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Overview

Ultrasound diagnostics of carotid and vertebral arteries

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Stroke is the third leading cause of death and the main cause of major disability worldwide. Each year more than 700,000 people experience a new or recurrent stroke and on average someone dies every 4 min of a stroke *(1)*. In Serbia stroke is the first cause of death among women and the second one among men.

While the percentage of strokes attributed to carotid disease is relatively low, the overall social and economic burden is high *(2)*. It is, therefore, important to identify and manage carotid atherosclerosis with the aim of stroke prevention.

The presence of an atherosclerotic lesion in the carotid bulb or in the extracranial internal carotid artery (ICA) is associated with elevated stroke risk *(3)*. Several mechanisms are attributable to the increased risk of cerebrovascular events including decrease in the blood flow resulting from critical stenosis or occlusion, or the stenotic lesion can also be the source of thromboembolic events.

In this article the authors are going to focus on some important aspects of ultrasound diagnostics of extracranial parts of brain arteries.

ULTRASOUND IMAGING OF CAROTID ARTERIES

Approximately 5–10% of all individuals aged 65 years or over has an asymptomatic ICA stenosis of 50% luminal narrowing or more *(4)*. An increasing degree of luminal narrowing is associated with an increasing risk of stroke in asymptomatic ICA stenosis. For every 10% increase in luminal narrowing, the stroke risk increases by nearly 31%, or 0.6% (in absolute terms) per year *(5)*. Stenoses with more than 95% luminal narrowing may be associated with a reduced stroke risk in comparison with stenosis of between 80 and 95% *(5)*. After an ischemic event in the territory of the stenosed ICA the annual major stroke risk increases to between 8 and 13% *(6)*. This risk is substantially higher within the first 6 months after the index event than thereafter. In symptomatic patients too, the degree of stenosis modulates the risk of stroke; for every 10% increase in ICA luminal narrowing, the stroke risk increases by approximately 10% (absolute risk increase of approximately 0.4% per year) *(6)*. Similarly, the risk decreases in cases of more than 90% luminal narrowing *(6)*.

Cervical ultrasound is therefore the diagnostic procedure most frequently used to detect and quantify atherosclerotic lesions in the ICA. It is not only important for determining stroke etiology in acute management but also for determining the individual stroke risk in asymptomatic

patients. In the future, the stented ICA could be closely monitored using only ultrasound technology.

Advanced plaque imaging techniques nowadays allow to analyze plaque morphology and its characteristics, as well as the presence of plaque's complications such as ulceration, hemorrhage and thrombus. The capability to identify plaques that are more prone to fragment and embolize is now vital for the early diagnosis, prevention, and treatment of stroke and neurological side effects *(7)*.

CAROTID STENOSIS

Degree of carotid stenosis

Indirect Signs

Indirect signs of an ICA stenosis derive mainly from hemodynamic alterations in the carotid system. It is therefore doubtless that these indirect signs may only be detectable in cases of high-grade ICA stenosis, with significant flow reduction (80% luminal narrowing) on the affected side. Under normal conditions, the blood flow in the periorbital arteries, mainly in the supratrochlear artery, is intracranial to extracranial. Owing to the higher perfusion pressure in the ophthalmic artery, originating from the intracranial portion of the ICA, than in the facial artery, as a branch of the external carotid artery, the blood flow in this anastomosis is directed towards the ultrasonic probe. A significant reduction of blood flow compared with the nonaffected side, an oscillating flow pattern, no flow, or most frequently, an inverse flow direction, all indicate increasing hemodynamic compromise in the case of ICA stenosis or occlusion *(8)*. Nevertheless, owing to the considerable variation in the flow pattern in the supratrochlear artery in the case of ICA disease, the accuracy of supraorbital Doppler, on its own, is only moderate. In cases of significant ICA stenosis, the Doppler flow pattern derived from the ipsilateral CCA changes showed an increase in the pulsatility index (decrease in diastolic velocity) and a reduction in the blood flow *(9)*. Comparing the CCA peak systolic (PSV) or mean velocity (MV) or pulsatility index of the affected with those of the nonaffected side can help to identify high-grade ICA stenosis.

In conclusion, the comparison of indirect parameters, such as supraorbital Doppler findings and CCA Doppler spectrum parameters, with the nonaffected side serves as a confirmatory test to affirm the direct findings in cases of highgrade ICA stenosis or occlusion (see below). The diagnosis and grading of carotid lesions should not be determined using this test alone.

Atherosclerosis of carotid artery: is the stenosis a sole predictor of stroke? Significance of »vulnerable plaque«?

In the recent past the degree of carotid artery stenosis was considered the only determinant factor to address patients to treatment *(6),* while at present several other factors are considered potentially important markers for future cerebro-vascular events *(10),* including plaque composition, presence and state of the fibrous cap (FC), intra-plaque hemorrhage, plaque ulceration and plaque location *(11)*.

In the past years, the degree of luminal stenosis has been used as a direct measure of atherosclerosis severity. However, in 1988, angiographic and subsequent histopathologic studies showed that plaque erosion and disruption were common morphologic features in symptomatic lesions, indicating that luminal narrowing was not the sole predictor of myocardial infarction *(12)*. Similar findings were later observed in the carotid arteries. Since low grade stenosis were demonstrated capable to produce cerebral ishaemic events, looking to plaque morphology beyond stenosis degree started to appear appropriate. For these reasons the concept of »vulnerable plaque« was introduced into surgical, histopathological and imaging areas, referring to atheromas containing large necrotic cores covered by a disrupted fibrous cap with a higher tendency to rupture, embolization and thrombosis.

In the 2007 Saba *et al. (11)* compared Multi-Detector CT-Angiography (MDCTA) techniques (MDCTA) and Ultra- Sound Echo- Color- Doppler (US ECD) in the

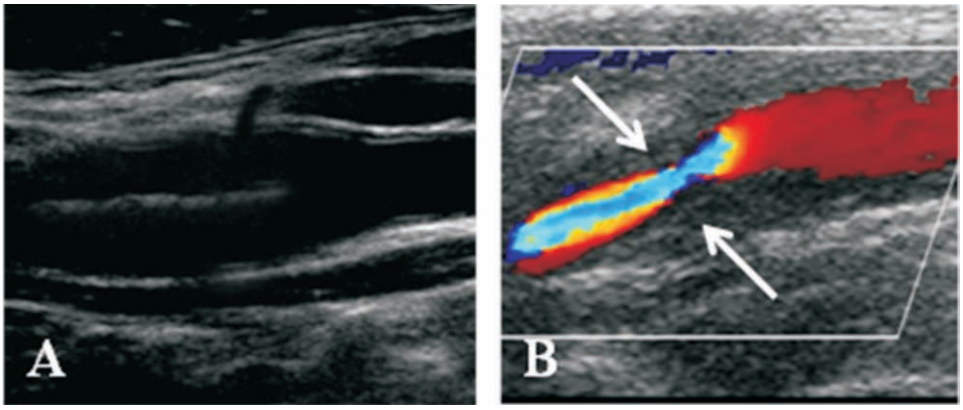

Figure 1. *A. Normal CCA bifurcation. B. Stenosed ICA (arrows).*

detection of plaque ulceration by using surgery as gold standard, demonstrating that the diagnostic accuracy of MDCTA is significantly higher (93% versus 37.5%).

Ulcerated plaques can be categorized according the classification described by Lovett *et al. (13)* where type 1 is an ulcer that points out perpendicular to the lumen, type 2 has a narrow neck and points out proximally and distally, type 3 has an ulcer neck proximally and points out distally, type 4 has an ulcer neck distally and points out proximally. Lovett *et al. (13)* demonstrated that type 1 and type 3 are the most frequent type of ulcers, however without any association with increased risk of adverse cerebrovascular events.

Plaque Surface Characteristics

Irregularities and Ulceration

Plaque surface disruption in the ICA, leading to plaque ulceration and intraluminal thrombus formation, is a key stage in the transformation of asymptomatic into symptomatic ICA lesions *(14)*. Detection of such pathoanatomical features may, therefore, be of clinical relevance. In a pathoanatomical validation study, it has been compared the ultrasonographic findings of plaque surface ulceration (i.e., plaque niche filled with reversed flow from both a longitudinal and transverse view without aliasing) with the corresponding pathoanatomical findings *(15)*. In conclusion, plaque surface characteristics cannot be diagnosed from ultrasound examinations with a sufficient degree of accuracy.

Intraluminal Thrombus Formation

Intraluminal thrombus formation is a major precursor of distal arterioarterial embolization *(14)*. In some cases, a mobile structure, mostly hypoechoic, can be found at the distal part of an atherosclerotic lesion. This is most probably caused by the tail of an intraluminal thrombus formation, originating from a ruptured plaque surface *(16)*. Nevertheless, the prevalence of this in symptomatic and asymptomatic patients with high-grade ICA stenosis has not yet been reported. Furthermore, there is some speculation that hypoechoic atherosclerotic plaque is partially composed of thrombotic material, thereby constituting an unstable lesion *(17)*. At present, the diagnostic accuracy of ultrasound in predicting intraluminal thrombus formation compared with a pathoanatomical standard of reference is still unclear.

Plaque remodeling and location of the plaque

Usually major atherosclerotic alterations occurs at the outer wall of the proximal segment and sinus of the internal carotid artery, in the region of the lowest wall shear stress. Plaque thickness is the least on the flow divider side at the junction of the internal and external carotid arteries where wall stress is the highest *(18)*.

The concept of remodeling considers the morphological and ultra-structural variation of a plaque in time. Thus, histological analysis of coronary plaques performed within 1 week after myocardial infarction demonstrated features of instability, while tissue evaluations performed within larger time intervals were similar to those in patients with stable angina. These observations point out that atherosclerotic plaques may change in time and that some determinants of instability may appear transitorily.

Recent studies indicated that carotid plaque eccentricity can predict the development of a cerebrovascular event. Ohara *et al. (19)* showed that eccentric stenosis was associated with a significantly increased incidence of ipsilateral events if compared with concentric stenosis. In the 2007 Hardie *et al.* (cit. u 7) demonstrated that expansive carotid remodeling is significantly greater in patients with cerebral ischemic symptoms than in asymptomatic patients, and that the extent of remodeling may indicate underling atherosclerotic plaque vulnerability.

Assessment of Plaque Morphology

Ultrasound B-mode is presently the best method for demonstrating arterial wall thickness and minor plaques, providing images of the wall itself and not only from the blood column.

In addition, moderate disease can be imaged in longitudinal and cross sectional planes. In severe disease, cross-sectional B-mode images are more difficult to generate because of shadowing and other artifacts. The same is true for color flow. Therefore, the more severe a stenosis, the more hemodynamic criteria are prevailing *(20)*. The relationship between area and diameter reduction depends on the type of stenosis, ie, whether it is concentric or eccentric. The latter is frequent if the plaque grows opposite to the flow divider. In this case, diameter and area reduction are similar; however, in concentric narrowing, degree of stenosis measured in percentage area reduction is higher than the measured diameter reduction *(20)*.

Quantification of carotid artery stenosis

It has been said previously that symptomatic patients with severe stenosis (>70%) benefit from CEA, and it is therefore vital to image and accurately measure the site of severe narrowing. However, pathological assessment of carotid plaques has also demonstrated that risk of embolism and thrombosis is not only associated with the size of the plaque but also with its composition *(7)*. The ability to image and identify the »vulnerable plaque« and especially those with hemorrhage will be vital in early diagnosis, prevention, and treatment of stroke and neurological side effects.

Toward the general attitude stenosis degree is currently considered a leading parameter for treatment decisions. Three large multi-centric randomized studies, NASCET (North American Symptomatic Carotid Endarterectomy Trial), ECST (European Carotid Surgery Trial) and ACAS (Asymptomatic Carotid AtheroSclerosis Group), provided cut-off values for degree of stenosis, indicating possible benefits of CEA *(21)*. The most used methods to quantify the degree of carotid artery stenosis are NASCET and ECST, both evaluating the degree of stenosis as the per-

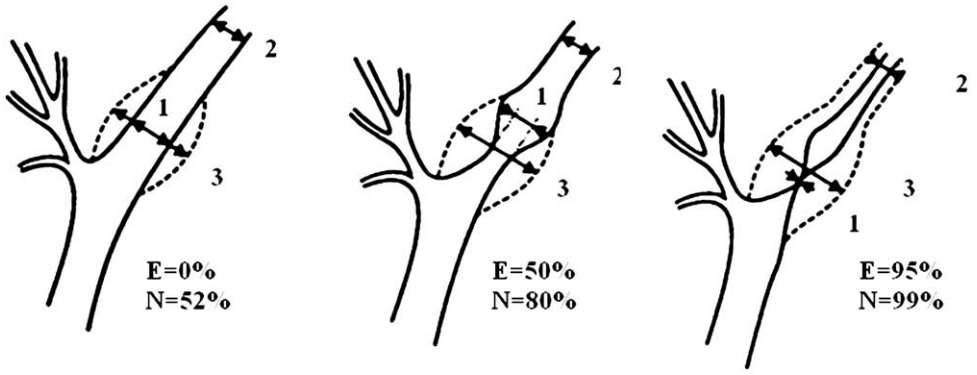

Figure 2. *Schematic comparison of NASCET and ECST methods of evaluating the degree of ICA stenosis. N – 'NASCET method'; E – 'ECST method'. See text for details.*

centage reduction in the linear diameter of the artery. To quantify the degree of the stenosis with NASCET and ECST methods, measurements must be performed on a strictly perpendicular plane to the longitudinal axis of the vessel; but it has to be underlined that some differences in the assessment of stenosis degree exist between NASCET and ECST and that the stenosis values derived from these methods on the same vessel **are not equal.** Namely, the NASCET method calculates the ratio between the lumen diameter at the stenosis site (1 in Figure 2) and lumen diameter of the distal, healthy ICA (2 in Figure 2), measured at the level of the II cervical vertebra) (Figure 2). The ECST method calculates the ratio between the lumen diameter at the stenosis site (1 in Figure 2) and the total carotid diameter (including the plaque) which is presumed former diameter of the same ICA segment (3 in Figure 2) (Figure 2). This measurement technique determines that ECST stenosis degree are larger compared to NASCET values (e.g. a 83% ECST usually is a 70% NASCET (22). These differences can not be overcome.

It is important to note that the NASCET method describes predominantly the hemodynamic significance of ICA stenosis (relation of the inflow to outflow diameter), whereas the ESCT method reflects more the amount of atherosclerotic tissue at the stenosed segment.

But recently one study *(23)* demonstrated that the entity of difference between NASCET and ECST measurements at different degree of stenosis varies markedly; generally, the entity of variation strongly and inversely depends on the degree of stenosis: even more, the proportional error tends to zero with the increase of stenosis degree.

Recently Jaff *et al. (20)* proposed that Computed angiography (CTA) may represent an appropriate first exam for patients with an high likelihood of vascular disease. On the other hand for screening patients with a lower likelihood of neurovascular pathology, Ultra-Sound Echo-Color-Doppler (US-ECD) should be selected. For asymptomatic patients scheduled for surgery as coronary artery bypass graft, abdominal aortic aneurysm and

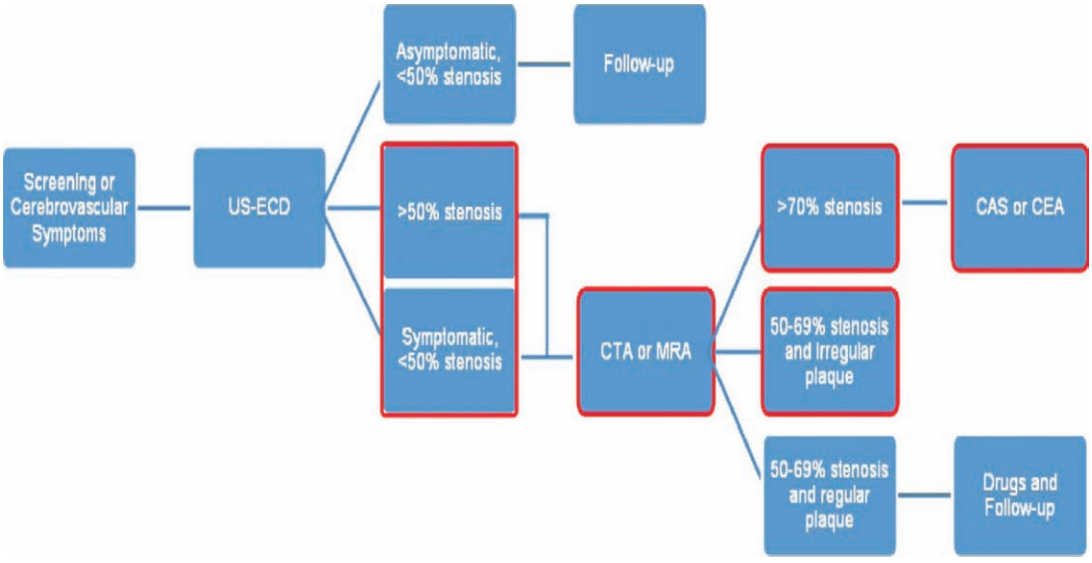

Figure 3. *Diagnostic flow-chart for determining degree of ICA stenosis (7).*

lower limb ischemia, US-ECD represents an accurate and cost-effective non-invasive screening tool *(20)*. If significant steno-obstructive disease of the ICA is detected with US ECD, international guidelines suggest that CTA as well as MRA can be used to confirm the diagnosis and to precisely determine the acurate degree of stenosis and ensure appropriate treatment planning

US-ECD is globally accepted as the standard imaging modality for first-line diagnosis of atherosclerosis of the carotid artery bifurcation. This high-resolution, non-invasive technique is readily available, rapidly applicable, and can be performed at relatively low cost.

Recommendations for carotid stenosis assessment

The NASCET method of measuring a stenosis should be the standard; the local narrowing (ECST) can be measured in addition, but it must be declared as such. This will avoid confusion. Grading of carotid stenosis by diagnostic ultrasound should be primarily based on morphological information (B-mode, color flow, or B-flow imaging) in low to moderate degrees of stenosis *(20)*. In addition to degree of narrowing, plaque thickness, plaque length, and residual lumen should be reported. Velocity measurements in a stenosis (PSV and carotid ratio) alone are not sufficient to differentiate a moderate from a severe (>70% NASCET) stenosis with sufficient clinical reliability. It is recommended that, in addition, a search for collateral flow is made in the ophthalmic artery branches (continuous wawe [CW] Doppler) or the anterior cerebral artery (transcranial Doppler or color-coded duplex sonography) *(20)*.

Furthermore, it is recommended that the poststenotic flow velocity distal to flow disturbances is examined, in which a reduction of velocities (comparison with the unaffected contralateral side or absolute reduction) allows additional grading within the category of severe stenosis *(20)*.

Hemodynamic criteria are appropriate for grading moderate to severe stenoses.

US-ECD, contrast-enhancement

Recent studies demonstrated that late onset of plaque enhancement at US after intravenous injection of microbubbles-based contrast agents is greater in symptomatic lesions than in asymptomatic ones *(24)*. This finding may merely represent the fact that symptomatic plaques have larger intra-plaque neovascularization than asymptomatic plaques and may thus more circulating microbubbles, as demonstrated by Coli *et al. (25)* in correlation with histological density analysis of microvessels. Furthermore, microbubbles have now been designed so that they can specifically bind to various molecules, therefore, allowing functional and molecular imaging. Recently perfusion imaging using micro-bubbles as contrast agents for US-ECD has been made feasible through developments in the ability to detect harmonics and overtones produced by the bubbles over tissue noise.

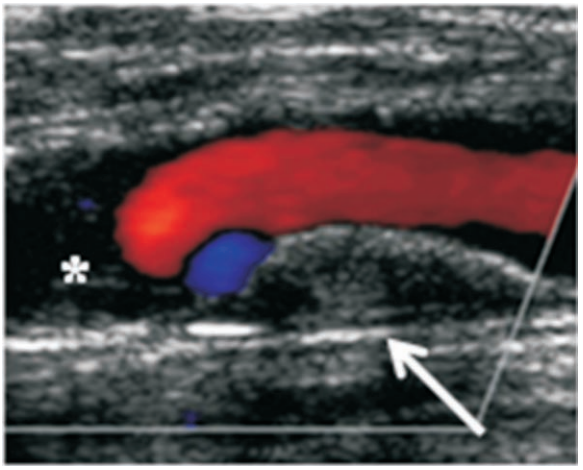

Figure 4. *ICA occlusion (asterix) with heterogeneous plaque (arrow).*

Carotid Occlusion

Ultrasonic Criteria

The complete atherosclerotic occlusion of the ICA is ultrasonographically characterized by *(1)* the absence of detectable flow within the former ICA lumen, *(2)* the presence of inhomogeneous, calcified material within the former vessel structure, *(3)* indirect signs of ICA lesions from hemodynamic alterations (see above), and *(4)* the detection, in almost all cases, of a socalled stump signal directly in front of the occluded segment (Figure 2d) *(26)*.

Using these criteria, ICA occlusion can be diagnosed with a sufficient degree of accuracy. The only moderate sensitivity is mainly attributable to the percentage of false-positive findings that arises because a very low flow in highly stenosed lesions is not always detected (Figure 4).

Carotid Ultra Sound Diagnostic: Pitfalls and Limitations

Calcifications and Shadowing

Extensive calcifications with shadowing can hamper the delineation of the residual lumen, thereby inhibiting the precise determination of the degree of stenosis, either by PSV or cross-sectional area reduction (CSAR). Consequently, previous authors have noted that imaging conditions are unsatisfactory in 8–13% of images generated by color Doppler-assisted duplex imaging (CDDI) *(18)*. The use of a transpulmonary stable intravenous contrast medium can significantly enhance the echogenicity of flowing blood. In high-grade ICA stenoses, use of a contrast medium can reduce the occurrence of 'insufficient image quality' from around 21 to 6% and improve the delineation of the entire residual lumen from 52 to 83% *(27)* (Figure 5).

Overestimation of the Degree of Stenosis in the Middle Range

All ultrasound methods tend to overestimate the degree of stenosis in comparison with intra-arterial digital sub-

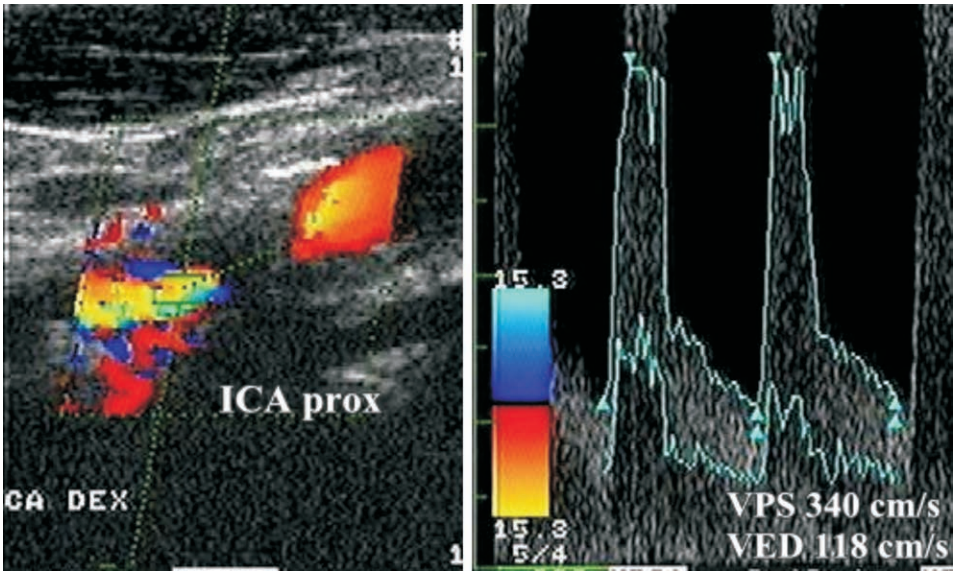

Figure 5. *Proximal ICA stenosis > 70% with heterogenous plaque and shadowing.*

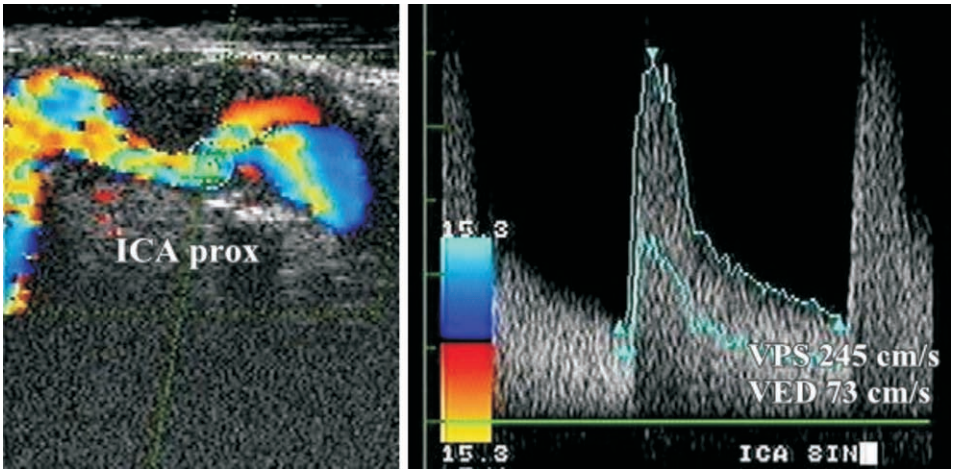

Figure 6. *Proximal ICA 70% stenosis with echolucent plaque.*

traction angiography (IA), especially in the 60–80% range. This is an important observation to note because the clinically most important threshold of 70% ICA stenosis lies within this range. The reasons for this are primarily physical, as the ultrasonic criteria rely predominantly on changes in blood flow volume and local area reduction, whereas the angiographic measurements rely on diameter measurements (Figure 5). It is therefore not surprising that, in some studies, the correlation of the degree of stenosis based on ultrasonic measurements and derived from pathoanatomical specimen is better than the correlation with IA *(28)* (Figure 6).

Detection of the 'Nearly Occluded' ICA

For a clinician-neurologist, the most common pitfall in neurosonography has always been the diagnosis of ICA occlusion when there is minimal residual blood flow, with percentages of false-positives ranging between 5 and 62% in reported series *(18)*. Compared with Doppler sonography and conventional B-mode imaging, CDDI has already improved the sensitivity for detecting minimal residual blood flow in preocclusive conditions *(18)*. Enhanced CDDI or power flow imaging (PFI), go one step further in that they are capable of detecting flow even in the narrowest parts of high-grade ICA stenoses and in the poststenotic flow segment, where flow signal intensities may be below the detection thresholds of non-enhanced CDDI.

II ULTRASOUND IMAGING OF VERTEBRAL ARTERIES

Despite the fact that ischemic stroke in the vertebrobasilar system (VBS) is significantly less frequent than in the carotid system, abnormalities found in Doppler and duplex examinations are about as prevalent in

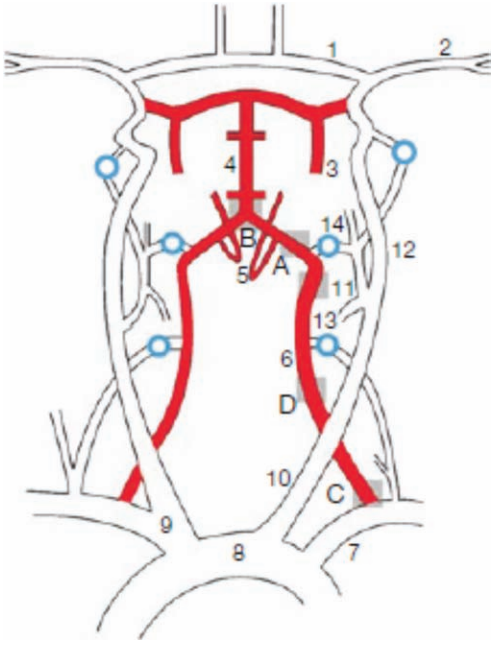

Figure 7. *Main vessels of the cerebral circulation. Vessels of the posterior circulation depicted in red. Collaterals to the vertebro-basilar system are shown as blue circles. Gray squares (A–D) refer to arterial segments shown in figures 2, 3, 5. 1 _ Anterior cerebral artery, ACA; 2 _ middle cerebral artery, MCA; 3 _ posterior cerebral artery, PCA; 4 _ basilar artery, BA; 5 _ posterior inferior cerebellar artery, PICA; 6 _ vertebral artery, VA; 7 _ subclavian artery, SA; 8 _ aortic arch; 9 _ brachiocephalic trunk; 10 _ common carotid artery, CCA; 11 _ external carotid artery (ECA) and branches; 12 _ internal carotid artery, ICA; 13 _ anastomoses between the cervical arteries and the VA; 14 _ anastomosis between occipital arteries and the VA (modified from (34).*

the VBS as in the carotid system. Because of the potentially severe clinical deficits associated with stroke of the VBS and the increased risk for stroke under conditions, such as underlying symptomatic vertebrobasilar stenosis and general anesthesia, it is highly desirable to have reliable methods available to identify pathological changes of the VBS. Furthermore, because the VBS via the circle of Willis can play a significant role as collateral blood supply system when vessels of the anterior circulation have been compromised, the knowledge of the VBS is necessary to estimate the overall integrity of the remaining blood flow to the brain (Figure 7).

The most frequent nontraumatic pathology affecting the VA is atherosclerosis *(29)*. There is significant association between VA stenosis and carotid stenosis, but the extent and severity of atherosclerosis is less in the VA *(30)*. The most frequent site of involvement is at the VA origin from the subclavian artery *(29)*. The gold standard for detection of ostial stenoses of craniocervical vessels is still conventional catheter angiography, although B-mode, colour and duplex ultrasound have also been employed to evaluate the VA. Direct visualisation of the VA origin is possible in up to 92% of patients on the right and 86% on the left *(31)*. The poorer results for the left reflects a combination of the higher incidence of proximal segment tortuosity and the variant origin of the left VA. Ostial stenosis can also be inferred from the duplex waveform of the VA. A tardus waveform or flow velocities in excess of 100 cm/s are suggestive of a stenosis. A prospective blind study of 158 patients found colour Doppler to have a sensitivity and specificity of 71 and 99%, respectively, for the detection of VA stenoses of more than 70% *(32)* (Figure 8).

Subclavian steal syndrome

Subclavian steal syndrome (SSS) occurs as a result of either occlusion or severe stenosis of the subclavian artery or brachiocephalic trunk proximal to the origin of the VA. This results in the shunting of blood from the contralateral VA, via retrograde flow in the ipsilateral VA, into the subclavian artery distal to the site of occlusion or stenosis. This phenomenon was first described in 1961 *(33)*. Atherosclerosis is the most common cause of SSS, accounting for close to 100% of cases. Rarer causes include congenital atresia of the first part of the subclavian artery and embolic, traumatic or iatrogenic interruption of the subclavian artery *(34)*. Inflammatory arteritis such

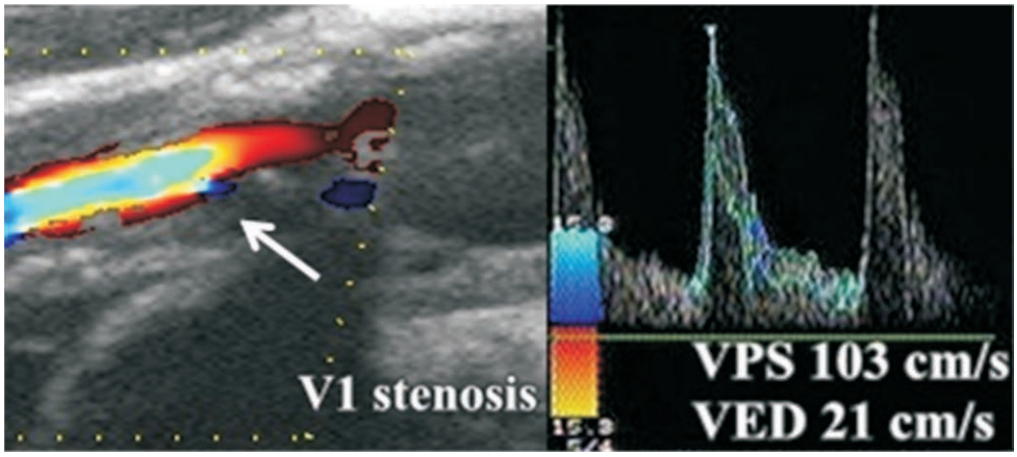

Figure 8. *Long vertebral artery V1 segment stenosis with heterogenous plaque (arrow).*

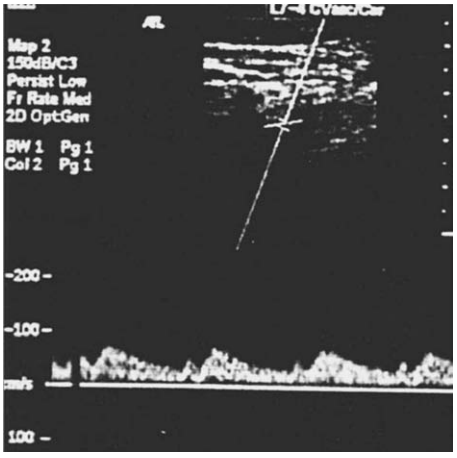

Figure 9. *SSS: extracranial vertebral artery segment with typical Doppler signal.*

as Takayasu arteritis is also a well-known cause of SSS *(34)* Up to 97% of patients would have ischemic symptoms involving the central nervous system or the ipsilateral upper limb or both. The most consistent clinical findings are a diminished or an absent pulse and asymmetrical blood pressure between the upper limbs *(34)* (Figure 9).

Inspite the fact that conventional angiography is still the gold standard for the investigation of SSS, ultrasound is an excellent noninvasive imaging modality for SSS. Duplex ultrasound has allowed the detection of earlier stages of SSS (pre-SSS) before the complete reversal of VA flow occurred. Intermediate waveforms have been identified which correlate moderately well with the degree of subclavian artery stenosis demonstrated on conventional angiography *(34)*. A sharp mid-systolic deceleration or flow reversal occurs between a sharp first systolic peak and a lower, more rounded second systolic peak when the subclavian artery stenosis reaches 45% or more *(34)*. Reversal or bidirectional flow has been shown to be 100% sensitive to either occlusion or high-grade stenosis of the subclavian artery or brachiocephalic trunk. Colour Doppler is usually enough for the detection of flow reversal, but will not demonstrate alterations in wave form prior to complete flow reversal. The disadvantage of duplex ultrasound is that it is operator-dependent; suboptimal or inaccurate determination of the direction of flow may occur owing to a wrong angle of insonation and especially so when the VA is tortuous. The use of reactive hyperaemia following brachial artery compression and release can be used to demonstrate further deterioration in the appearance of both the duplex waveforms and the pathological flow patterns on conventional angiography *(34)*. Duplex ultrasound is also very useful for the follow-up of patients after surgical or percutaneous treatment for SSS.

Instead of a conclusion

Regardless described limitations and potential pitfalls, diagnostic ultrasound may certainly be used to classify and grade carotid disease with high reliability, taking into account morphological and complex hemodynamic parameters. These parameters represent pathophysiological variables with evidenced correlation with patients' prognosis.

The role of surface-imaging modalities in diagnostic vertebral pathology, like ultrasound, although safe and noninvasive, are of limited use because unlike the carotid vessels they are relatively deep seated with numerous musculo-fascial structures surrounding them. Developing techniques exploring morphological and functional characteristics of carotid atherosclerotic plaques also have the potential to be adapted to imaging the vertebrobasilar system.

In summary, ultrasound imaging, using gray scale imaging, Doppler spectral analysis, and color Doppler imaging, is a proven and useful procedure for evaluating the extracranial cerebrovascular system. While it is not possible to detect every abnormality, adherence to the following guidelines will maximize the probability of detecting most extracranial cerebrovascular abnormalities. Occasionally, an additional and/or specialized examination may be necessary. Carotid Doppler ultrasound is an essential tool in the armamentarium of the stroke physician.

Indications for Ultra Sound diagnostic of extracranial part of brain arteries (35)

At the end there are indications for an ultrasound examination of the extracranial carotid and vertebral arteries including but not exclusively limited to:

1. Evaluation of patients with hemispheric neurologic symptoms, including stroke, transient ischemic attack, and amaurosis fugax[1–4];
2. Evaluation of patients with a cervical bruit;
3. Evaluation of pulsatile neck masses;
4. Preoperative evaluation of patients scheduled for major cardiovascular surgical procedures;
5. Evaluation of nonhemispheric or unexplained neurologic symptoms;
6. Follow-up of patients with proven carotid disease;
7. Evaluation of postoperative patients after cerebrovascular revascularization, including carotid endarterectomy, stenting, or carotid-to-subclavian bypass;
8. Intraoperative monitoring of vascular surgery;
9. Evaluation of suspected subclavian steal syndrome[5];
10. Evaluation for suspected carotid artery dissection,[6] arteriovenous fistula, or pseudoaneurysm; and
11. Patients with carotid reconstruction after extracorporeal membrane oxygenation bypass.

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