The Usefulness of High-Resolution Carotid Ultrasonography for the Detection of Subclinical Atherosclerosis.

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Abstract: Background: This study aimed to evaluate diagnostic possibilities of the high-resolution carotid ultrasonography for determining early manifestations of atherosclerosis taking into account gender and lipid profile differences of patients. Patients and methods: In this case-control setting, we included 431 subjects aged 55 to 79 years with no history of hypertension, ischemic heart disease, heart attack, stroke and other cardiovascular diseases. Non-invasive assessment of carotid intima-media thickness (CIMT) was held by high-resolution carotid ultrasonography. Results: We detected the atherosclerotic lesions in more than 50% of the patients. The appearance of atherosclerotic plaques in carotid arteries was associated with gender and alterations in the lipid spectrum of blood. Conclusion: The high-resolution carotid ultrasonography combined with blood lipid spectrum test could be considered as a screening method to reveal early atherosclerosis.

Key Words: Atherosclerosis, Carotid intima-media thickness, High-resolution carotid ultrasonography.

Introduction:
Cardiovascular pathology steadily takes first place among the mortality causes in the population of Russia. Clinical and socio-economic significance of the cardiovascular diseases (CVDs) has been increasing since average age of the population and influence of risk factors are growing.(1) There were described more than 200 factors contributing to the atherosclerosis development or adversely affecting its flow. The most important risk factors of atherosclerosis are hypertension, obesity, insufficient physical activity, smoking and gender.(2) Atherosclerosis is the morphological substrate of CVDs. Atherosclerosis is a chronic disease of the large and medium caliber arteries, defined by the sedimentation and accumulation of the atherogenic apoprotein B-containing plasma lipoproteins in the intima with subsequent connective tissue reactive proliferation and fibrous plaques formation.(3) Women considered to be less prone to coronary atherosclerosis than men.(4, 5) This fact could be substantiated by a favorable women estrogenic background.(6) It is remained unclear whether there are gender differences associated with early manifestation of carotid atherosclerotic lesions. Furthermore, atherosclerotic vascular alterations in one area can be extrapolated to another area. Thus, in the study of the carotid arteries duplex scanning relevance for the coronary atherosclerosis early detection the presence and severity of coronary atherosclerosis with the presence and severity of carotid arteries atherosclerosis were compared.(7) As a result, it was found that marked atherosclerotic vascular lesions in one organ are accompanied by pronounced arteries alterations in another. The coronary arteries lesions were revealed in 92.6% of cases, in the presence of carotid arteries lesions, which determines the high sensitivity of carotid arteries duplex scanning at a relatively low specificity – unimpaired carotid arteries were detected with coronary arteries pathology in 29.6% of cases. It is known that risk factors modification primarily brings benefit to persons with high initial risk.(8) However, at the...
population level, the majority of deaths occurred in the group at low or moderate cardiovascular risk. This is because the number of people at high risk is small (so-called "the prevention paradox"). Consequently, it is necessary along with preventive interventions in groups at high risk to identify in a population patients with initial manifestations of atherosclerosis. In the early diagnosis of in evel is still time for adjustment to the patient’s lifestyle and prevention manifestations of the disease. If atherosclerosis is diagnosed at an early subclinical stage it can be prevented already with reorientation of patient’s lifestyle.

The aim of this study was to determine the diagnostic capabilities of high-resolution carotid ultrasound scanning for atherosclerosis early manifestations diagnosis together with gender differences and lipid spectrum of blood alterations clarification.

**Materials and Methods**

The study included 431 individuals (50 – 83 years, in average 65.1±0.29 years) who were screened at clinical diagnostic center «Nauka». Male group included 92 (21.3%) patients, female – 339 (78.7%). The study was approved by the Ethics Committee of the Academy of biology and biotechnology. All participants gave written informed consent.

The main method for the atherosclerotic status assessing was the carotid intima-media layer thickness measurement by high-resolution B-mode ultrasound scanning (10), using a high-resolution tomographic ultrasound machine VOLUSONE8 equipped with a 7.5 MHz linear array transducer. The inquiry protocol included scanning of the left and right carotid arteries and the carotid sinus area with a focus on the posterior artery wall in three fixed projections: anterolateral, lateral and posterolateral.(11)

All measurements were performed sequentially in a single session. The scanning procedure was recorded in the form of frozen shots in JPG format to external media.

After the main survey the patients were divided into two groups: group 1 - patients with initial atherosclerosis manifestations with intima-media thickness values from 0.9 mm to 1.3 mm (Figure 1) and group 2 - with severe atherosclerosis manifestations, when intima-media thickness values were 1.3 mm and higher (Figure 2). Individuals with absence of carotid arteries intima-media complex thickening (Figure 3) were combined into the control group. The first and second groups patients were separated by sex. Lipid spectrum of blood alterations were evaluated in each group.

Blood lipid spectrum was evaluated by homogeneous enzymatic colorimetric test using automatic biochemical analyzer Furuno CA-400.

**Statistical analysis:** The collected data statistical analysis was carried out using windows version of Statistica 10 (StatSoft, USA). A p value <0.05 was regarded as statistically significant.

**Results and Discussion**

Among 431 patients absence of blood lipid spectrum alterations and CIMT was detected in 35 individuals (8.1%), only adverse lipid profile alterations in blood were detected in 155 (35.9%), CIMT alone was determined in 41 (9.5%), and simultaneously both early atherosclerotic aberrations were revealed in 200 subjects (46.4%). Thus, the most numerous group was one with patients who had lipid profile and ultrasonic changes which testified to the atherosclerosis development.

In the present study, 206 individuals (47.8%) (group 1) had atherosclerosis initial manifestations namely CIMT from 0.9 mm to 1.3 mm, 48 patients (11.1%) (group 2) had acute form of atherosclerosis. CIMT was absent in 177 subjects (41.1%) (control group).

Distribution of three studied groups patients according to sex is presented in Table 1.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Control group</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Total</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>153 (45.8%)</td>
<td>150 (44.9%)</td>
<td>31 (9.3%)</td>
<td>334 (100%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>24 (27.9%)</td>
<td>56 (55.8%)</td>
<td>17 (16.3%)</td>
<td>97 (100%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>177 (41.1%)</td>
<td>206 (47.8%)</td>
<td>48 (11.1%)</td>
<td>431 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

Assessment of p value was held by the criterion M-L Chi-square.
Among control group patients who have no carotid arteries walls lesions there were more women than men (48.2% vs. 27.9%). Groups 1 and 2 more frequently men have CIMT. Evaluation of conjugation between the carotid arteries wall atherosclerotic alterations severity and sex was performed using the Pearson's Chi-square test with Mantel–Haenszel correction for the continuity (M-L Chi-square). It has been proved the association between male sex and the symptom frequency like CIMT by statistical analysis of two qualitative traits pairing. While CIMT quantitative traits did not differ between men and women. Thus, CIMT average values of men and women in control group were 0.78±0.005 mm and 0.77±0.035 mm, in group 1 – 1.03±0.02 mm and 1.05±0.007 mm, in group 2 – 1.45±0.0272 mm and 1.52±0.07 mm, respectively. Hence only the qualitative traits pairing analysis using crosstabulation allowed to reveal the relationship between sex and the severity of the carotid arteries wall atherosclerotic alterations.

Previously after ultrasound scanning of the internal carotid arteries diameter, linear velocity and resistance of 647 people of both sexes aged from one year to 74 years there were marked another hemodynamic variations depending on sex. The authors noted that in the period from early childhood to adolescence and from age of puberty to advanced age there is an increase of the internal carotid arteries diameter. The internal carotid arteries diameter, vascular resistance index, volumetric blood flow rate were higher in men than in women in most age periods.(12)

The parameters of blood lipid spectrum of three studied groups patients are shown in Table 2.

Table 2: Blood lipid spectrum of study subjects depending on CIMT severity

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total cholesterol (mmol/l)</th>
<th>High density lipoprotein cholesterol (mmol/l)</th>
<th>Low density lipoprotein cholesterol (mmol/l)</th>
<th>Triglyceride (mmol/l)</th>
<th>Atherogenic index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>6.00±0.01</td>
<td>1.69±0.03</td>
<td>3.38±0.08</td>
<td>1.21±0.04</td>
<td>2.59±0.06</td>
</tr>
<tr>
<td>Group 1</td>
<td>6.22±0.09</td>
<td>1.48±0.02</td>
<td>3.64±0.07</td>
<td>2.29±0.85</td>
<td>3.32±0.07</td>
</tr>
<tr>
<td>Group 2</td>
<td>6.46±0.16</td>
<td>1.37±0.07</td>
<td>3.73±0.10</td>
<td>1.76±0.11</td>
<td>3.63±0.18</td>
</tr>
<tr>
<td>All patients</td>
<td>6.16±0.06</td>
<td>1.57±0.02</td>
<td>3.54±0.04</td>
<td>1.73±0.38</td>
<td>3.04±0.05</td>
</tr>
<tr>
<td>p value</td>
<td>0.084</td>
<td>&lt;0.001</td>
<td>0.42</td>
<td>0.63</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Assessment of p value was held by the Fisher criterion (F). At the same time conducted analysis of variance allowed to determine multiple difference of one indicator among several groups. Group 1 patients had significantly (p<0.05) decreased high density lipoprotein cholesterol levels in blood, increased atherogenic index, in other words, they had unfavorable tendency of blood lipid spectrum alteration.

In the comparative analysis course of three groups subjects depending on CIMT severity and sex the blood lipid spectrum differences intensified (Table 3).

Table 3: Blood lipid spectrum of study subjects depending on CIMT severity and sex

<table>
<thead>
<tr>
<th>Groups</th>
<th>Sex</th>
<th>Total cholesterol (mmol/l)</th>
<th>High density lipoprotein cholesterol (mmol/l)</th>
<th>Low density lipoprotein cholesterol (mmol/l)</th>
<th>Triglyceride (mmol/l)</th>
<th>Atherogenic index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>Female</td>
<td>6.10±0.11</td>
<td>1.72±0.03</td>
<td>3.41±0.08</td>
<td>2.23±0.04</td>
<td>2.56±0.06</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>5.43±0.21</td>
<td>1.59±0.07</td>
<td>2.44±0.20</td>
<td>1.70±0.10</td>
<td>2.78±0.19</td>
</tr>
<tr>
<td>Group 1</td>
<td>Female</td>
<td>6.18±0.10</td>
<td>1.63±0.03</td>
<td>3.71±0.08</td>
<td>2.54±0.15</td>
<td>3.28±0.08</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>5.73±0.12</td>
<td>1.35±0.07</td>
<td>4.35±0.13</td>
<td>1.56±0.17</td>
<td>2.43±0.13</td>
</tr>
<tr>
<td>Group 2</td>
<td>Female</td>
<td>6.40±0.20</td>
<td>1.65±0.08</td>
<td>3.77±0.13</td>
<td>1.50±0.13</td>
<td>3.40±0.21</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>6.12±0.21</td>
<td>1.13±0.06</td>
<td>4.70±0.15</td>
<td>1.75±0.22</td>
<td>4.41±0.20</td>
</tr>
<tr>
<td>p value</td>
<td>0.004</td>
<td>&lt;0.001</td>
<td>0.81</td>
<td>0.94</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Assessment of p value was held by the Fisher criterion (F). Total cholesterol was higher in women with CIMT than in men (groups 1 and 2). However, due to the higher values of high density lipoprotein cholesterol in blood atherogenic index in women was lower than men. Significant differences were observed for total cholesterol (p=0.004), high density lipoprotein cholesterol (p<0.001) and atherogenic index (p<0.001) between all groups.

Conducted ANOVA analysis of variance for the impact factors (sex, blood lipid spectrum alterations) force research has showed that sex exercised a significant influence on the CIMT severity. This was evidenced by the high value of Fisher test (F=83.7) at p<0.001. The impact force of blood lipid spectrum as an influencing factor was also significant (p=0.028), while Fisher test was 4.1.

**Conclusion:**
According to the obtained data it was revealed using neck vessels ultrasonography that in tentatively clinically healthy subjects group 56.2% of people had signs of atherosclerosis. These results make non-invasive high-resolution carotid ultrasonography as the priority method for the detection of subclinical atherosclerosis. The carotid intima-media thickness severity was associated with male sex and adverse blood lipid spectrum alterations – decreased high density lipoprotein cholesterol levels and increased atherogenic index.

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**Conflict of interest:** None.

**References**