ULTRASOUND OF CAROTID ARTERIES, WHAT ARE PLAQUES, STENOSIS: LATEST NEWS AND FUTURE TASKS

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Abstract
In recent decades, cardiovascular diseases are the main cause of mortality in developed and developing countries. The diagnosis and especially the assessment of the degree of risk of these pathologies constitute today the challenges that modern medicine dictates to us. One of the imaging examinations that is receiving attention in recent years in terms of cardiovascular risk assessment is the doppler ultrasound of carotid arteries. The knowledge about this examination, the indications and especially the correct interpretation of the data, will be a valuable tool in helping the work of the clinician.

Keywords: Doppler Ultrasound; Carotid arteries; Carotid plaque; Carotid stenosis.

EKOGRAFIA E ARTERIEVE KAROTIDE, ÇFARË JANË PLLAKAT, STENOZAT: TË REJAT E FUNDIT DHE DETYRAT E TË ARDHMES

Abstrakt
Në dekadat e fundit sëmundjet kardiovaskulare janë shkaku kryesor i vdekshmërisë në vendet e zhvilluara dhe në ato në zhvillim. Diagnostikimi dhe sidomos vlerësimi i shkallës së rrezikut të këtyre patologjive, përbëjnë sot sfidat që na dikton mjekësia bashkëkohore. Një nga ekzaminimet imazherike që po merr vëmendje vitet e fundit në drejtim të vlerësimit të rrezikut kardiovaskular është edhe ekografia doppler e arterieve karotide.
Sfondi: Ekografia Doppler është zhvilluar në sajë të bashkëpunimit shumëvjeçar midis mjekëve dhe inxhinierëve. Që prej futjes në praktikën klinike në vitet '70 të shekullit të kaluar, ky ekzaminim ka përjetuar përmirësime të ndjeshme në teknikë dhe është sot një nga testet më të besueshme dhe praktike në vlerësimin e sëmundjeve vaskulare. Duke ndërthurur imazhet *B-mode* dhe teknologjinë Doppler, ekografia Doppler e arterieve karotide lejon mjekun të vlerësojë nga ana sasiore dhe cilësore pllakat dhe stenozat e arterieve karotide. Qëllimi i këtij artikulli është të njohë mjekët klinicistë me indikacionet, interpretimin e të dhënave dhe të rejat e fundit për ekografinë Doppler të arterieve karotide.
Metodat. Rishikim i literaturës dhe imazhe ekografike nga puna me pacientë në Shërbimin e Mjekësisë Interne dhe Hipertonisë në Qendrën Spitalore Universitare "Nënë Tereza", Tiranë.
Përfundim. Ekziston nevoja e ndërtimit të një protokolli mjekësor kombëtar në lidhje me shkallëzimin e pllakave dhe stenozave të arterieve karotide, për të bërë të mundur më tej edhe një

vlerësim të standardizuar të riskut kardiovaskular të pacientit, bazuar edhe në vecoritë e popullatës shqiptare.

Fjalë kyçe: Ekografia Doppler; Arteriet karotide; Pllakat karotide; Stenozat karotide.

Introduction

Anatomy of the carotid artery

CCA

The common carotid arteries (CCA) are paired branchless arteries of the neck that supply blood to the head, face and neck. Each common carotid bifurcates into internal and external carotid arteries. Although the left and right common carotid arteries follow the same course through the neck, their origin differs. On the left, the CCA arises directly from the aortic arch whereas, on the right, the origin is from the brachiocephalic trunk. The left CCA can be thought of as having two distinct parts: thoracic and cervical. Since the right CCA arises cranially, it only really has a cervical portion. The cervical portion of both CCAs follows a similar course. Each vessel passes obliquely upwards from behind the sternoclavicular joint to the level of the upper border of the thyroid cartilage, at approximately the C4 level (Fig. 1) (1).

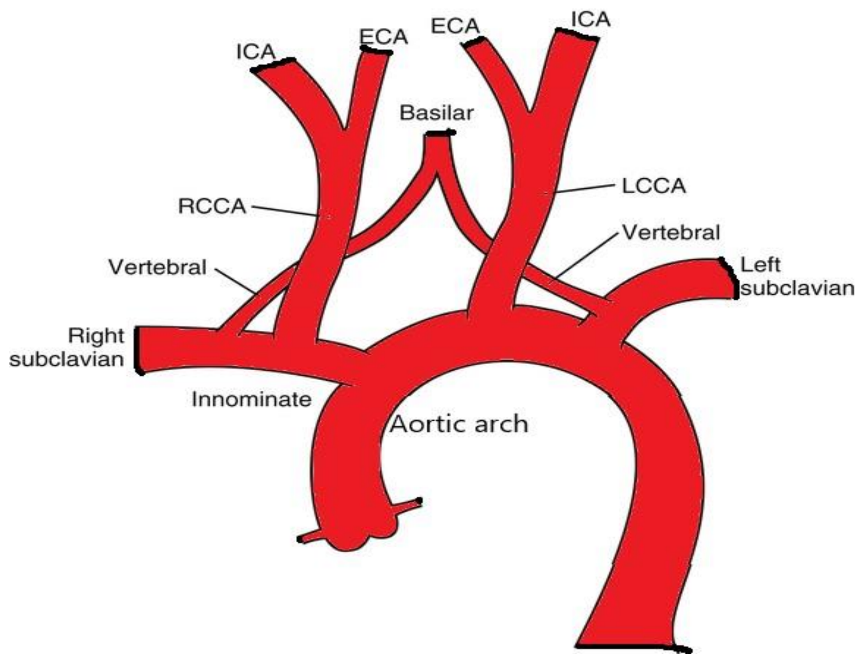


Figure 1. Carotid artery anatomy

The internal carotid artery (ICA) is one of two terminal branches of the common carotid artery (CCA) which supplies intracranial structures.

Origin

The common carotid artery branches to form the internal carotid artery (ICA) and the external carotid artery (ECA). Immediately after its origin, the ICA has an expansion called the carotid bulb or sinus. In the carotid body there is a small collection of chemoreceptor cells located immediately after the bifurcation (2).

In most cases, the carotid bifurcation occurs between the levels of the C3 and C5 vertebrae, or between the levels of the hyoid bone and the upper border of the thyroid cartilage. However, there is a wide variation (2).

Vertebral artery

Paired vertebral arteries provide blood supply for the upper part of the spinal cord, brainstem, cerebellum, and posterior part of the brain. Each artery originates from the first part of the subclavian artery, it then courses superiorly along the sides of the neck, merging with its companion at the pons level to form the single, midline basilar artery as shown in Fig. 2 (3).

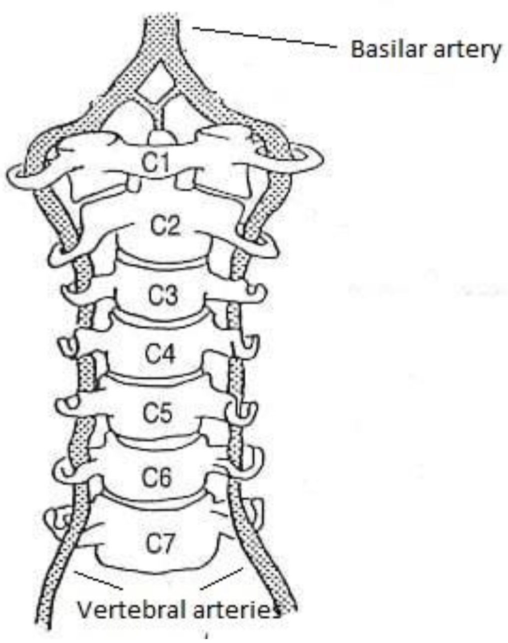


Figure 2. Vertebral arteries anatomy

Circle of Willis

The basilar artery and ICA give off numerous communicating branches which anastomose with each other at the base of the brain, forming the hexagonal vascular network called the circle of Willis. The circle of Willis connects the anterior and posterior circulations of the brain. This reflects the importance of the vertebral artery for the human body.

The circle of Willis (cerebral arterial circle or circulus arteriosus) is an anastomotic ring of arteries located at the base of the brain. This arterial anastomotic circle connects the two major arterial systems to the brain, the internal carotid arteries and the vertebrobasilar (vertebral and basilar arteries) systems. It is formed by four paired vessels and a single unpaired vessel with numerous branches that supply the brain (Fig. 3) (3).

The main function of the circle of Willis is to provide a collateral blood flow between the anterior and posterior arterial systems of the brain. Additionally, it offers the alternate blood flow pathways between the right and left cerebral hemispheres. This way the circle protects the brain from ischemia and stroke in cases of vascular obstruction or damage (3).

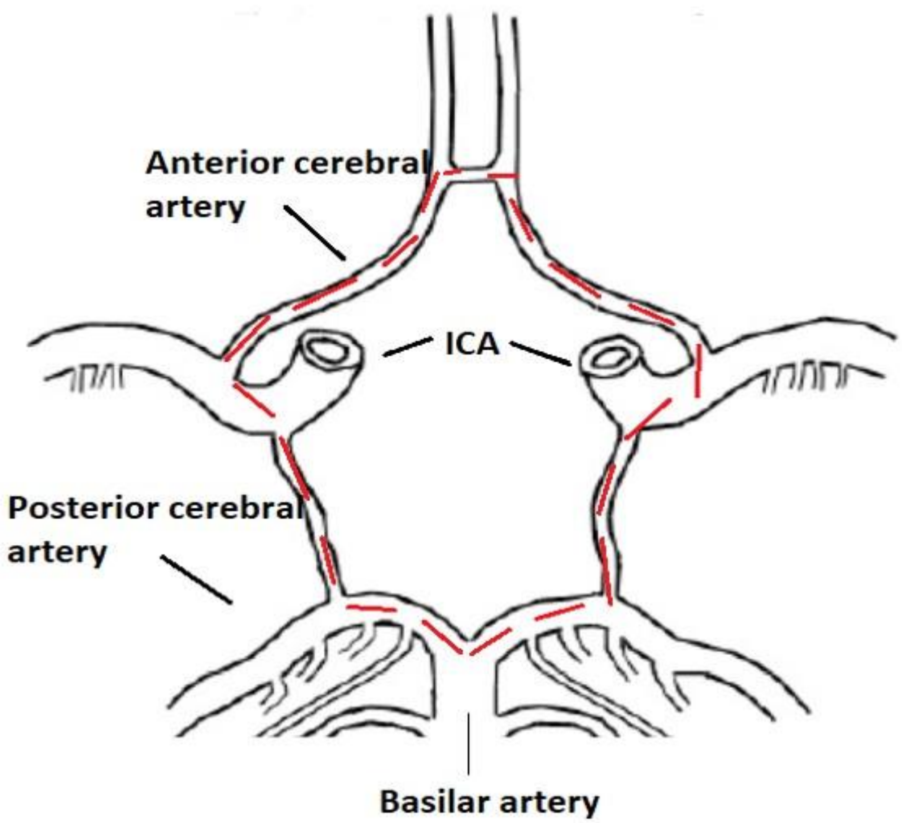


Figure 3. Circle of Willis

Carotid ultrasound

Carotid ultrasound, also called Doppler ultrasound or carotid duplex ultrasound, (DUS) is a painless and harmless test to evaluate the carotid arteries. Carotid ultrasound assesses the presence of atherosclerotic plaques in the arteries. The plaque consists of substances such as: cholesterol, calcium, different cells, and an increase in its size can cause narrowing of the lumen of the diseased artery (4).

Common Indications

Common indications for performing this examination include:

- Transient ischemic attacks (TIA)
- Amaurosis fugax
- Carotid bruit
- Cerebrovascular Accident (CVA)
- Follow-up of known carotid stenosis
- Post intervention follow-up e.g. carotid endarterectomy, stent or bypass

- Trauma in the distribution of the carotid artery e.g. suspected dissection, arteriovenous fistula or pseudoaneurysm
- Pre-operative assessment for high risk patients e.g. coronary artery bypass surgery (CABG)
- Pulsatile neck masses
- Evaluation of suspected subclavian steal syndrome
- Pre- maxillo-facial surgery (5)
- Dizziness alone is not sufficient indication for this exam (6).

Contraindications and Limits

Contraindications for extracranial cerebrovascular duplex ultrasound are few; however, some limitations exist and may include the following:

- Patients with short, thick muscular necks
- Patients who have had recent surgery, ultrasound visualisation may be limited due to oedema, haematoma, surgical staples, dressings etc
- Calcified plaque may cause acoustic shadowing limiting Doppler and B-mode image assessment
- Patients who are unable to lie flat due to pre-existing co-morbidities e.g. chronic obstructive pulmonary disease (COPD) and arthritis – although these patients may be able to tolerate being examined seated in a chair or with the head of the bed raised
- Patients who are unable to cooperate or those with involuntary movements
- Examinations undertaken portably at the patient's bedside may be limited due to equipment and room dimensions (5).

General Guidelines:

A complete examination includes evaluation of the bilateral common, extracranial internal carotid, and proximal external carotid arteries as well as the extracranial portions of bilateral vertebral arteries.

•The examination must be bilateral unless otherwise contraindicated

•A complete examination includes evaluation of the entire course of the accessible portions of each vessel

•Variations in technique must be documented (i.e., stents) (6).

Measurement of intima media thickness

Intima-media thickness (IMT) is a marker of subclinical atherosclerosis (asymptomatic organ damage) and should be evaluated in every asymptomatic adult or hypertensive patient at moderate risk for cardiovascular disease. Intima-media thickness values of more than 0.9 mm (ESC) or over the 75th percentile (ASE) should be considered abnormal. A carotid artery ultrasound scan is the method of choice, and results are reliable, provided certain standards are followed (7).

Atherosclerosis most often develops gradually and slowly, starting from childhood and proceeding into adulthood with varying velocity and susceptibility to complications. The first structural change that can be detected in atherosclerosis is an increase in IMT.

Intima-media thickness is an important atherosclerotic risk marker. However, this increase is not synonymous with subclinical atherosclerosis, but is related to it. Indeed, increase in IMT is also the result of nonatherosclerotic processes such as smooth muscle cell hyperplasia and fibrocellular hypertrophy leading to medial hypertrophy and compensatory arterial remodeling. Therefore this process may be an adaptive response to changes in flow, wall tension, or lumen diameter. The uniform thickening progresses in straight arterial segments as the patient ages and all known vascular risk factors accelerate this process. Therefore IMT is an important atherosclerotic risk marker but cannot be accepted as a risk factor and should not be subjected to treatment (7).

How is the measurement done?

IMT is defined as a double-line pattern visualised by echo 2D on both walls of the common carotid artery (CCA) in a longitudinal view as shown in Figure 4. Two parallel lines (leading edges of two anatomical boundaries) form it: lumen-intima and media-adventitia interfaces (7).

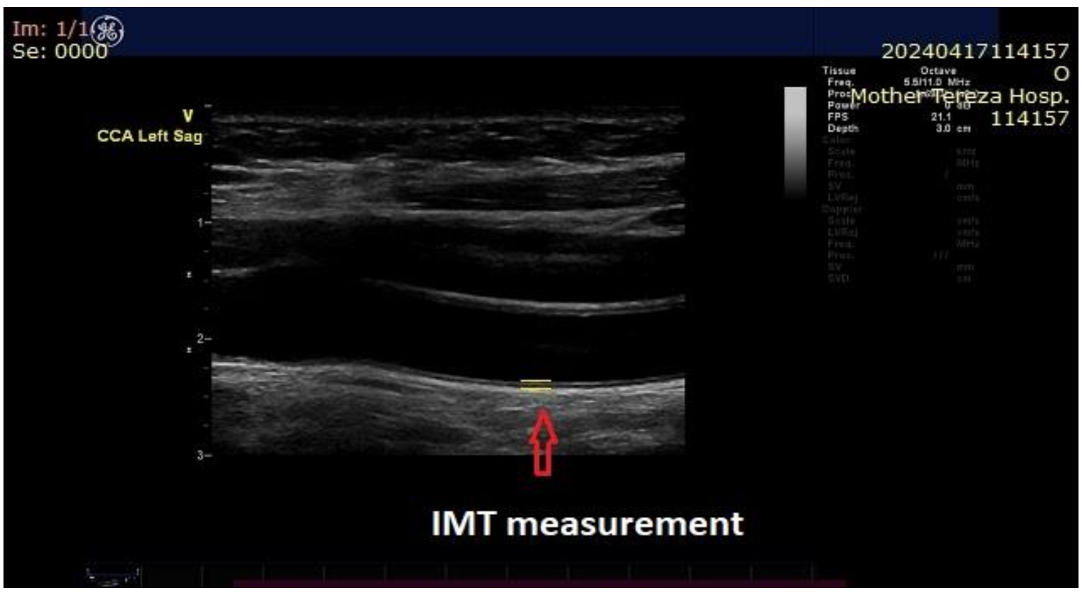


Figure 4. Intima-media thickness measurement

IMT is measured as the distance between lumen-intima (first yellow line) and media-adventitia (second yellow line) interfaces (7).

Where should the measurement be done?

The measurement is made at a distance of 10-20 mm from the branching of the CCA to the ICA and ECA. One of the main problems in interpreting IMT results from clinical trials is the differences in measurement methodology. These discrepancies can refer to either one or more of these parameters: the precise definition of the investigated carotid segment, the use of mean or maximal IMT, the measurement of near and far wall or only far wall IMT, the insonation at a single or different angles, employing manual tracking or an automated software, including carotid plaques or not and uni- or bilateral measurements. To avoid this problem standards for IMT measurement have been developed (7). According to recent guidelines, an IMT >1.5 mm thick will be classified as plaque (Fig. 5).

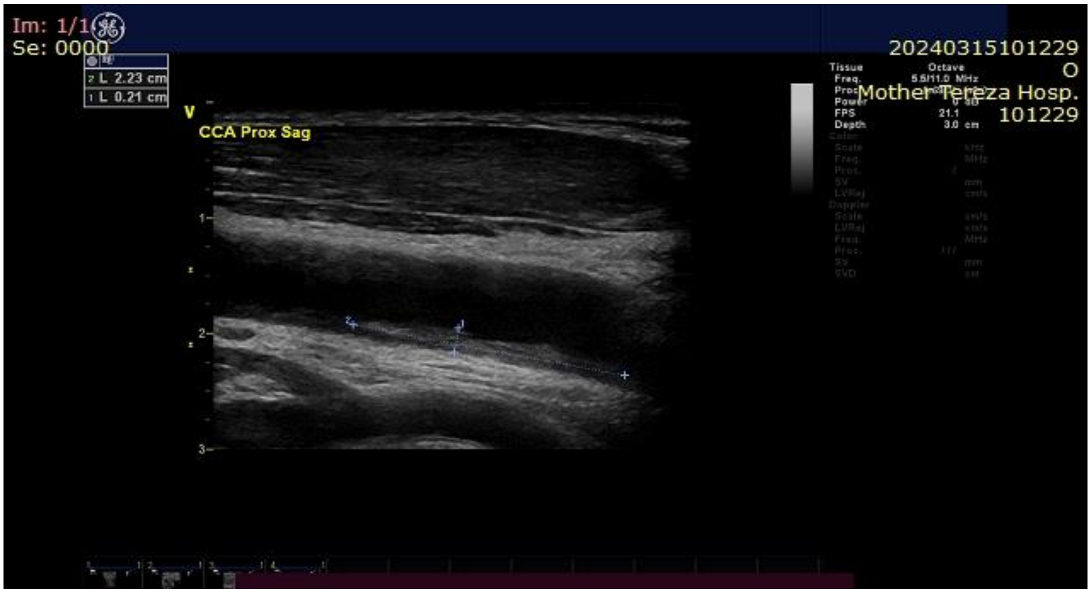


Figure 5. Intima-media thickness (plaque)

The bifurcation is one of the areas most affected by the formation of atherosclerotic plaques, due to the blood flow gaps that are created in this segment.

What is a carotid plaque?

Plaque is made up of deposits of fatty substances, cholesterol, cellular waste products, calcium, and fibrin.

Pathology

The plaques formed in the carotid vessels can be divided into four types:

- type I: predominantly hemorrhage, lipid, cholesterol, and proteinaceous material
- type II: dense fibrous connective tissue with >50% volume of hemorrhage, lipid, cholesterol, and proteinaceous material
- type III: dense fibrous connective tissue with <50% volume of hemorrhage, lipid, cholesterol, and proteinaceous material
- type IV: dense fibrous connective tissue (8)

Ultrasound

On grayscale, characterization of plaques can be performed:

- type I: predominantly hypoechoic with thin echogenic rim
- type II: echogenic plaque with >50% hypoechoic areas
- type III: echogenic plaque with <50% hypoechoic areas
- type IV: uniformly echogenic plaque (8)
- type V: calcified plaque

They can be termed as:

- homogeneous (type I and IV)
- heterogeneous (type II and III) (8)

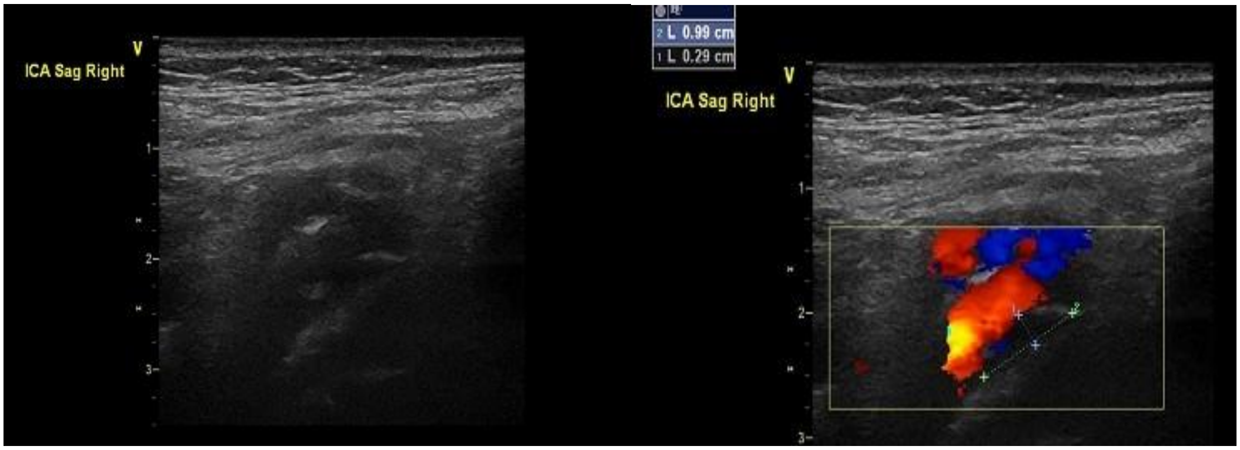


Figure 6. Types I plaque (Grayscale)

Grayscale features that are associated with unstable plaques (plaques at highest risk for rupture and sequela for CVD events) are low grayscale median value, black areas near the lumen surface of the plaque, and the presence of discrete white areas (DWAs) within the plaque (Fig. 6). The size of the plaque (as measured by calculating plaque area [two-dimensional imaging] and volume [three-dimensional imaging]) has also been used to examine associations with CVD risk factors and risk for future CVD event (9).

Several studies have demonstrated that these grayscale features are associated with plaque tissue composition when comparing ultrasound grayscale findings with surgical and histopathology findings post-carotid endarterectomy. Lower GSM values (more hypoechoic) are associated with more lipid content and inflammatory cells. Plaques with higher grayscale median values are associated with a higher percent of calcium. Plaques with black areas (areas of very low echogenicity) near the lumen surface of the plaque are associated with higher ulceration scores by the surgeon at the time of carotid endarterectomy. DWAs are white areas within a plaque (higher grayscale values – typically 126-255) and are not associated with an acoustic shadow. DWAs are thought to represent areas of increased macrophages and/or neoangiogenesis and have been associated with increased inflammation and hemosiderin scores when comparing their presence on ultrasound images to carotid plaque histopathology findings (9).
Plaque grayscale findings have also been shown to be associated with imaging findings of brain infarct, associations with CVD risk factors, and can be predictive of future events.
Plaques with lower GSM values were associated with an increased incidence of cerebral infarction on brain computed tomography examination compared to patients with higher GSM values (9). Studies have also demonstrated that GSM values are lower in patients with diabetes compared to nondiabetic patients (9). In summary, ultrasound plaque grayscale features are associated with histopathologic findings of inflammation, ulceration, hemorrhage, and calcification. Studies have demonstrated that these features, along with clinical history, can be used to risk stratify patients. Research studies have demonstrated that these features (especially plaque area) are associated with CVD risk factors (9).

Carotid artery stenosis

Methods of assessing the degree of stenosis vary depending on the technique and accuracy of the assessment. Angiography has been considered for many years as the most accurate method for evaluating carotid artery stenosis. The two large clinical trials evaluating the benefit of endarterectomy in symptomatic patients (NASCET and ECST) used different methods to measure carotid stenosis although both relied on catheter angiography.

Both the NASCET and ECST trials used angiography and calculated the percentage of stenosis as a ratio of diameters measured from the angiogram (Figure 7). The NASCET method compared the diameter of the residual lumen in the stenosis with the diameter of the normal ICA lumen distal to the bulb. The ECST method compared the residual lumen in the stenosis with an estimate of the diameter of the artery at the point of the stenosis. As the point of maximum stenosis is commonly found within the bulb, the ECST method typically yields a higher value for a stenosis with a given residual lumen than does the NASCET method (10). Duplex ultrasound has been shown to have good correlation with both NASCET and ECST methods of calculating percentage stenosis and with an appropriate choice of diagnostic criteria each has similar sensitivity and specificity (10) as indicated in Fig. 8.

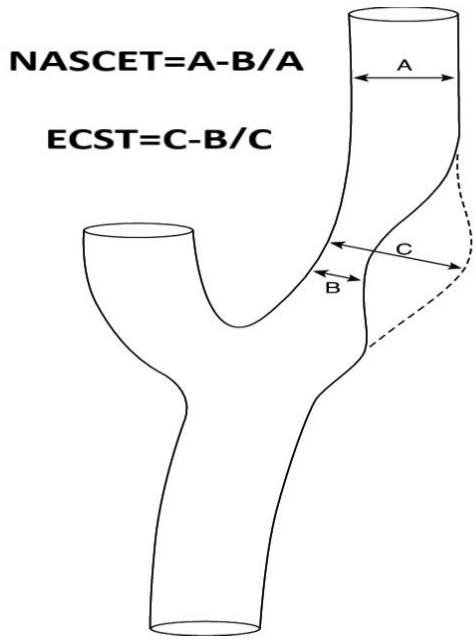


Figure 7. Stenosis measurement (angiography)

Using a regression analysis, Rothwell et al.found the relationship between the ECST and the NASCET values to closely approximate: ECST%=0.6, NASCET%+40% (Figure 8).

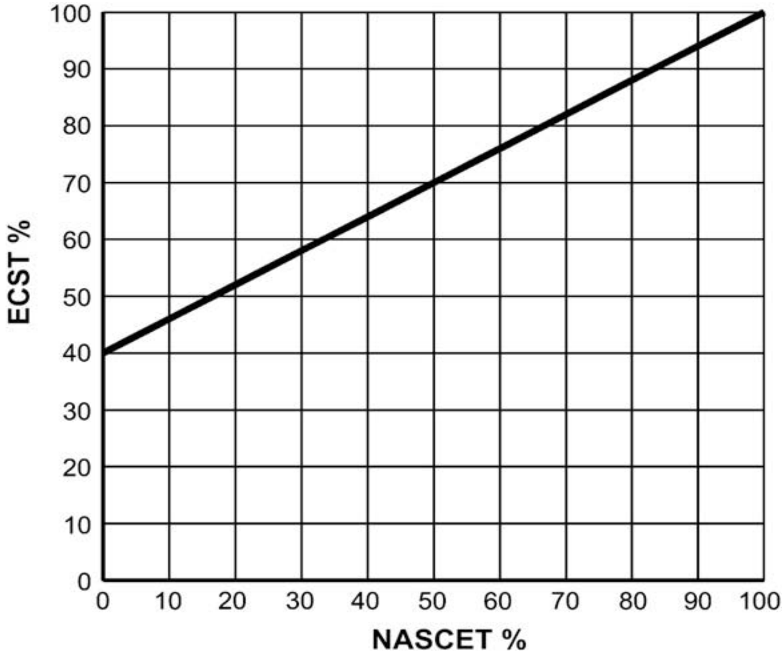


Figure 8. The relationship between percentage diameter stenosis calculated using the ECST and NASCET methods using formula of Rothwell et al. (10)

However, in recent years with the development of biomedical technology, new ways of evaluation and diagnosis have been introduced into the daily routine. The same assessment methodology of Carotid artery stenosis can also be applied in ultrasound and is defined as anatomical stenosis (Figure 9). A complementary method is the measurement of the area of the stenosis. However, due to the low accuracy, such a method is not very advisable (Fig.10).

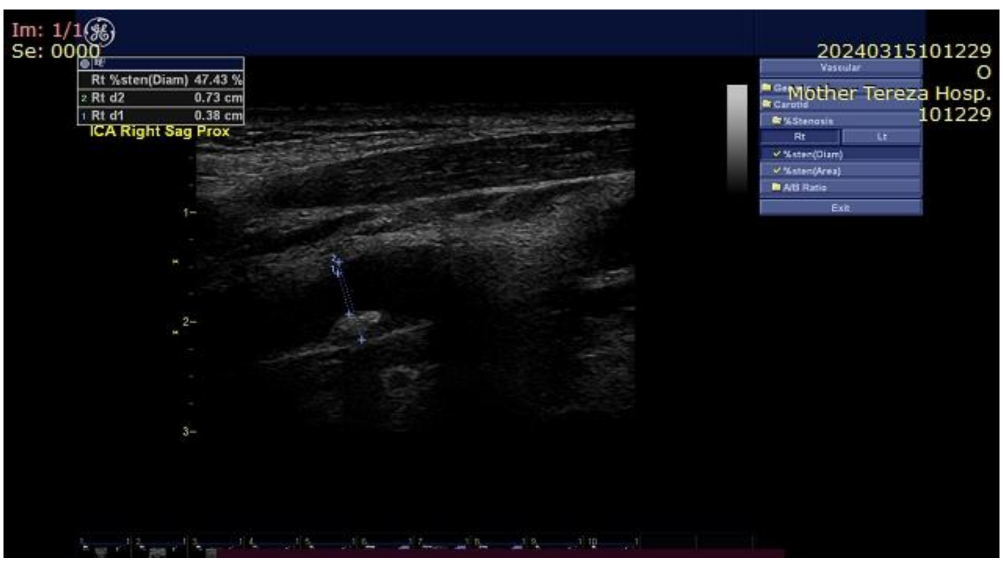
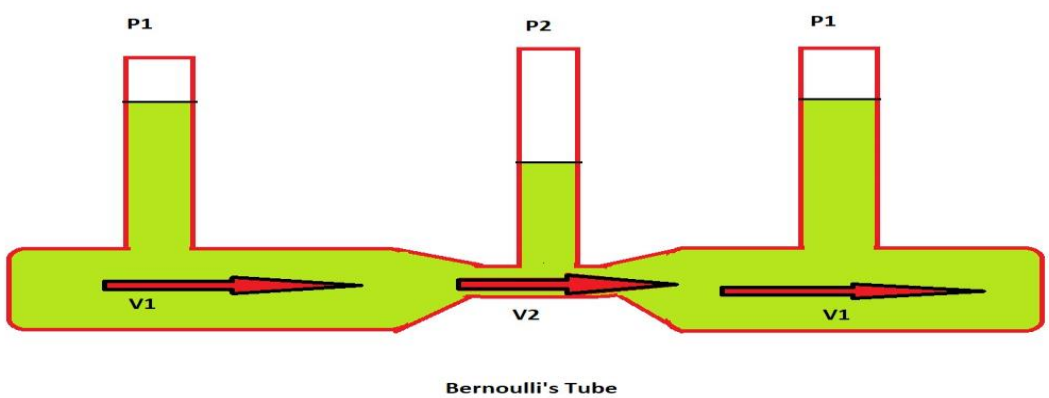


Figure 9. Evaluation of stenosis using diameters (ECST method)

Figure 10. Evaluation of stenosis using area

Using longitudinal plane with colour and spectral Doppler the extracranial carotid arteries should be assessed for any areas for velocity increase or turbulence from the CCA to the distal ICA, and the vertebral artery (11).

Let's recall Bernoulli's principle, which states that: *when the speed of a moving fluid increases, the pressure inside the fluid decreases.* More specifically: the fluid velocity increases in segments with narrowing of the section (Fig. 11).



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igure 11. Bernoulli’s tube

This is also the principle on which the evaluation of stenoses (hemodynamic) is based by measuring the speed of blood flow at the point of stenosis. Through various studies and comparison of velocities with measurements made by other methods (angiography, interventional and post-mortem measurements) a direct relationship between the degree of stenosis and the measured velocities has been determined. Haemodynamically significant stenoses are diagnosed by using the standard criteria (5) as shown in the Table 1.

Table 1. Stenosis-grading scheme Internal Carotid Artery (Oates CP et al.) (5)

Stenosis-grading scheme ICA			
Stenosis %	PSV	PSV ratio	St. Mary ratio
NASCET based	PSVICA (cm/s)	PSVICA/PSVCCA	PSVICA/EDVCCA
<50%	<125	<2	<8
50-59%	>125	2-4	8-10
60-69%			11-13
70-79%	>230	>4	14-21
80-89%			22-29
>90%	>400	>5	>30
Near occlusion	High, low or string flow	Variable	Variable
Occlusion	No flow	Not applicable	Not applicable

Velocity measurements should be made at several points: before stenosis, at stenosis and after stenosis (12). To fully enable clinical decisions to be made regarding patient management, it is advisable to define the degree of stenosis within a band of 10%, ranging from 50% to 99% stenosis (10).

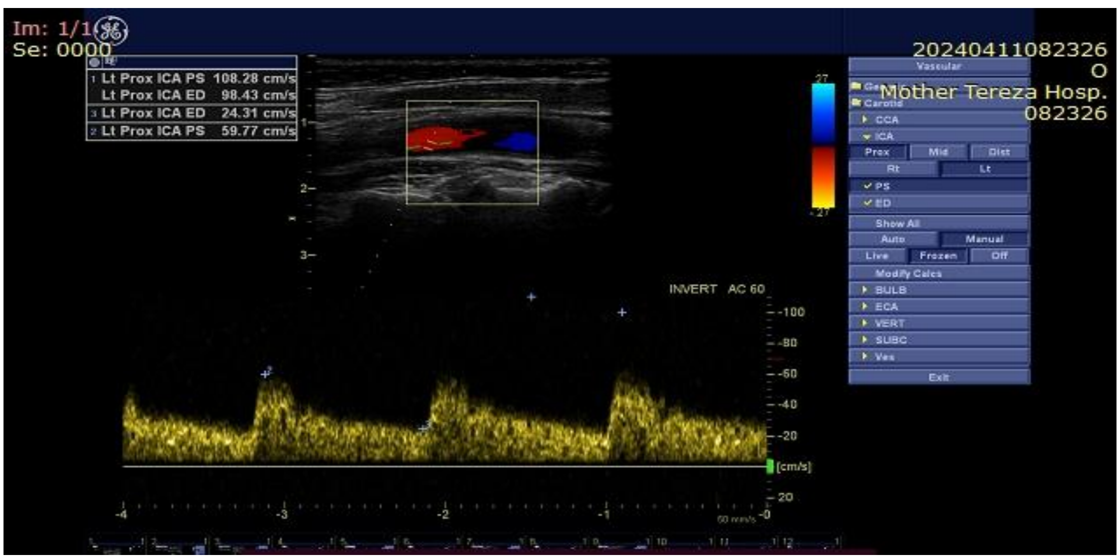

Figure 12. Peak systolic velocity, end diastolic velocity measurement

ICA peak systolic velocity has historically been the primary diagnostic criteria applied to carotid disease (10).
There are a number of potential sources of variability in the internal carotid artery peak systolic velocity. Such factors as:

- variation in the geometry of the bifurcations and the size of bulb
- variation in the vessel size that reflects body size
- collateral flow effects including intracranial/ECA

- collateral flow
- change in ICA flow over the menstrual cycle
- change with age and blood pressure
- the physical parameters of the ultrasound machine (10).

The effect of these factors on blood velocities in diseased vessels is mitigated by the use of velocity ratios. Velocity ratios will also mitigate inter-machine differences (10). The Peak Systolic Velocity Ratio (PSVR), the ratio of the PSV in the ICA to the PSV in the distal CCA, has been widely used (Fig. 12) (10). The St Mary's ratio is formed from the ratio of the PSV in the ICA as the numerator, a value that increases with degree of stenosis, over the EDV in the distal CCA as the denominator, a value that decreases with increasing ICA resistance caused by a progressively severe stenosis. This produces a graph with a wide range of values for the index and sufficiently low data spread so as to allow grading in deciles (10).

New technologies in the evaluation of carotid artery plaques and stenoses

Among diagnostic methods, contrast enhancement ultrasound (CEUS) which uses a contrast medium based on sulfur hexafluoride, has emerged in the last decade as a reliable technique not only due to its ability to quantify the grade of stenosis, but also for its superior capability in depicting the vulnerability features of the plaque, thus providing an accurate qualitative assessment and stratification of the risk of rupture. It also represents a valid method in the evaluation of carotid dissection. CEUS uses an intra-vascular contrast agent consisting of microbubbles (1–8 μm) filled with perfluorinated gas with low solubility injected to acquire high contrast ultrasonic images of the carotid artery. It allows some limitations of DUS to be overcome, such as the detection of low blood flow and insonation of deep vessels (13).

3-D ultrasound

New perspectives are being gained through the 3D technique. While providing a model in three spatial planes, the software provides a read-out of the quantitative analysis of maximum stenosis and plaque volumetric measurement of the plaques; this can be made with a 3D-US system based on 2D-US image acquisition and can be measured accurately and with low variability, making it a useful tool in clinical studies of the progression and regression of carotid plaques (13).

Conclusion

Doppler ultrasound of the carotid arteries is a simple examination, without risks and easily accessible. By correctly recognizing the indications, and correctly evaluating the results of the DUS, the clinician can determine the degree of the patient's cardiovascular risk, the risk of cerebrovascular diseases, determine the medication as well as the indications for surgical intervention in cases of carotid artery stenoses.

Because of the different ways of evaluating and calculating carotid artery stenoses that are in use today, as well as because of changes in lifestyle or life expectancy in different countries, it is recommended that a standard be established for the evaluation of stenoses of the carotid arteries, as well as the stratification of cardiovascular risk based on carotid artery assessments for the Albanian population. The compilation of medical protocols for the determination of risks and treatment by associations and professionals in the field is the need of the hour.

Conflict of interest: None declared.

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