Ultrasound Screening of Multifocal Atherosclerosis

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Key words: Multifocal atherosclerosis (MFA); Color Duplex; ischemic heart disease (IHD); Intima-media thickness (IMT).

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Abstract

Aim. The aim of our study was to perform ultrasound screening of multifocal atherosclerosis (MFA), in patients with coronary atherosclerosis.

Material and methods. Color duplex screening (CDS) and continuous wave (CW) doppler was used to study 32 clinically healthy persons and 87 patients with clinical data for ischemic heart disease (IHD).

Results. We have found high frequency of MFA simultaneously affecting coronary, carotid and femoral arteries. Intima-media thickness (IMT), which is a coronary atherosclerosis marker, had verifiable increasing in the common carotid artery (CCA) and common femoral artery (CFA) in the case of patients with chronic heart disease (CHD). In patients with CHD using ultrasound we established high frequency of clinically non-manifested asymptomatic stenosis and thromboses of the internal carotid artery (ICA) and common femoral artery, as well as aneurysms of the abdominal aorta (AAA). Markers for CHD with high sensitivity were the atherosclerosis plaques of ICA and CFA as well as IMT of the CFA. The most sensitive and specific markers for CHD were the combination of the IMT and atherosclerosis plaques of CCA, ICA and CFA.

Conclusion. Ultrasound diagnostic is the method of choice for simultaneous non-invasive screening of carotid, peripheral and MFA and has sensitive markers for coronary atherosclerosis.

Introduction

Atherosclerosis is one of the most serious and socially consequential conditions – a leading cause of death in the developed countries. Its basic forms are the coronary, cerebro-vascular and peripheral (1, 2). Besides these forms, there are also less familiar forms of atherosclerosis, such as the visceral atherosclerosis, which affects superior mesenteric artery, trunks celiacus and their renal arteries, as well as the aneurysms of the abdominal aorta. Any of the above forms of atherosclerosis in sufficient time could progress to grave invalidity or death.

One of the main characteristics of atherosclerosis is its multifocality (3, 4). The atherosclerotic process affects simultaneously or consecutively different organs of the body. A combined form of atherosclerosis - coronary, carotid and peripheral, is ascertained in
20-50% of the cases in a one-moment examination. If the condition is traced down its frequency increases considerably. The multifocality of atherosclerosis represents a diagnostic and therapeutically problem because of the fact that the different areas affected are investigated by different types of specialists: cardiologists, neurologists, angiologists, and gastroenterologists. Another important problem is the fact that in many of the patients with coronary atherosclerosis, carotid artery disease and peripheral arterial disease (PAD), the condition progresses for a very long time asymptotically. Probably only less than half of the patients have any clinical manifestations of the condition – stable angina, transitory ischemic attack (TIA) and claudication intermittent (5, 6). Atherosclerosis frequently is presented by severe thrombosis and/or attack (heart attack / stroke / critical ischemia of the limbs) at the patients who had not any complaints before. In such cases the arteriosclerotic plaque – the stenosis - often turns into thrombosis and a serious organic lesion occurs. In cases when an attack (heart attack, stroke, visceral or peripheral attack) has already occurred and the patient has survived its severe form, the treatment is extremely difficult and invalidity of the organs and limbs is usually unavoidable. Coronary, carotid and peripheral surgery, regardless of all its successes, can only partially and temporarily solve the problem and is, moreover, often too late to try even that. From this point of view, it is extremely important that an early diagnostic of atherosclerosis is carried out at the early asymptomatic stage of the condition.

In this respect, ultrasound screening has tremendous advantages compared to the other diagnostic methods. It can be carried out in a non-invasive and mass way at risk groups within ambulatory treatment. Moreover, the carotid artery disease and PAD, as well as the affected abdominal aorta and its visceral branches, can be simultaneously screened (7-10). This kind of examination has a high diagnostic quality. Unfortunately, coronary atherosclerosis is practically unreachable through such non-invasive investigation. The only reliable diagnosis here is achievable through coronaryography, but the indication for its implementation is usually a clinically manifest ischemic heart disease (IHD), which considerably limits the circle of patients screened for coronary atherosclerosis. The familiar risk factors – hypertonia, dyslipidemia, diabetes, smoking, stress – did not give a hundred percent reliable indications for the presence of an arteriosclerotic process (11, 12). This is the reason why a number of new markers for coronary atherosclerosis have been introduced recently.

In the last decades, the changes in the intima-media thickness (IMT) of the carotid and - less frequently – femoral artery are used as a marker of coronary atherosclerosis (13, 14). A number of multicentre studies established a correlation between the increase of IMT over 1 mm at common carotid artery (CCA), internal carotid artery (ICA) and common femoral artery (CFA) and the occurrence of coronary atherosclerosis (5-17). It is clear that there is a correlation between the increase in IMT and the frequency of the cardio-vascular complications. This makes IMT not only a marker of coronary sclerosis, but also a risk factor for the development of a heart attack or stroke – a marker of multifocal atherosclerosis (MFA) (18, 19).

According to some studies, IMT of the femoral artery is more sensitive marker, than IMT of the common carotid artery (5, 7). Others say that the carotid plaque is much more sensitive marker than IMT5. In this respect it must be keep in mind that the thickening of IMT does not necessarily mean an occurrence of an atherosclerotic process. It can be caused by the proliferation of the intima, as in the case of arterial hypertension. The increase of the IMT can also be caused by factors that do lead to atherosclerosis. This makes IMT a risk factor or a marker of atherosclerosis, but is not atherosclerosis itself, while the arteriosclerotic plaque is a sign of atherosclerosis.

Another marker of atherosclerosis is ankle-brachial index (ABI). In many screenings it is used as a marker of coronary and carotid atherosclerosis (20, 21).

Discussions are going on about the importance and sensitivity of the different markers of atherosclerosis. This requires an additional study of the problem, comparing the sensitivity and potential of the different markers of atherosclerosis. Such a study involves the diagnostics by ultrasound Doppler screening.

The aim of the current study was to carry out ultrasound screening of multifocal atherosclerosis in the case of patients with coronary sclerosis, so the evaluation of the sensitivity and potential of the different markers of atherosclerosis can be established.

Material and methods

A total of 119 patients with an average age of 61.4 ± 10.9 were examined, 90 of them were male and the rest 29 were female. The patients were divided into two groups.

Group À - 32 patients - clinically healthy, no indications of atherosclerosis and risk factors (arterial hypertension, diabetes, dyslipidemia, smoking, family
anamnesis). The patients had an average age of 60.4 years ± 9.8, male were 18 and female 16.

Group B – 87 patients with clinical indications of IHD, with an average age of 61.4 years ± 11.2 (29-80 range), 72 of them were male and 15 female.

The patients from groups A and B were examined anamnestically and clinically for the following risk factors of atherosclerosis: arterial hypertension, diabetes, dyslipidemia, family anamnesis (heart attack, stroke and vascular gangrene), obesity, stress, as well as for an additional factor – belief in God. An anamnesis concerning possible coronary conditions, operations and stenting in the past was taken too. Also, was taken an anamnesis of possible cerebrovascular disease (CVD) - TIA, stroke, as well as PAD (+/- claudicatio intermittet), gangrene, peripheral and heart operations or stenting.

The patients from the two groups were examined one time using Color Duplex screening (CDS) and bidirectional continuous wave (CW) doppler.

By the Color Duplex the following parameters were examined:

CDS – examination of carotid arteries (common and internal):

Atherosclerotic plaques, stenosis and thromboses of CCA and ICA were looked for. Standard methods of evaluation for the carotid artery disease were used involving B-mode, Color Doppler and power wave (PW) doppler. The thickness of the plaque was measured in tenths of the millimeter. The degree of stenosis was measured in terms of European Carotid Surgery Trial (ECST). It is a method in which the diameter of the vessel is measured in the place of its maximum constriction and not distally, in a "healthy" section.

The IMT of CCA was measured using standard methods by measuring IMT of the distal vascular wall, in 10 mm-long section before the bifurcation. Totally 3 - 5 measurements were made and the average result was taken.

CDS – examination of common femoral artery:

IMT was examined using standard methods, 10 mm long section before the bifurcation of CFA and 3 - 5 measurements were made to count an average result.

CDS - examination of the abdominal aorta (AA):

The patients from groups A and B were screened for aneurysms of the abdominal aorta (AAA) by measure of the maximum diameter of the aorta.

Using PW Doppler the systolic pressure of anterior tibial artery (ATA) and posterior tibial artery (PTA) were measured in all patients. Ankle-brachial index (ABI) was measured by following method: average pressure between the two arteries and / the higher brachial pressure.

All patients from group B – with clinical indication of IHD – were examined with coronarography. The degree of injury was estimated by screening coronary stenosis/thromboses, as well as the number of arterial branches affected with disease. An echocardiography examination was carried out at all patients from group B.

The results obtained were processed statistically.

Results

Following the examination by coronarography, 87 patients from group with clinical indications of IHD, was divided into two subgroups: B1 subgroup with 74 patients with coronary atherosclerosis and B2 subgroup with 13 patients without coronary atherosclerosis.

Three groups/subgroups (A, B1, B2) arrived regarding the past vascular conditions (coronary, cerebral and peripheral) or heart operations and stenting undergone (Table 1).

Table 1: Anamnestic data on IHD, CVD and PAD – subgroups B1 and B2.

<table>
<thead>
<tr>
<th>Group B</th>
<th>IHD n (%)</th>
<th>Stenocardia n (%)</th>
<th>Heart attack n (%)</th>
<th>ACB n (%)</th>
<th>Stent n (%)</th>
<th>CVD n (%)</th>
<th>PAD n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup B1 (74 pts)</td>
<td>74 (100)</td>
<td>13 (17.5)</td>
<td>37 (50)</td>
<td>10 (13.5)</td>
<td>14 (18.9)</td>
<td>9 (12.1)</td>
<td>13 (17.5)</td>
</tr>
<tr>
<td>Subgroup B2 (13 pts)</td>
<td>0</td>
<td>13 (100)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

IHD - ischemic heart disease; ACB – aortocoronary bypass; CVD – cerebrovascular disease; PAD – peripheral artery disease.

It was found out that in the case of subgroup B1 (coronarography proven atherosclerosis) about 50% of the patients had undergone a heart attack and about 32% a coronary bypass or stenting. Over 80% of the patients from subgroup B1 had an anamnesis for advanced coronary atherosclerosis. In the same group 12% of the patients reported CVD and 17% - PAD. Patients from subgroup B2 had not anamnestic data.
for an advanced atherosclerotic process. All patients from this subgroup had had clinical suspicions of stenocardia, but the diagnosis was not confirmed by coronarography. In the group A all patients had not clinical or anamnestic data of atherosclerosis.

Patients from group B were also examined regarding the different risk factors to atherosclerosis (Table 2).

Table 2: Risk factors to atherosclerosis in the case of patients from group B.

<table>
<thead>
<tr>
<th>Group</th>
<th>HTA n (%)</th>
<th>D n (%)</th>
<th>DL n (%)</th>
<th>S n (%)</th>
<th>O n (%)</th>
<th>FA n (%)</th>
<th>Stress n (%)</th>
<th>B n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subgroup B1</td>
<td>72 (97.2)</td>
<td>18 (24.3)</td>
<td>62 (83.7)</td>
<td>43 (58.1)</td>
<td>43 (58.1)</td>
<td>37 (50)</td>
<td>17 (22.9)</td>
<td>26 (35.1)</td>
</tr>
<tr>
<td>Subgroup B2</td>
<td>11 (84.6)</td>
<td>0 (8.7)</td>
<td>6 (48.1)</td>
<td>7 (53.8)</td>
<td>6 (48.1)</td>
<td>3 (23.8)</td>
<td>7 (53.8)</td>
<td></td>
</tr>
</tbody>
</table>

HTA – hypertension arterialis; D – diabetes; DL – dyslipidemia; S – smoking; O – obesity; FA – family anamnesis; B – belief in God.

A much higher frequencies of risk factors to atherosclerosis (diabetes, dyslipidemia, smoking and arterial hypertension) were ascertained in the case of subgroup B1 compared to subgroup B2. The difference concerning diabetes and dyslipidemia is particularly distinctive. Clearly evinced difference was also established regarding to the factor “belief in God”, believers in God from group B1 being largely outnumbered by believers in God from group B2. The relative risk RR of development of coronary atherosclerosis in the case of non-believers is RR = 1.4, CI = 0.95 (0.76-2.58)

Using CDS the IMT parameter of the common carotid and femoral artery was examined in all three groups of patients (Table 3).

Table 3: Size of IMT of CCA and CFA in the case of the different groups.

<table>
<thead>
<tr>
<th>IMT – (mm)</th>
<th>Group A</th>
<th>Subgroup B1</th>
<th>Subgroup B2</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCA</td>
<td>0.78±0.13</td>
<td>1.21±0.26</td>
<td>0.79±0.14</td>
</tr>
<tr>
<td>CFA</td>
<td>0.81±0.14</td>
<td>1.46±0.41</td>
<td>0.85±0.16</td>
</tr>
</tbody>
</table>

A statistically reliable increase of IMT of the two examined arteries was found in subgroup B1 (patients with coronary atherosclerosis), compared to the control group and the group with negative coronarography.

Parallel to the IMT examination, the carotid and common femoral arteries were examined by Color Duplex regarding to atherosclerotic plaques, stenotic and thrombotic processes (Table 4).

In the subgroup B1 (with proven coronary atherosclerosis) a high frequency of atherosclerotic carotid and femoral artery disease was established. Low or no such pathology was found in the case of subgroups B2 and group A (without coronary atherosclerosis). The frequency of the plaques and stenosis of the arteries examined in the subgroup B1 was very high: 93.2% in the ICA and 81% in the CFA, while a relatively high frequency of thrombosis in ICA - 9.4 % and superficial femoral artery (SFA) 16.2%, was established. These facts make clear in a categorical way the multifocality of the atherosclerotic process. When coronary atherosclerosis is the case here in the majority of cases concomitant carotid and femoral atherosclerosis also occurs. The risk of development of carotid atherosclerosis when there is coronary atherosclerosis is RR=4.97, OR = 59.8. Also, high is the risk of development of atherosclerosis in the case of the femoral artery RR=3.5, OR=14.2. Within our examination 3 out of 13 cases of femoral thromboses (23%) were diagnosed for the first time. These cases had developed asymptomatically or were not diagnosed on time. Even more unexpected was the result we got at in the case of carotid artery disease. All thromboses of carotid artery were diagnosed only within our screening, 6 out of 7 had developed asymptptomatically (85.7%) or with no demonstrative clinical manifestations. There were no anamnestic data for being a stroke undergone, except one case with thrombosis where TIA had been reported. The high frequency of light, medium or heavy carotid artery disease affecting almost 100% of the patients with coronary atherosclerosis was not reflected in the anamnesis for cerebral-vascular disease

Table 4: Frequency of stenotic-thrombotic processes in CCA, ICA and CFA.

<table>
<thead>
<tr>
<th></th>
<th>CCA</th>
<th>ICA</th>
<th>ICA</th>
<th>CFA</th>
<th>CFA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Subgroup B1</td>
<td>14 (1.9)</td>
<td>68 (83.2)</td>
<td>7 (9.4)</td>
<td>60 (81)</td>
<td>12 (16.2)</td>
</tr>
<tr>
<td>Subgroup B2</td>
<td>0 (0)</td>
<td>3 (23)</td>
<td>0 (0)</td>
<td>3 (23)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Group A</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

CDS - color duplex screening; CCA – common carotid artery; ICA – internal carotid artery; CFA – common femoral artery; SFA – superficial femoral artery.

Figure. 1 Screened asymptomatic thrombosis of ICA.
—only in 12% of the cases in terms of anamnestic data. It could be said, that carotid atherosclerosis does not entail any disturbances in the supply of blood to the brain or that the brain has not undergone any complications. Rather, the atherosclerosis has developed for a long time asymptptomatically or with very discreet symptoms making it hard for clinicians to diagnose it.

Using Color Duplex the following frequency and character of atherosclerosis of ICA was determined in the subgroup B1: stenosis<50% had 49 patients (66.2%), stenosis = 50-70% had 10 pts. (13.5%), stenosis>70% had 8 pts. (10.8%) and thrombosis had 7 patients (9.4%).

Those data show a relatively high frequency of serious carotid artery disease with stenosis>50%, comprising 1/3 of the cases. In all cases there was a higher risk of development of embolic or thrombotic stroke.

By CW Doppler the step systolic pressure of all patients was measured and the ABI of the different groups of patients was determined using the methodology described.

The values of ABI in the cases of group A and subgroup B2 were normal 1.03±0.15 and 1.02±0.16 respectively, while in the case of the subgroup-B1 (patients with proven coronary atherosclerosis) the index was 0.76±0.21, which was considerably and verifiably reduced (p<0.001). This is made clear by the fact that along with coronary atherosclerosis multifocal atherosclerosis develops, which affects the peripheral arteries of the lower limbs.

Using Color Duplex the abdominal aorta of all patients under the renal arteries was examined. The maximum diameter of the aorta was measured (Table 5).

| Table 5: CDS - measuring the maximum diameter of the abdominal aorta (AA) in the case of the different groups of patients. |
|------------------|------------------|------------------|
|                  | Group A          | Subgroup B1      | Subgroup B2      |
| AA-maximum diameter (mm) | 17 ± 4           | 23* ± 8          | 18 ± 5           |
| Aneurysm of AA – over 3 cm | 0                | 6 (8.1 %)        | 0                |

AA: abdominal aorta; *p<0.001.

Moderate but statistically reliable increase of the maximum diameter of the abdominal aorta was established in the case of patients from subgroup B1 compared to the other group/subgroup. At 6 patients with abdominal aneurysm a maximum diameter of over 3 mm was found.

Very important is the fact of the relatively high frequency of asymptomatic abdominal aneurysms was found in the cases of the subgroup of patients with atherosclerosis. This fact is indicative, on the one hand, of the combination of the two diseases as well as of being common ethiopathological mechanisms between arteriosclerosis and the aneurysms of the aorta. On the other hand, the fact is indicative of the existence in the case of patients with coronary atherosclerosis of asymptotically progressing aneurysms of the abdominal aorta (AAA), which could undergo rupture as they grow.

In accordance with the norms accepted by most authors in examining the following parameters, to be considered pathological are: for the IMT of the two arteries - values over 1 mm, for plaque - thickening of the intimate over 2 mm, for the ABI - values under 0.9 (8, 22), for aneurysms of the abdominal aorta – diameter over 3 cm, and for dilatation – diameter over 2 cm. Sticking to the aforementioned norms, the following frequency of pathological values of IMT in the case of group B1 were established: IMT in CCA and CFA were pathological at 27 (36.4%) and 68 (91.8%) patients, respectively. Pathologic plaques in the same subgroup were found at 69 (93.2%) patients in their ICA and at 60 (81%) patients in their CFA. Pathologic plaques in the both arteries (CCA+CFA) were found in 72 (97.2%) patients, while pathologic IMT and plaque in the both arteries were found at 74 (100%) patients.

On the basis of the frequency established and the interrelation between the parameters examined by Color Duplex in subgroups B1 and B2, the sensitivity, specificity and other characteristics for IMT can be established. The presence of plaques in ICA and CFA and ABI can be established too, used as markers for coronary atherosclerosis (Tables 6 and 7).

| Table 6: Characteristics and potential of evaluation markers at IHD. |
|------------------|------------------|------------------|
| Markers of IHD  | IMT – CCA | IMT-CFA | ABI  |
| Sensitivity  | 0.36         | 0.91         | 0.24  |
| CI 95%        | 0.31-0.38    | 0.87-0.95    | 0.19-0.24 |
| Specificity  | 0.84         | 0.63         | 0.99  |
| CI 95%        | 0.56-0.97    | 0.34-0.85    | 0.74-1.0 |
| Positively predicted value | 0.93 | 0.94 | 0.99 |
| CI 95%        | 0.80-0.98    | 0.90-0.97    | 0.81-1.0 |
| Negatively predicted value | 0.19 | 0.53 | 0.18 |
| CI 95%        | 0.12-0.21    | 0.29-0.72    | 0.14-0.18 |
| Accuracy      | 0.43         | 0.88         | 0.35  |
| Relative risk | 1.1          | 2.0          | 1.2   |
| Odds Ratio    | 3.1          | 19.6         | 417.8 |

IHD - ischemic heart disease; IMT – CCA = Intima media thickness in common carotid artery; IMT-CFA = Intima media thickness in common femoral artery; ABI – ankle brachial index.
The sensitivity of IMT in ICA as a marker of atherosclerosis is unexpectedly low - 0.36, its specificity being relatively high - 0.84. The accuracy of the method is low, its relative risk being relatively normal. Higher is the sensitivity of IMT in CFA – 0.84, the accuracy of the method being – 0.88, RR = 2 and OR = 19.8. ABI is a marker with a very low sensitivity - 0.24, but with high specificity - 0.99 and high OR. As a marker of coronary atherosclerosis, the plaque of ICA has high sensitivity - 0.93 and specificity - 0.69, high accuracy - 0.89, RR =2.6 and OR=31. The plaque of CCA as a marker has relatively lower sensitivity but higher specificity. The combination of markers considerably increases the possibilities for screening for coronary atherosclerosis. The presence of plaques on the inner carotid artery and the common femoral artery is a marker with 0.97 sensitivity, 0.84 specificity, 0.95 accuracy of the method, RR being 6.3 and OR - 198. A combination of markers determined (thickness of IMT of CCA and CFA over 1 mm, combined with the presence of plaques on ICA and CFA) almost certainly marks the presence of coronary atherosclerosis: sensitivity – 1.0, specificity - 0.92, positive predictive value – 0.98, negative predictive value – 0.99, accuracy of the method – 0.98, very high values of RR and OR.

The changes in the abdominal aorta, found more often in the case of patients from group B1 than in the case of patients from groups A and B2, can be added to the aforementioned markers. At 26 patients from group B1, 35% dilatation of AA exceeding 3 cm was found much more frequently than in the case of patients from the other groups. It was found out while studying the potential of this parameter as a marker for coronary atherosclerosis that its sensitivity is relatively low – 0.35, but its specificity is very high – 0.99, the accuracy of the method being – 0.44, its positive prognostic value – 0.86, its relative risk – 1.2 and Odds ratio – 70.4. Clearly, regardless of its unimpressive sensitivity, the pathological distension of the abdominal aorta can be used as a marker of coronary atherosclerosis.

The data we got about the high frequency of the risk factors contributing to atherosclerosis – arterial hypertonia, diabetes, dyslipidemia, smoking, obesity and family anamnesis – in the case of patients with coronary atherosclerosis supported their importance for the occurrence of the process. The relatively low percentage of believers in God in the case of group B1, compared to group B2, is a fact that needs closer examination within a larger study. The fact could be explained in terms of the hypothesis that believers adapt more easily to stress than non-believers.

**Discussion**

The reliably ascertained thickening of IMT of CCA and CFA in the case of the group of patients with coronary atherosclerosis, in contrast to the group of patients without coronary atherosclerosis, proves the link between the changes in IMT and coronary atherosclerosis. Such pathological changes have been established by a number of studies investigating the problem (15, 19, 23, 24). IMT of CCA is more frequently used as a marker and risk factor of coronary atherosclerosis. There are studies investigating the two arteries - the common carotid artery and the common femoral artery - in which it is asserted that IMT of CFA is the more sensitive marker, though. Many studies prove the existence of a correlation between the pathological increase of IMT of CCA and the frequency of myocardial heart attack and stroke at the patients being monitored within a period of 3 - 9 years. In most studies a high frequency of the relative risk of coronary and cerebro-vascular incidents has been established (25, 26, 27).

**Table 8: Correlation between carotid IMT and cerebro-vascular incidents in the case of asymptomatic patients (19, 23, 24, 28).**

<table>
<thead>
<tr>
<th>IMT</th>
<th>Study</th>
<th>Gender (M/F), age (years)</th>
<th>Duration (years)</th>
<th>Complication</th>
<th>RR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 1 mm</td>
<td>KID Finland</td>
<td>m, 40-40</td>
<td>3</td>
<td>Myocardial attack</td>
<td>2.2 (0.7-4.3)</td>
</tr>
<tr>
<td>Over 1 mm</td>
<td>ARC USA</td>
<td>m, 45-64</td>
<td>4-7</td>
<td>IH</td>
<td>1.9 (1.3-2.7)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>m, 45-64</td>
<td>6</td>
<td>Stroke</td>
<td>5.1 (1.3-8.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>m, 45-64</td>
<td>6</td>
<td>Stroke</td>
<td>3.6 (1.9-6.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.5 (0.5-5.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>CHS USA</td>
<td>m/f over 64</td>
<td>6</td>
<td>Attack Stroke</td>
<td>2.9 (2-4)</td>
</tr>
<tr>
<td>For 0.16</td>
<td>Rotterdam</td>
<td>m/f over 50</td>
<td>3</td>
<td>Attack Stroke</td>
<td>1.4 (1.2-1.8)</td>
</tr>
<tr>
<td>mm</td>
<td>Holland</td>
<td>m/f over 55</td>
<td>3</td>
<td>1.4 (1.3-1.8)</td>
<td></td>
</tr>
</tbody>
</table>

IHD - Ischemic heart disease; IMT – Intima media thickness.
It is clearly seen from the table that the risk of myocardial attack and stroke in the case of asymptomatic patients with thickening of IMT over 1 mm is heightened, the effect in the case of women being more clearly evinced. The Rotterdam study proves also that each increase in IMT with 0.16 mm increases the relative risk of heart attack and stroke with 1.4. Similar studies have been carried out with regard to IMT of CFA as well as with regard to the two arteries. The importance of IMT as a predictor of coronary and cerebrovascular complications and a risk factor and marker of coronary and multifocal atherosclerosis has been proven. Nevertheless, some authors point out that the increase in the IMT cannot be with absolute certainty attributed to initial atherosclerotic changes in the intima since the thickness of the media is measured too. Besides, the thickening of the intima can be due to an intimal hyperplasia and intimal hypotrophy, two compensatory reactions to hemodynamic stress. This phenomenon is more clearly evinced in the area of the arterial bifurcation and can only provoke the development of intimal hypertrophy or the development of atherosclerotic plaque. Hence, our assertion that it cannot be stated with certainty that the changes in IMT are due to early atherosclerosis, the two changes (IMT and the atherosclerotic plaque), may have a partly common pathogenesis.

Some researches have proven the direct correlation between the thickening of IMT and the development of atherosclerotic plaque of the carotid artery (25, 29).

We can summarize that the changes in IMT of the carotid and common femoral artery have to do with coronary atherosclerosis and are a risk factor and predictor of the development of coronary and cerebrovascular complications. But, are these changes a sensitive marker of coronary atherosclerosis really (30).

The data arrived at by us did not corroborate such a supposition. Only 27 patients (36%) from subgroup B1 turned out to have pathological changes in IMT exceeding 1 mm. The sensitivity of the method as a marker of atherosclerosis is low—0.36; the relative risk involved being 1.1. Much higher is the sensitivity of IMT of CFA, the relative risk involved being 2.0. This ours finding correlate with other authors too (9, 10, 17, 31).

Studying ABI as a risk factor, predictor and marker of coronary atherosclerosis (32, 33) very low sensitivity was established, only 0.24, but the specificity was very high 0.99. A number of researches confirm the existence of a correlation between pathological ABI and coronary atherosclerosis as well as the role of pathological ABI as a risk factor and predictor of coronary and cerebro-vascular complications (9, 22, 32). This is due to the fact that the values of ABI bellow 0.9 are determined only in the case of hemodynamic stenosis or thromboses in the peripheral arteries of the lower limbs and are usually the result of PAD (peripheral arterial disease) caused by atherosclerosis. Consequently, ABI registers one of the basic forms of atherosclerosis - PAD, which is often in combination with coronary and cerebro-vascular atherosclerosis. In the case of pathological ABI in almost a 100% of the cases there is concomitant coronary atherosclerosis, but in the case of the present study only 25% of the cases with manifested coronary atherosclerosis had pathological ABI. Because of this finding for ABI and also for IMT, ABI should not be used as independent markers of coronary atherosclerosis.

A very high frequency of the atherosclerotic pathology was established in studying the group of patients with coronaryography proven atherosclerosis in terms of atherosclerotic plaques, stenosis and thromboses of the inner carotid artery and the common femoral artery. When the plaque or the thrombosis of ICA is used as a marker of coronary atherosclerosis, the sensitivity of the method is very high – 0.93. When the plaque of CFA is used as a marker of coronary atherosclerosis, the sensitivity of the method is relatively lower but its specificity is higher. These data are confirmed by studies carried out by other authors. Preceding from the assumption that atherosclerosis is a multifocal process, it is logical to assume the following. When an advanced atherosclerotic process (plaque) is ascertained in one or two key arteries of the body it can be with a very high degree of probability assumed that a third group of arteries – the coronary arteries – are affected too. In order that the sensitivity and specificity of the markers is increased, it is appropriate that the markers are combined. When two markers are used in combination, high sensitivity – 0.97 and high specificity – 0.84 is manifested. The relative risk and IR are high too.

Because IMT is a specific marker (different from the atherosclerotic plaque) we studied by Color Duplex the two types of markers - IMT and plaque of the two arteries the carotid and common femoral. Thus very high sensitivity was achieved - 0.99, as well as very high specificity - 0.93, the RR being extremely high for coronary atherosclerosis.

While by the ultrasound method studying patients with proven coronary atherosclerosis with regard
to the multifocality of the process, a very high frequency of concomitant atherosclerosis with other localizations was established. Atherosclerotic carotid artery disease was found in the case of 93% of the patients with coronary atherosclerosis. The common femoral artery was afflicted in 81% of the cases. As a result of the development of the diagnostic methods very early atherosclerotic changes in the vessels are detected, hence the much higher frequency of the concomitant multifocal atherosclerosis. Most studies, our own inclusive, establish 20%, 30% up to 50% multifocal atherosclerosis. More precise researches with extended criteria for diagnosing the disease (plaque over 1.5 mm) prove not only the multifocality of the process, but also the almost one-moment affliction (in a different degree, though) of the arteries of the body. The three basic forms of atherosclerosis — coronary, cerebro-vascular (carotid) and peripheral (PAD) develop simultaneously.

The problem is that the frequency of the asymptomatic forms of atherosclerosis is very high, 6 out of 7 (85%) carotid thromboses and 25% of the femoral thromboses diagnosed within our study had developed asymptotically and were only detected through the screening we carried out. The thromboses discovered by us within 6 of the patients from the group with coronary atherosclerosis, AAA had developed asymptotically too. Unfortunately, rupture is the first serious clinical manifestation of this condition. This specificity of the atherosclerosis (its long asymptomatic development) makes very difficult its timely clinical diagnosing. As a result, treatment often starts at a stage when serious organic damages (heart attack, stroke, and gangrene) have already been undergone. From this point of view, it is extremely important that an early diagnosing of the atherosclerosis in its different forms and localizations is carried out. The screening of the hidden atherosclerotic damages in the case of high-risk groups patients is extremely important too (13, 34, 35, 36). In this respect, the ultrasound Doppler diagnostic (the Color Duplex and PW Doppler) are methods with tremendous potential both in the field of mass screening and the field of precise vascular diagnosing (8, 13, 14, 19, 25, 37). The method is harmless, quick, can be repeated many times. Its diagnostic value is high and it is moreover cheap. Within one research the following markers of atherosclerosis can be examined: IMT of CCA and CFA, plaques and stenosis of the two arteries, ABI and the diameter of AA under the renal arteries. All these parameters are diagnosing multifocal atherosclerosis, the presence of an atherosclerotic process in the carotid, femoral or peripheral arteries. They can also be used as highly sensitive markers of coronary atherosclerosis and predictors of future complications. As a result the complex examination of the patient and the use of combined markers can improve considerably the potential of early diagnosis. They also improve our capacity to discover early forms of multifocal atherosclerosis, our capacity to screen for coronary atherosclerosis in particular.

Our own observation led to the finding that IMT has certain sensitivity to CCA as a marker of atherosclerosis, but this sensitivity increases considerably when combined with IMT of the carotid and femoral artery. The most reliable marker of coronary atherosclerosis is the combination of atherosclerotic plaques of the carotid and femoral arteries, with or without changes of IMT of the two arteries. In addition to these markers ABI should be used too. Here are the advantages of such a complex ultrasound examination (CDS and CW Doppler) for the diagnosing of atherosclerosis: It is non-invasive, carried out ambulatory and is handy for mass screening. It has high diagnostic sensitivity and specificity with regard to diagnosing of multifocal atherosclerosis, as well as a marker of coronary atherosclerosis.

The carotid and femoral bifurcations are studied in one moment for atherosclerosis, and the arteries of the lower limbs were screened for atherosclerosis with ABI.

Such a study can be supplemented with screening for aneurysms of the abdominal aorta and for stenosis of renal artery, mesenteric superior and trunks celiacus.

As far as the femoral and carotid bifurcations in particular are concerned, the method shows very high sensitivity and can detect the very early stages of the atherosclerotic process — plaques with a width exceeding 1.5 mm.

The discovered stenotic plaques of the carotid and femoral arteries can be also used as markers of coronary sclerosis. IMT of CCA and CFA can be used as markers for the same purpose too.

Thus using ultrasonic diagnosing several problems concerning atherosclerosis can be solved.

In the first place, the study is complex. It involves the simultaneous screening of the carotid, peripheral and abdominal-visceral form of atherosclerosis.

In the second place, the very early or asymptomatic forms of atherosclerosis are detected.
In the third place, by using a whole complex of ultrasound markers, we can prognosticate the presence of a hidden form of atherosclerosis — coronary atherosclerosis.

In the fourth place, the method is appropriate for the conduction of mass screening of risk groups. This advantage is extremely important, considering the aforementioned characteristics and specifics of atherosclerosis as a problem.

And at the last, it must be mentioned that the method is relatively inexpensive.

The following risk groups must be subjected by ultrasound screening for multifocal atherosclerosis: patients with a manifested form of atherosclerosis — coronary, carotid or PAD — for screening for other forms of atherosclerosis and patients with manifest risk factors to atherosclerosis — arterial hypertension, dyslipidemia, diabetes, smoking, family anamnesis, age over 55 years for male and 60 years for female.

After discovering pathological markers for atherosclerosis, the markers can be used as an indication for carrying out coronarography of patients who have no clinical indications of IHD:

**Absolute indication:** The presence of at least two of the markers for coronary atherosclerosis, one of which has to include the carotid artery, though: - atherosclerotic plaque of carotid artery; - atherosclerotic plaque of femoral artery; and ABI < 0.9.

**Relative indication for coronarography:** - IMT over 1 mm of NCA and CFA (or both of them); - the presence of atherosclerotic plaque of CCA or CFA, combined with thickening over 1 mm of a IMT of one of the two arteries, but not from the area of the stenosis; IMT of carotid artery over 1 mm, combined with pathological ABI.

On the basis of the study conducted the following major conclusions can be drawn:

Atherosclerosis is a multifocal condition affecting simultaneously the coronary, carotid and peripheral arteries and occurring clinically as IHD, cerebrovascular disease (CVD) and PAD. This presupposes looking for other hidden forms of atherosclerosis when some basic form of atherosclerosis has already been clinically evicted.

Using CDS and coronarography, the frequency of MFA was determined (81%), this involving the one-moment affecting of coronary, carotid or femoral arteries.

The employing of CDS in the case of patients with coronary atherosclerosis led to the establishment of a high frequency of Coronary artery disease (CAD) 93% and PAD (of the femoral artery) 81%, including its early preclinical forms.

A statistically reliable increase of IMT of CCA and CFA in the case of patients with CHD was ascertained. IMT is a marker of coronary atherosclerosis.

There is a correlation between the frequency of occurrence of the carotid and femoral atherosclerotic plaques (stenosis) and the occurrence of the coronarographically proven IHD. Patients with CHD stand a high relative risk of developing carotid (RR=5) and peripheral atherosclerosis - PAD (RR=3.5).

In the case of patients with CHD high frequency of clinically asymptomatic stenosis and thrombosis of ICA — 86.9% and CFA — 78.3%, as well as of aneurysms of the abdominal aorta — 8.1% was ascertained by ultrasound. This entails the necessity of screening for MFA in the case of all patients with IHD.

It was ascertained a relatively low sensitivity of IMT towards CCA (0.36) and ABI (0.24) and a high specificity as markers of IHD.

Highly sensitive markers of CHD are the atherosclerotic plaques of ICA (0.93) and CFA (0.81), as well as IMT of CFA (0.84).

The most sensitive and specific markers for IHD are the combination of the examination of IMT and the atherosclerotic plaques of CCA, ICA and CFA (100% sensitivity and 0.92 specificity).

Ultrasound diagnosing is a method of choice of a one-moment non-invasive screening of the carotid, peripheral or multifocal atherosclerosis and has sensitive markers for coronary atherosclerosis. When it is positive, represent a highly sensitive ultrasound marker of coronary atherosclerosis.

The complex and early diagnosing of MFA employing coronary markers can make treatment with medications and endovascular treatment much more efficient. The mass ultrasound screening of risk groups for atherosclerosis would change dramatically our approach to that serious condition. It would redirect our attention towards the early asymptomatic manifestations of the condition thus reducing the high mortality and invalidity rate involved. The future of the treatment of atherosclerosis is in the prophylaxis of the condition and its opportune treatment with medications and by endovascular treatment. Such an approach can make
coronary, carotid and peripheral vascular surgery a thing of the past.

References


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