COMPLEX UTRASOUND STUDY OF THE ATHEROSCLEROTIC PLAQUE

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COMPLEX UTRASOUND STUDY OF THE ATHEROSCLEROTIC PLAQUE (Abstract): Carotid surgery concept is winning ground both among neurologists who recommend and vascular surgeons who perform an increased number of interventions. Regardless of the technique used (open surgery, stenting) we were interested in the tendency of the plaque to grow and determine stenosis. Ultrasound (US) is 91-94% sensitive and 85-99% specific in detecting a significant stenosis of the internal carotid artery. Aim: To establish a correlation between the preoperative US and intraoperative plaque characteristics in order to determine the restenosis rate. Material and methods: From January 1, 2012 to December 31, 2012, 70 consecutive patients were included in this study. Two groups were formed: 35 patients with stenotic ICA and 35 patients presenting stenosis at the femoral artery bifurcation (control group). The comparison between these two groups started from the premise of a similar pattern for internal carotid artery – deep femoral artery and external carotid artery- superficial femoral artery. US scans were performed on admission in all patients. All images were normalized and Gray Scale Median (GSM) was calculated. Results: Femoral plaque GSM values were higher in relation with hyperechogenicity highlighting the intensely calcified structure. Unstable plaques were more heterogenic, with higher transparency and lower GSM than stable plaques. This was the case of carotid plaques. During follow-up US revealed no restenosis. Conclusions: Femoral bifurcation plaques are calcified and determine chronic ischemic symptoms, while carotid bifurcation plaques are unstable and determine cerebral symptoms. US remain the gold standard non-invasive technique both for screening and diagnosis and set the therapeutic coordinates. Keywords: CAROTID PLAQUE, CAROTID ARTERY ULTRASONOGRAPHY, GRAY SCALE MEDIAN.

Carotid surgery concept is winning ground both among neurologists who recommend and vascular and cardiovascular surgeons who perform an increased number of interventions. Regardless of the technique used (open surgery, stenting) we were interested in the tendency of the plaque to grow and determine stenosis.

The prevalence of significant internal carotid artery (ICA) stenosis (more than 50%) is 0.5% among the age range 50 - 59 years, 10% in elderly over 80 years and 20% in patients presenting lower limb peripheral arterial disease (1).

Worldwide stroke is the third common cause of death. The prevalence of stroke after a transient ischemic attack (TIA) is 7% per year and the prevalence of stroke in an asymptomatic patient with a carotid stenosis larger than 80% is 3% per year (1).
The main cause of stroke is atheroembolism followed by the low blood flow through the stenosis.

The benefit from surgery in terms of stroke prevention in patients with symptomatic 70 - 99% stenosis (NASCET criteria) is higher than the one obtained from medical treatment (1). The available level I evidence suggests that in symptomatic patients surgery is currently the best option. The recommendation was based on a meta-analysis by The Cochrane Collaboration of eight randomized trials comparing carotid artery stenting with carotid endarterectomy (2). Patients with recent symptomatic stenosis (70-99%) are at highest risk of subsequent stroke. The efficacy of CEA falls with time (2).

Duplex ultrasound is the gold standard technique for carotid arteries evaluation. Ultrasound (US) uses B-mode US imaging and Doppler US to detect focal increases in blood flow velocity indicative of high grade carotid stenosis. The peak systolic velocity is the most frequently used to measure the severity of stenosis. Color Doppler technique increases the efficiency of the test, but it has not been shown to improve accuracy. US is 91-94% sensitive and 85-99% specific in detecting a significant stenosis of the ICA (3, 4, 5). Doppler US is also useful in obtaining information about plaque composition. Intraplaque hemorrhage, which may increase the risk of embolism and impact on prognosis, can be visualized on high resolution B-mode (3, 4, 5, 6, 7, 8). The ratio of ICA peak systolic velocity to the common carotid artery (CCA) velocity predicting a high grade stenosis sets the indication for surgery (9).

MATERIAL AND METHODS

The patients entering this study were selected from: patients referred by neurology departments with a high probability of advanced ICA lesion, patients with peripheral vascular disease already hospitalized in the vascular surgery department screened positive for significant carotid or femoral stenotic lesions, patients with arteriopathy hospitalized in cardiology and internal medicine departments diagnosed with significant femoral artery stenosis. 98% of the patients were diagnosed and selected in the Vascular Surgery Department. Before surgery all patients benefited from a new Doppler US (performed on Siemens Echodoppler XP 300 Premium - 2010).

All patients gave their informed consent for the study.

Two groups were formed: patients with stenotic ICA and patients presenting stenosis at the femoral artery bifurcation. The inclusion criteria for the first group were: asymptomatic ICA stenosis greater than 70%, history of TIA, history of minor stroke with self-sufficiency and 50-95% ICA stenosis. The patients in the second group meet the following inclusion criteria: arteriopathy stage III and IV with atherosclerotic lesions at the femoral bifurcation, regardless of the chosen surgical procedure.

The exclusion criteria were: autoimmune diseases, hypothyroidism, osteoporosis, hepatic insufficiency (GOT higher than 2.5 U / l), chronic kidney disease (creatinine above 2.0 mg / dl), ischemic heart disease class III, IV NYHA, atrial fibrillation and malignancies.

The comparison between these two groups started from the premise of the existence of a similar pattern for ICA – deep femoral artery (DFA) and external carotid artery (ECA) - superficial femoral artery (SFA). Thus, the bifurcation of the
CCA into the ICA and ECA anatomically resembles the bifurcation of common femoral artery (CFA) into DFA and SFA at each bifurcation there is an artery that will face increased resistance (ECA and SFA) and an artery that faces low resistance in the periphery (the ICA and DFA). Because of this, plaques at the two bifurcations are supposed to have a similar structure. Although clinically the manifestations of obstruction/stenosis of the ICA are much more severe than in obstruction/stenosis of DFA, the two models can be studied together in terms of atheromatous plaque progression.

US scans were performed on admission in all patients in both groups. B-mode settings were adjusted and then saved to ensure uniformity throughout the study (fig. 1). The stenosis grade was measured both in transversal and longitudinal section (fig. 2, 3).

Two reference points were used for normalization of B-mode images, blood (black), and adventitia (white). Patients were examined supine with the neck-rotated 45 degrees to the opposite side. A peripheral vascular transducer was used. The image was “frozen”, stored and transferred to a computer in order to calculate the Gray Scale Median (GSM). All images were normalized according to the method proposed by El-Atrozy et al. eliminating sonographic gain-induced variability of echogenicity in which the entire image is changed by a process of linear scaling to two reference points (blood and adventitia) with computer software (Adobe Photoshop 7.0). The GSM of the blood was set to 0, and the GSM of adventitia was set to 255. To determine the GSM for each stenotic plaque we acquired the histogram (10, 11, 12, 13, 14) (fig. 4, 5).
The results were used to compare the groups with one another and to draw conclusions from each group.

All patients underwent surgical interventions (endarterectomy and angioplasty in the patients with carotid artery stenosis or femoral artery stenosis and endarterectomy associated with bypasses in the patients with femoral artery stenosis)

US was performed postoperatively and as follow-up at 1, 3, 6, 9 and 12 months (fig. 6, 7).

**RESULTS**

From January 1, 2012 to December 31, 2012 we included in the study 70 consecutive patients meeting all criteria, 35 patients in each group.

Twelve patients with carotid lesions showed ICA stenosis greater than 90% stenosis. Patients with femoral lesions had CFA stenosis greater than 50% associating in 13 cases DFA stenosis greater than 70%.

No statistically significant differences in demographic characteristics, vascular risk factors or therapy were identified.

Post-Hoc analysis (paired analysis) comparing the femoral or carotid plaque area before and after the normalization
revealed the absence of statistical difference. The difference between prenormalization and normalization GSM values in each group were statistically significant (tab. I, II).

The average carotid plaque area was twice as big as the average femoral plaque area (tab. III).

### TABLE I

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<thead>
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<th>Newman-Keuls test</th>
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<tbody>
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*P - 95% confidence interval, ss = statistically significant, ns = not statistically significant

### TABLE II

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*P - 95% confidence interval, ss = statistically significant, ns = not statistically significant

### TABLE III

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*pre-N prenormalized, N normalized, SD standard deviation, SE standard error, Md median

Femoral plaque GSM values were higher in relation with hyperechogenity, highlighting the intensely calcified structure.

Unstable plaques were more heterogeneous, with higher transparency and lower GSM than stable plaques.

Carotid plaques average GSM was lower than the femoral one, meaning the carotid plaques are less stable.

Minimum-maxim differences reveal a high grade of heterogeneity in both groups (tab. IV).

Patients showed no carotid or femoral restenosis during the 1, 3, 6 and 12 months of US follow-up. Patients remained under surveillance.
Complex ultrasound study of the atherosclerotic plaque

### TABLE IV
Statistical GSM values [mm] pre-normalized vs. normalized

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<th>SE</th>
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*pre-N prenormalized, N normalized, SD standard deviation, SE standard error, Md median

**DISCUSSION**

Our study showed higher GSM values than those reported in the literature (15, 16). This is a consequence of the patients’ tendency to present to the vascular surgeon in advanced disease stages.

The correlation of a lower GSM with plaque instability needs to be proved. During the US follow-up we aim at detecting the occurrence of restenosis.

**CONCLUSIONS**

Bifurcation plaques occurring in peripheral atherosclerotic disease are calcified and determine chronic ischemic symptoms (intermittent claudications, rest pain), while carotid bifurcation plaques are unstable and determine cerebral symptoms either by TIA or ischemic stroke. US remain the gold standard noninvasive technique both for screening and diagnosis and set the therapeutic coordinates. The GSM analysis is a new and versatile tool used to establish plaque characteristics and to assess the risk for acute events.

**REFERENCES**


NEW GENE INVOLVED IN ANEMIA

Some forms of congenital anemia are caused by the deficiency in heme biosynthesis. Heme is a constitutive element of hemoglobin that is a protein in red blood cells responsible for transporting oxygen. Americans researchers have discovered a new gene that regulates heme biosynthesis. This gene named mitochondrial ATPase inhibitory factor 1 (Atpif1) is involved in the enzymatic activity of ferrochelatase, the terminal enzyme in heme biosynthesis. Using an animal model, the researchers found that loss of Atpif1 reduces ferrochelatase activity and increases mitochondrial pH which leads to deficiency in heme biosynthesis and causes anemia. Understanding of the mechanisms regulating heme biosynthesis may contribute to development of improved therapies for certain type of anemia such as congenital sideroblastic anemia and mitochondrial disease (Shah DI, Takahashi-Makise N, Cooney JD et all. Mitochondrial Atpif1 regulates haem synthesis in developing erythroblasts. Nature. 2012; 491(7425): 608-12).

Cătălina Luncă