

INVESTIGATION OF THE REFERENCE VALUES OF THE ANKLE-BRACHIAL INDEX IN ASYMPTOMATIC SEVERE HYPERCHOLESTEROLEMIA

Lyudmila G. Vladimirova-Kitova,
Clinic of Cardiology
Medical University, Plovdiv, Bulgaria

ABSTRACT:

The issue with the different levels of ankle-brachial index, which are in the normal reference range is less studied, but quite interesting. There have not been any studies on ankle-brachial index in patients with severe hypercholesterolemia in Bulgaria. **Aim:** To study the relationship between the ankle-brachial index and the lipid markers of the atherogenic risk (routine lipid profile, Apolipoprotein-B, Apolipoprotein-A) in asymptotically severe hypercholesterolemia (without peripheral vascular disease). **Methods and materials:** 50 patients with documented severe hypercholesterolemia >7.5 mmol/l satisfying the Simon-Broom criteria for clinically established and probable Familial Hypercholesterolemia were studied. All of the patients had a negative stress echocardiography and not known coronary artery disease. There were 30 controls without hypercholesterolemia. The laboratory used was the Clinical Laboratory at the Medical University Plovdiv. The total cholesterol and triglycerides were measured with enzyme-colorimetry and cholesterol in high density lipoprotein and cholesterol in low density lipoprotein with direct automatic analyses. Apolipoproteins were calculated by immunoturbidimetric method. The biochemical analyzer Konelab 60i was used in all the measurements. **Results:** The median baseline ankle-brachial index in both groups differ significantly, 1.06 ± 0.12 in the hypercholesterolemia group and 1.25 ± 0.03 in the controls ($u=2.44$, $p<0001$) The ankle-brachial index reference range divides them in borderline 0.9-0.99, low normal 1.0-1.29 and normal 1.1-1.29. The first two groups were combined in one including 35 patients (70 %) and the third included 15 patients (30 %). There is a very strong inverse relationship between ankle-brachial index value and age. It reflects the age related changes in the vessel structure and function in subclinical atherosclerotic accumulation, in this case affecting the circulatory system of the lower extremities. A strong inverse statistically significant relationship was found between ankle-brachial index and Apolipoprotein-B, ankle-brachial index and Apolipoprotein-B/A₁ index. These two variables explain the variations in ankle-brachial index.

Conclusion: In the population with manifested hypercholesterolemia, Apolipoprotein-B and not the routine lipid profile and atherogenic indexes, is a predictor of structural blood vessel damage, verified through ankle-brachial index.

Key words: hypercholesterolemia, ankle-brachial index, peripheral vascular disease, biomarkers,

INTRODUCTION:

The ankle-brachial index (ABI) is the first non-invasive test for atherosclerotic accumulations (1) It has been used for numerous years to identify individuals with a compromised blood supply to the lower extremities. (2). The frequently asymptomatic course of peripheral vascular disease (PVD) and the inaccuracy of the physical examination necessitates the use of ABI as a routine part of the clinical evaluation. (2). It correlates with the measurement of the blood pressure. (3) It is highly informative for stenoses of the lower extremities of $> 50\%$. (3-6). The reference values were presented at TransAtlantic Intersociety Consensus Working Group in 2005: Normal is 0.9, mild PVD; 0.5-0.75, moderate PVD; less than 0.5 severe PVD. More than 1.3 – falsely elevated (non-compensated vessels) It has been proven that the low (<0.9) as well as the high (>1.3) ABI are related to an increased cardiovascular risk. Identifying individuals with extreme values may be used for an evaluation of the cardiovascular risk. ABI values less than 0.9 have a sensitivity of 95% and specificity of 99% for PVD. (3-5)

The issue with the different levels of ABI, which are in the normal reference range is less studied, but quite interesting. There are only few data available on the significance of the atherosclerotic burden when dealing with normal range values. The case with the different levels of ABI when they are in reference range is intriguing. These "normal" ABI levels are less well studied. Data on the impact of normal ABI's on atherosclerosis burden is available in few studies only. There have not been any studies on ABI in patients with manifested hypercholesterolemia in Bulgaria. (4-10)

AIM:

To study the relationship between the ABI and the lipid markers of the atherogenic risk (routine lipid profile, Apolipoprotein-B, Apolipoprotein-A-i) in asymptotically severe hypercholesterolemia (without PVD).

METHODS AND MATERIALS:

50 patients with documented severe hypercholesterolemia >7.5 mmol/l satisfying the Simon-Broom criteria for clinically established and probable Familial Hypercholesterolemia were studied. All of the patients had a negative stress echocardiography and not known coronary artery disease. There were 30 controls without hypercholesterolemia. The laboratory used was the Clinical Laboratory at the Medical University Plovdiv. The total cholesterol and triglycerides were measured with enzyme-colorimetry and cholesterol in high density lipoprotein (HDL-cholesterol) and cholesterol in low density lipoprotein (LDL-cholesterol) with direct automatic analyses. Apolipoproteins were calculated by immunoturbidimetric method. The biochemical analyzer Konelab 60i (Thermo-Electron-Co USA) was used in all the measurements.

RESULTS

The median baseline ABI in both groups differ significantly, 1.06 ± 0.12 in the hypercholesterolemia group and 1.25 ± 0.03 in the controls ($u=2.44$, $p<0001$) The ABI reference range divides them in borderline $0.9-0.99$, low normal $1.0-1.29$ and normal $1.1-1.29$. The first two groups were combined in one including 35 patients (70 %) and the third included 15 patients (30 %).

There is a very strong inverse relationship between ABI value and age. It reflects the age related changes in the vessel structure and function in subclinical atherosclerotic accumulation, in this case affecting the circulatory system of the lower extremities. (Figure 1)

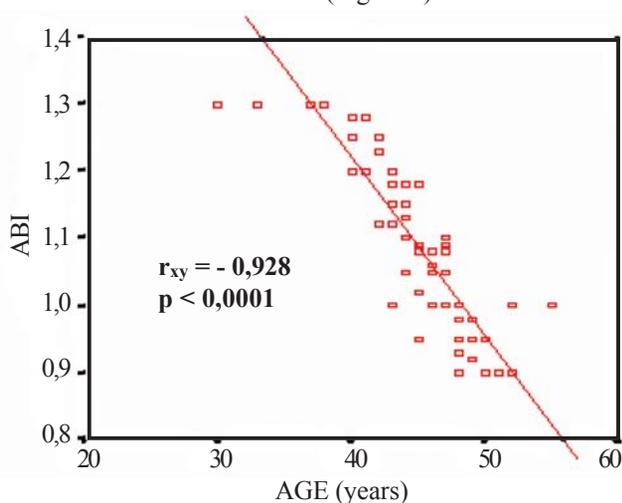


Figure 1. Correlation between ankle-brachial index and age

We can calculate ABI in respect of age and gender in investigation patients with severe hypercholesterolemia.

$$\text{male: ABI} = 2,285 - 0,026 \times \text{age,}$$

$$\text{female: ABI} = 2,279 - 0,026 \times \text{age.}$$

We differentiated all patients in two group in respect of age (≤ 45 and > 45 years old). There are most patients with normal level (> 1.1) of ABI in the group with ≤ 45 years old (97%), as most patients with low-normal level of ABI (97.5 %) in patients group with > 45 years old. The results present on the Figure 2.

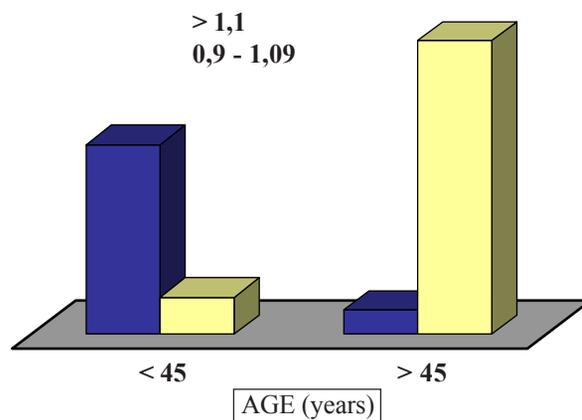
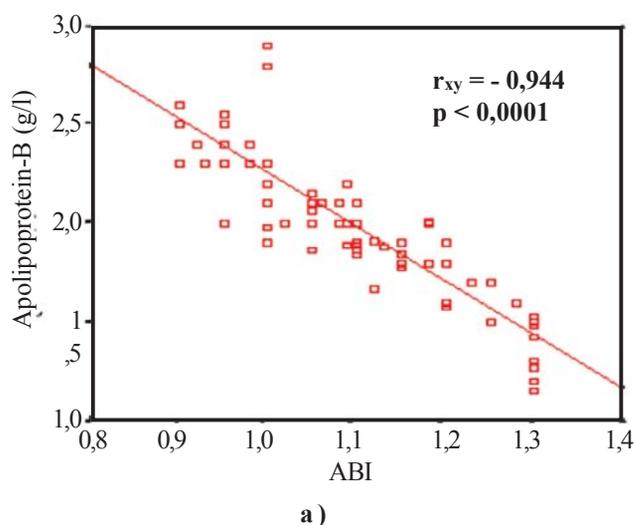


Figure 2. Distribution on the two groups of ABI in respect of the age

A strong inverse statistically significant relationship was found between ABI and Apo-B, ABI and Apo-B/Apo-A₁ index. These two variables explain the variations in ABI. (Figure 3-a,b)



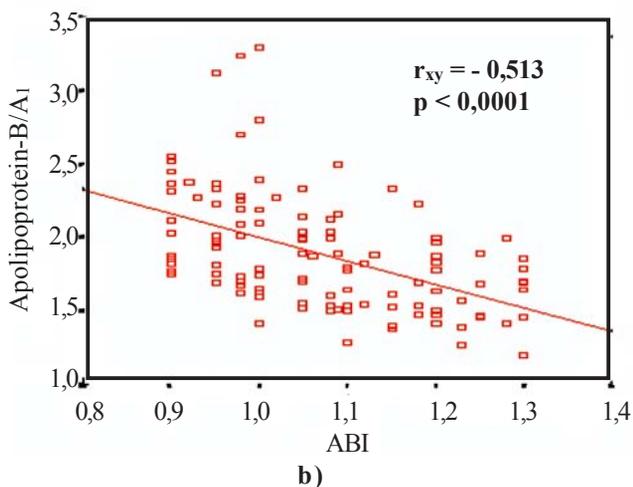


Figure 3. Statistical significant strong correlation between ankle-brachial index and atherogenic biomarkers **a)** – Apolipoprotein-B, **b)**- Apolipoprotein-B/ Apolipoprotein-A₁ index

We found a weak, but statistically significant connection between ABI and the lipid parameters and the derivative atherogenic indexes in the studied high risk population sample with hypercholesterolemia and we appreciate the risk level of these patients in the daily practice (Table 1).

Table 1. Weak statistical significant correlation between ABI with routine lipid profile and atherogenic indexes

	r _{xy}	p
Total cholesterol	-0,148	0,050
HDL-cholesterol	0,255	0,002
LDL / HDL-cholesterol	0,225	0,007
HDL / triglyceides	0,147	0,050

DISCUSSION

Apolipoprotein B appears most statistical significant factor of ABI in asymptomatic manifested hypercholesterolemia, i.e. without PVD according to the reference range values of ABI. The routine lipid profile and the atherogenic indexes gives us an idea about the number of the LDL particles, while the Apolipoproteins express their number per density, in other words it is an indirect measurement of the quantity of the oxygenated LDL (11-14).

In the selected studied population with severe hypercholesterolemia, Apolipoprotein-B appears to be a major predictor of the structural abnormalities in the vessel wall, verified via ABI measurement. This leads to the finding that ABI values in the reference range Apolipoprotein-B is most important factor for ABI from measurements atherogenic biomarkers.

CONCLUSION

In the population with manifested hypercholesterolemia, Apo-B and not the routine lipid profile and atherogenic indexes, is a predictor of structural blood vessel damage, verified through ABI.

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Address for correspondence:

Lyudmila G. Vladimirova-Kitova

Department of Cardiology, Medical University, Plovdiv, Bulgaria

E-mail: kitov@vip.bg