, with its ability for continuous monitoring, is the only test for detection of cerebral microembolic signals (MES), harbingers of stroke, that may be present in various cardiovascular and cerebrovascular disorders and procedures.

MES are particles of thrombus or atheromatous plaque or particles of air in cerebral circulation: they can derive from ulcerated plaques, from atrial thrombus, from prosthetic heart valves, as well as during TEA or arterial stenting. The US monitoring allows the assessing of the source of embolism and provides important pathophysiological information and the evaluation of the risk for embolic stroke [28, 29].

In conclusion, TCCD, in stroke patients, is noninvasive, relatively inexpensive, easily repeatable diagnostic test ideal in the diagnosis and monitoring of the effectiveness of therapy. While the neuroimaging, in acute stroke, is principal in the space domain, TCCD has introduced the time domain into the management of stroke patients by providing serial imaging and monitoring reperfusion of intracranial arteries after stroke [30].

CDU and TCCD limits

CDU has some limitations; although this technique is excellent in initial evaluation of the extracranial cerebral vessels, the presence of calcifications in the carotid plaque tends to make the study less accurate.

Also, because US cannot assess the intracranial portion of the ICA, CDU cannot recognize the non-hemodynamic stenosis of this segment and tandem lesions may be missed. In a similar manner, proximal stenosis of the left CCA and of the innominate artery cannot be evaluated for their origins from the aortic arch.

The major limitations of TCCD are the high operator dependency and a 10–15 % rate of inadequate temporal windows, particularly in older women, due to the thickness of the skull. Other limitation is related to the difficulty in studying distal segments and non-hemodynamic stenosis.

These limitations can be corrected through training and the use of contrast agents [31].

Of course, when it is clinically appropriate, other neuroimaging modalities are necessary for the final confirmation of the US diagnosis.

Conclusion

CDU and TCCD are inexpensive, easily repeatable, fast, noninvasive, reliable tools for evaluating the extra- and intracranial arteries and may be considered as the stethoscopes of stroke neurologist who manages patients with acute CVD.

The US imaging of the extra cranial and intracranial vessels can identify, in less than 15 min in the emergency room, the underlying mechanism of the stroke allowing the immediate start of effective therapy.

In symptomatic patient, CDU should be performed rapidly to identify patients with unstable plaque, with a high-grade stenosis and morphologic features of high risk for intracranial embolization and to select patients who may require CEA/angioplasty and stenting or medical therapy.

CDU is very useful in the initial assessment of patients with a suspected CAD: it is impossible to recommend neuroradiological (NR) test in every patient with unilateral headache without focal neurology, since the yield would be extremely low. So early US diagnosis allows the selection of patients for early NR tests and the initiation of a proper treatment in patients with CAD before the neurological symptoms.

TCCD is important to detect, in real time, the site of the intracranial stenosis/occlusion and may be crucial to determine the type of acute therapy and monitor its effectiveness.

Conflict of interest Franco Accorsi declares that he has no conflict of interest.

Informed consent All patients provided written informed consent.

Human rights All procedures followed in accordance with ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5).

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