

SUBCLINICAL ATHEROSCLEROSIS: GENERAL CONCEPTS AND ASSESSMENT METHODS

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Abstract: The subclinical atherosclerosis, together with its complications (stenosis, thrombosis, embolism) is one of the most important pathological condition found in cardiology and neurology. Having a growing incidence, it has a devastating influence not only regarding the life expectancy, but also regarding its quality, becoming the main cause of morbidity and mortality. It is presented the most successful assessment method in order to reveal subclinical vascular damage and organ dysfunction.

Cuvinte cheie:

ateroscleroza,
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Rezumat: Ateroscleroza subclinică, împreună cu complicațiile sale (stenoza, tromboza, embolia) constituie una din cele mai importante stări patologice întâlnite în cardiologie și neurologie. Cu o incidență în continuă creștere, ea are influență devastatoare nu numai asupra speranței de viață, dar și asupra calității ei, constituind principala cauză de morbiditate și mortalitate. În articol sunt prezentate metodele de evaluare cele mai utile pentru relevarea afectării subclinice vasculare și a organelor țintă.

INTRODUCTION

The atherosclerosis and its complications is the major cause of morbidity and mortality with myocardial infarctions and strokes which they cause. The atherosclerosis, per se, does not cause special events, the plaque disruption of atheroma being the one that leads to the diminuation or the interruption of the blood flow by distal embolization or arterial occlusions (1).

The detection and the assessment of atherosclerosis in a subclinical stage has a special importance because it allows more rigorous and applied approaches of primary preventive measures that aims in the diminuation of the number of cardiovascular events.

General concepts

The atherosclerosis is a cronical disease of the arteries with a long evolution, decades, characterized by a slow deposition of fats accompanied by a progressive fibro-conjunctive reaction which thickens the artery wall and determines a progressive narrowing of its lumen, having as a final result its occlusion. It has as a characteristic damage **the plaque of atheroma** and the changing of the elastic components of the arteries. It is characteristic to the arteries and veins having a medium or large diameter. The emergence and the development of the atherosclerosis is facilitated by so called risk factors (2).

The morphofunctional peculiarities, together with the local changes (inflammatory, structural etc) have a role if not determinant, at least favorable for the preferential localization of the atheromatosis lesions (1).

Stadialization of the atherosclerotic damages

The current concept is that the atherosclerosis starts as a response at the minimum chronic injury of the vascular endothelium – the continuous single cell stratum which coats the arterial wall – and that the interactions between the monocytes, the lipoproteins, the platelets, the lymphocytes and the smooth muscle cells at the level of the arterial intima and media will continue the pathological process. The main "battlefield" of the atherosclerotic process is the intima, which is located right under the endothelium (3).

There are 8 development stages of the atherosclerotic plaque, these stages corresponding each to a histological type of a atheroma lesion.

St. I – III (initial lesion → lipidic groove → preatheroma): lipids accumulation, intra- and then extracellular;

St. IV – V (atheroma → fibroatheroma): fibrosis around the lipidic core, forming the atherosclerotic plaque;

St. VI – VIII (complicated lesion → calcified → fibrous): the plaque of atheroma having complications like breaking, bleeding or thrombosis, showing clinical signs (1,3).

The stages I-V of the plaque of atheroma (lipidic groove → fibroatheroma) is in fact **the subclinical atherosclerosis**.

Stages VI-VIII of the plaque of atheroma (complicated plaque, calcified and fibrous plaque) define the **clinical atherosclerosis** manifested in stenosis, occlusions or arterial embolism at the level of the target organs (heart, brain, kidneys, inferior limbs).

The atherosclerosis is in fact a systemic disease which affects all the arterial territories, but with specific clinical manifestations at the level of the target organs. It is known that 40% of the patients having a cerebral vascular disease and 60% of the patients having a symptomatic peripheral arterial disease also have affected other vascular territories. In addition these patients are not optimum treated, there are high percentages of patients who does not achieve the therapeutic targets of the correction of the risk factors.

Assessment Methods

The proofs of the subclinical affection can be achieved through a non-invasive assessment and an invasive assessment. The subclinical damage means vascular damage and/or organ damage.

The subclinical vascular damage can be demonstrated using some parameters, easily to be measured, that we are able to verify to all the "healthy" patients but having high risk factors concerning the atherosclerosis.

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1. The ankle-arm index (ABPI, ankle brachial pressure index)

It is a simple index, an easily measured index and definitely it is necessary a Doppler pen that can rapidly notify the pulse wave at the pedial artery or at the posterior tibial artery. The ankle-arm index consists in the ratio between the systolic blood pressure of the inferior limb (measured in the ankle) and the superior one (measured in the arm). The determination of the ankle-arm index is made on the right part and on the left part, at rest and after 5 minutes of walking or riding a medical bike.

The interpretation of the levels of the ankle-arm index:

- over 1.2 = arterial stiffness in the case of severe forms of arteriopathy (also encountered at the patients with diabetes mellitus, 50% of them having peripheral arteriopathy)
- between 1 and 1.2 = normal
- between 0.9 and 1 = acceptable levels
- between 0.8 and 0.9 = mild arteriopathy, it is required the risk factors management
- between 0.5 and 0.8 = moderate arteriopathy, it is required specialized treatment
- below 0.5 = severe arteriopathy it is required emergency treatment

The test has a sensitivity of 90% and a specificity of 98% concerning the detection of the hemodynamically significant arterial stenosis (over 50%) in the main arteries of the inferior limb.

2. IMT, intima-media thickness

The increasing of the index of the intima-media thickness is the first noticeable sign of the vascular damage in the atherosclerosis, the substratum of this one being represented by the fibrocellular hypertrophy and the hypertrophy of the smooth muscle cells found in the arterial media. It represents the cumulative thickness of intima and media measured at the level of the common carotid artery, on the distal wall, at about 10 mm before the carotid bifurcation. The measurement is made on an ultrasound image of the carotid axis, using B mode, in longitudinal section. It is an index that is measured mandatorily during the Doppler ultrasound examination of the cervical-cerebral arteries (4,5) (fig. 1).

Figure no. 1 The intima-media thickness measured at the ACC level



The interpretation of the intima-media thickness levels:

- between 0,4 and 0,6 mm = normal at children and youth
- between 0,6 and 0,9 mm = acceptable levels at adults
- between 0,9 and 1,5 = pathological levels, mild and moderate atherosclerosis
- over 1,5 mm = the plaque of atheroma, it is required

specialized treatment (5)

3. PWV, pulse wave velocity

The determination of the pulse wave velocity (PWV) represents the most simple and non invasive method of the arterial stiffness determination. The technique consists in the recording of the pulse wave using two electrodes, one of them situated at the basis of the neck at the level of the common carotid artery and the other one placed on the forearm at the level of the radial artery. The time interval when the pulse wave crosses the distance between the two electrodes is measured by the device and a PWV over 10 m/s is considered as having a pathological value (6).

4. The calcium score

The calcium score (scorul Agatston) is an indirect marker of the atherosclerotic load of the coronary arteries which was recently introduced as a diagnostic method for the ischemic heart disease. It is determined using a CT-scan examination and it reflects the calcifications from the plaques of atheroma at the level of the coronary arteries predicting the vascular damage better than age, sex and ethnic origin. The calcium score has a diagnostic value even before the occurrence of the first symptoms or signs of the cardiac ischemia; in fact, the current guides ACC/AHA (American College of Cardiology/American Heart Association) recomands the determination of the calcium score also at the asymptomatic patients having an intermediate risk of coronary artery disease based on the Framingham score.

5. Trans-esophageal ultrasound and intravascular ultrasound (IVUS)

They are semi-invasive examinations which highlights atherosclerotic lesions at the level of the ascending aorta and of the coronary arteries and they are also able to specify quite exactly the dimensions and the types of the plaques of atheroma at these levels, this way quantifying the risk of further ischemic events. The APRIS study (Aortic Plaque and Risk of Ischemic Stroke) published in 2008 outlines that a 4 mm plaque in the ascending aorta highlighted by ultrasounds is associated with a 3 times higher risk of AVC, especially if it is ulcerated or with adjacent thrombus. Unfortunately these medical investigations are more difficult to be performed (7).

The subclinical atherosclerosis can be highlighted not even by vascular damage but also by tracking the signs of the damage of the target organs: the heart, the brain and the kidneys.

The subclinical damage of the heart can be highlighted by the following investigations considered to be "classical" ones:

- The resting electrocardiogram: the left ventricular hypertrophy is an element which reflects the subclinical damage of the heart and it is an independent predictor for the cardiovascular events.
- The effort electrocardiogram: for the clinically silent ischemia.
- The echocardiography: the wall hypertrophy, left ventricular mass > 125 g/m², remodeling of the cavities, the diastolic function modified.

The subclinical damage of the brain can be assessed by:

- Cognitive Assessment Tests: reveals the cognitive disorders and the risk of dementia.
- RM (the magnetic resonance): highlights the clinically silent incomplete infarcts and lesions of the white substance.

The subclinical damage of the kidney is revealed by:

- The microalbuminury: 30-300mg/24h or the ratio microalbuminury/creatinine > 22 in men and > 31 in women.
- The glomerulus filtration rate: < 60ml/min/1,73m²

- The serum creatinine slightly higher: men 1,3-1,5 mg/dl, women 1,2-1,4 mg/dl

In conclusion the subclinical atherosclerosis is an intermediate condition in the cardiovascular continuum which starts with the occurrence of the risk factors (dyslipidemia, HTA, diabetes, smoking, obesity), continues with the subclinical atherosclerosis and finalises with a multitude of clinical manifestations (coronary disease, myocardial infarction, cerebral infarction, heart failure, renal failure etc.).

The determination and the assessment of the subclinical damage, can be made and must be made, during daily activities, using the following "simple" methods, for a clinician: the electrocardiogram, the echocardiogram, the intima-media thickness assessment, the ankle / arm index, the microalbuminuria, the serum creatinine; the CT evaluation, the MRI or the IVUS making it less frequently and only regarding the selected cases.

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