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 asymptomatically 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 immunoturbodimetric 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 Apolipoprotien-B/A_1 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-$_1$) in asymptomatically 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 immunoturbodimetric 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)

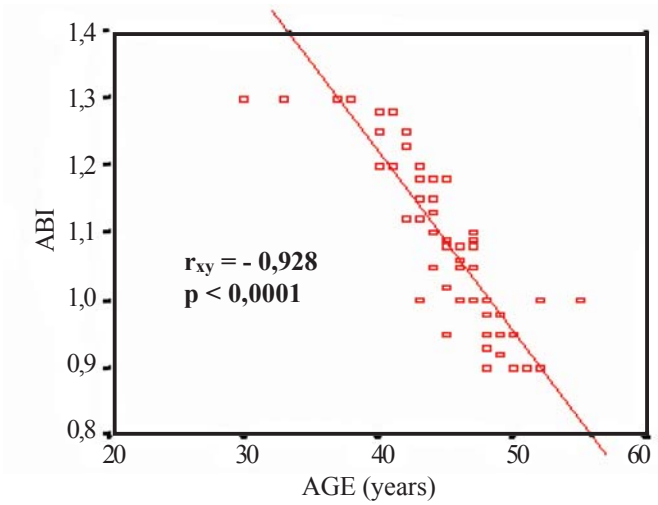


Figure 1. Correlation between ankle-brachial index and age

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

male: ABI = 2,285 - 0,026 x age,
female: ABI = 2,279 - 0,026 x 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.

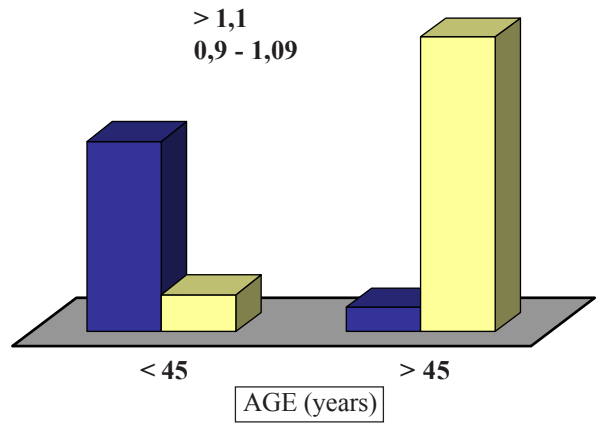
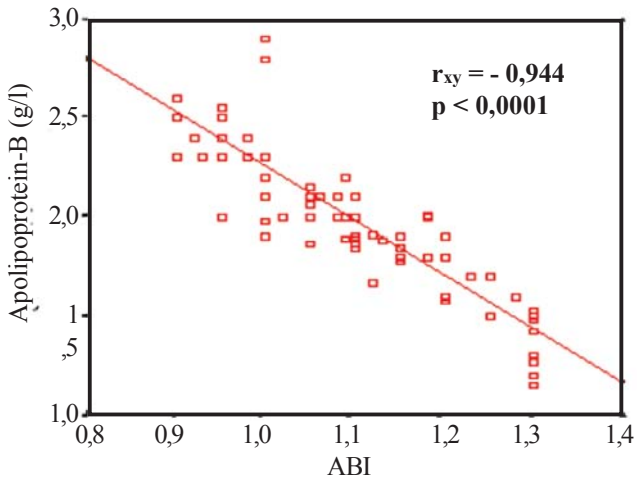


Figure 2. Distribution on the two groups of ABI in respect of the age

A strong inverse statistically significant relationship was found between ABI and Apo-B, ABI and Apo-B/Apo-A$_1$ index. These two variables explain the variations in ABI. (Figure 3-a,b)



a)

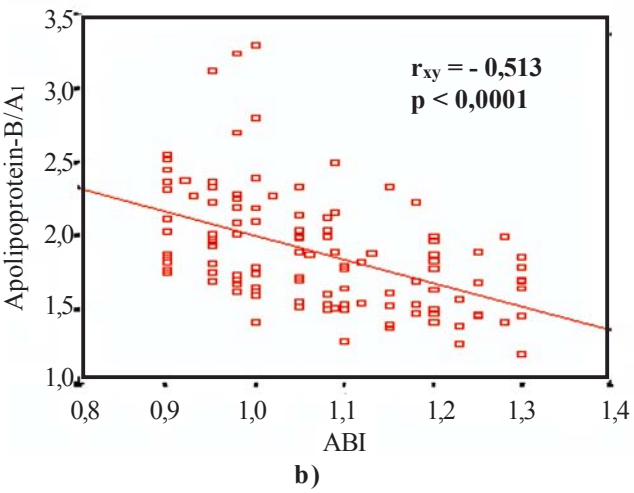


Figure 3. Statistical significant strong correlation between ankle-brachial index and atherogenic biomarkers
a) – Apolipoprotein-B, **b)**- Apolipoprotein-B/ Apolipoprotein-A_1 index

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 measuments 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 .

REFERENCES:

1. Rader DJ. Noninvasive Procedures for Subclinical Atherosclerosis Risk Assessment.The Am J Med, 1999; 107; (2A) 25S-27S.

2. Hooi JD, Stoffers HE, Kester AD et al. Peripheral arterial occlusive disease: prognostic value of signs, symptoms, and the ankle-brachial pressure index. Med Decis Making. 2002; 22(2): 99-107.

3. Management of peripheral arterial disease (PAD). TransAtlantic Inter-Society Consensus (TASC). Int Angiol. 2000; 19 (Suppl 1): 1-304.

4. Стайков И, Петрова Ю. Проучване на индекса глезен-ръка при пациенти с мозъчно-съдова болест Съвременна медицина 2005;3:13-9.

5. Doobay AV, Anand SS. Sensitivity and Specificity of the Ankle-Brachial Index to Predict Future Cardiovascular Outcomes. A Systematic Review. Arterioscler Thromb Vasc Biol. 2005; 25: 1463.

6. Duprez D. HOPE brings hope for the use of the ankle-brachial index as cardiovascular risk marker. Eur Heart J. 2004; 25: 1-2.

7. Sacks D, Bakal CW, Beatty PT, Becker GJ, Cardella JF. Position statement of the use of the ankle-brachial index in the evaluation of patients with peripheral vascular disease: a consensus statement developed by the standards division of the Society of Cardiovascular & Interventional Radiology. J Vasc IntervRadiol. 2002; 13:353.

8. Zheng ZJ,Sharret AR,Chambless LE et al. Associations of ankle-brachial index with clinical coronary heart disease, stroke and preclinical carotid and popliteal atherosclerosis:The atherosclerosis risk in communites (ARIC) study. Atherosclerosis 1997;131:115-25.

9. McDermott MM, Liu K,Criqui MH, et al. Ankle-brachial index and

subclinical cardiac and carotid disease. Am J Epidemiol 2005;162: 33-41.

10. Newman AB, Shemanski L, Manolio TA, et al. Ankle-arm index as a predictor of cardiovascular disease and mortality in the cardiovascular health study. Arterioscler Thromb Vasc Biol. 1999; 19: 538-45.

11. Denke MA. Weighing in Before the Fight. Low-density lipoprotein cholesterol and non-high-dnesity lipoprotein cholesterol versus apolipoprotein B and the best measure of therapy. Circulation 2005; 112: 3368-70.

12. Dunder K, Lind L, Zethelius B, Berglund L, Lithell H. Evaluation of a scoring scheme, including proinsulin and the Apolipoprotein B/apolipo-protein AI ratio, for the risk of acute coronary events in middle-aged men: Uppsala Longitudinal Study of Adult Men (ULSAM). Am Heart J 2004; 148: 596–601.

13. Grundy SM. Low-Density Lipoprotein, Non-High-Density Lipoprotein, and Apolipoprotein B as Targets of Lipid-Lowering Therapy. Circulation. 2002; 106: 2526.

14. Jadhav UM, Kadam NN. Apolipoproteins: correlation with carotid intima media thickness and coronary artery disease. J Assoc Physicians India 2004; 52: 370–5.

Address for correspondence:
Lyudmila G. Vladimirova-Kitova
Department of Cardiology, Medical University, Plovdiv, Bulgaria
E-mail: kitov@vip.bg

The ankle-brachial index should be measured routinely in patients at risk of cardiovascular disease who are seen at internal medicine departments. Key words: Peripheral arterial disease. Ankle-brachial index.Â The natural history of atherosclerosis includes an asymptomatic first phase of lengthy duration, followed by a clinical phase that.Â Factors Related to the Ankle-Brachial Index The correlations between ABI values and the various quantitative parameters studied are shown in Table 3. The prevalence of a low ABI (<0.9) or pathological ABI (<0.9 or >1.4) according to the presence of risk factors, as well as the associations between them are shown in Table 4. The. All patients underwent investigation of the state of the peripheral arteries using the device VaSera VS-1000 (Fukuda Denshi, Japan). Patients evaluated the presence of cardiovascular disease, previously vascular events, type and subtype of stroke. Also assessed neurological status with neurological scales: NIHSS, Barthel, Rankin, Ashworth, mobility index Rivermid and test swallowing.Â Ankle-brachial index, cognitive impairment and cerebrovascular disease in a chinese population. // Neuroepidemiology. 2014;42 (2):131-8. 19. Moon JH, Lim S, Han JW, et. al.Â Predictive value of the Essen Stroke Risk Score and Ankle Brachial Index in acute ischaemic stroke patients from 85 German stroke units. // J. Neurol. Neurosurg Psychiatry. 2008 Dec;79 (12):1339-43. 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 asymptomatically severe hypercholesterolemia (without peripheral vascular disease). Methods and materials: 50 patients with documented severe hypercholesterolemia