



Full Length Research Article

EARLY PREDICTIVE MARKERS OF ATHEROSCLEROSIS IN THE YOUNG

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ABSTRACT

With a long time ago atherosclerosis it was considered a disease of the elderly and never imagined that could debut in youth. The reality is that the process of atherosclerosis start earlier comparative with what we believe in this moment. I will present a study conducted per 321 young hypertensive patients with age between 18-35 years per a period of three years 2007-2010, in the County Bihor, Romania. All these patients were investigate clinical and paraclinically. The results of the study shown that an increase percent of the young had dyslipidemia and risk for atherosclerosis. We must to discover also other predictive markers of atherosclerosis in youth excepting the dyslipidemia.

INTRODUCTION

Until a very long time ago, in the history of medicine, atherosclerosis it was considered a disease of old age and wasn't take into account that could be present in the young. The question is how early atherosclerosis process begins? The atherosclerosis can be considered only a disease of old age? How early we must be careful with our lifestyle to prevent atherosclerosis and all its complications? Could be present ischemic heart disease with severe stenosis of the coronary arteries in the young people with risk of acute myocardial infarction? If they would have done several studies on sudden deaths in the young persons in the car accidents or from other reasons and would have performed several autopsies at young ages, maybe we would were surprised to notice that atherosclerotic plaques are present inside of the wall of the vessels very early and we should be more carefully with our lifestyle much earlier. If we can discover an early predictive marker for early detection of atherosclerosis, except dyslipidemia, could be use as a screening test in the young. Abdominal obesity in young people represents a risk factor for dyslipidemia and early atherosclerosis. Dyslipidemia in youth may be also hereditary.

The question is whether the atherosclerosis in young people can be considered a genetic disease with hereditary transmitted or is it just acquired because of our abusive lifestyle? The presence of the xanthelasma and xanthomas at youth are safe signs for dyslipidemia and early atherosclerosis markers.

- May influence the thyroid dysfunction – hypothyroidism the process of atherosclerosis?
- Diabetes type I insulin-dependent and diabetes MODY at young greatly accelerates the process of atherosclerosis in youth.
- We can consider increase level of glycosylated hemoglobin at youth an early marker for atherosclerosis?
- We can consider the increased level insulinemia an early marker for atherosclerosis in youth?
- We can consider the big-baby more than 4Kg a candidate for early atherosclerosis?
- The congenital aneurysms with different locations can be an early risk factor for the atherosclerosis in young people?
- We can consider the carotid echo-Doppler at youth a marker for early atherosclerosis in young people?
- The ankle-arm index can be considered a marker of early atherosclerosis in young people?

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MATERIALS AND METHODS

I present a study conducted per 321 young hypertensive patients with age between 18-35 years per a period of three years 2007-2010 in the County Bihor, Romania. The measurement of blood pressure was performed three weeks repeated to avoid white coat phenomenon very common at young peoples and if persist increase more than 140/90mmHg at three repeated measurement or was high >170/90mmHg from the first moment, the young was considered hypertensive. All these patients were investigate clinical and paraclinically.

RESULTS

The results of the study show that a percentage of young hypertensive patients had dyslipidemia (Table 1) and risk for atherosclerosis at the young age.

- 24,29% had cholesterol increase level more than 250mg/dl
- 26,79% had HDL cholesterol increase than 40mg/dl
- 23,67% had LDL cholesterol increase than 60mg/dl
- 32,71% had triglycerides level increase than 150mg/dl
- 17,75% had uric acid increase than 5g/dl
- 21,18% had increase level of glycemia more than 110mg/dl

Table 1.

Analysis – blood tests	No cases	Percent %
Glycemia increase	68	21,18%
Cholesterol increase	78	24,29%
HDL cholesterol decrease	86	26,79%
LDL cholesterol increase	77	23,67%
Triglycerides increase	105	32,71%
Uric acid	57	17,75%

Table 2.

EKG appearance	No cases	Percent %
Secondary changes depolarization - ST segment sub elevate and negative T wave	35	10,90%
Old anterior-septum myocardial infarction and ischemic changes (inverted T wave)	12	4,8%

Table 3.

Echocardiography changes	No cases	Percent%
Low ejection fraction below than 55 %	27	8,41%

Table 4.

The carotid Eco Doppler	No. cases	Percent%
Stenosis of carotid artery 25%atheroma plaque	35	10,90%

Table 5.

Analysis-blood tests	No. cases	Percent%
Insulinemia	58	19,18%
Glycosylated hemoglobin DM type I	38	12,82%
Glycosylated hemoglobin MODY	8	2,81%

These results demonstrate that there may be a cardiovascular risk in the young hypertensive patients, especially if associated with other cardiovascular risk factors such as dyslipidemia which at young can be genetically transmitted or results of disorder life style. So, the process of atherosclerosis starts at the young age in this situation. The appearance of EKG confirmed safe at 35 patients (10,90%), obese and hypertensive the presence of ischemic change – secondary change depolarization such as: ST segment sub elevate and negative T wave (Figure 1). and at 12 young obese and hypertensive patients (4,8%) with an old anterior-septum myocardial infarction and ischemic changes (inverted T wave) (Figure 2). (Table 2) These results shown, that the process of atherosclerosis start at young age, develops coronaries arteries stenosis, ischemic heart disease and risk for heart attack in youth. The echocardiography examination shown unexpected low ejection fraction below than 55 % at 27 young hypertensive patients respective 8,41%. (Table 3) Of course, the number of cases is low 27 and the percent is low 8, 41% (Table 3) but, at the young age we expect that the percent of the patients with low ejection fraction below than 55% to be absent.

These suggest that can appear manifestations of cardiac failure at young age. All young hypertensive patients, 35 obese (10, 90%), who had ischemic - lesion changes on ECG, also had 25 % carotid artery stenosis after the carotid Doppler ultrasound was conducted (Table 4). This is another important proof that the process of atherosclerosis start at young age. The level of the insulinemia and glycosylated hemoglobin increase (Table 5) is other important markers for early atherosclerosis in the young. These results shown that 58 young obese hypertensive patients (19,18%) had insulinemia level increase than 14 μ U/ml. and 38 young hypertensive patients with diabetes mellitus type I (12,82%) and 8 patients with MODY diabetes mellitus (2,81%) not have a good control of the value of glycemia, because have the level of glycosylated hemoglobin increase than 7%. 35% of young hypertensive patients had xanthelasma (Figure 3, Figure 4), xanthomas or lipomas (Figure 5, 6, 7, 8, 9, 10) at the objective examination.

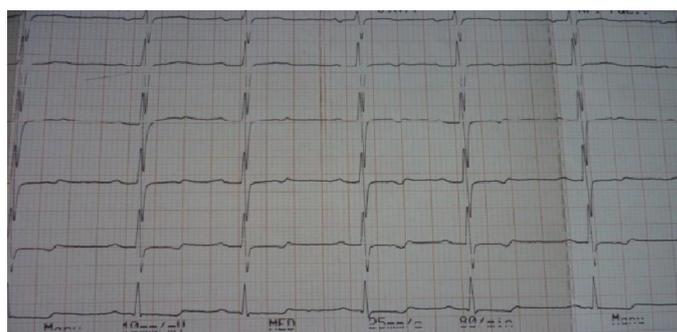


Figure 1. EKG young man obese, hypertensive 28 years old, asymptomatic, with severe dyslipidemia, flat T wave in leads V1, V2, V3 and inverted T wave in leads V4, V5, V6. (silent ischemia)

These represent the early markers of atherosclerosis in the young. The results of this study shown that if a young hypertensive patient had an increase level of cholesterol, HDL cholesterol increase, LDL cholesterol increase, triglycerides increase, uric acid, glycemia, glycosylated hemoglobin, insulinemia, secondary changes depolarization - ST segment

sub elevate and negative T wave on EKG, stenosis of carotid artery 25% atheroma plaque, the presence of xanthelasma, xanthomas and lipomas, all these represents early predictive markers for the atherosclerosis in the young.

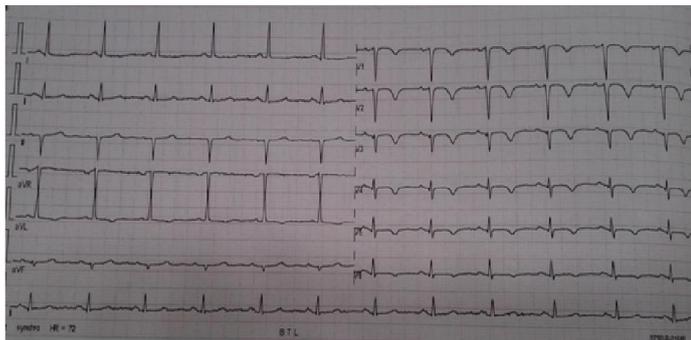


Figure 2. EKG young man obese, hypertensive patient 29 years old QS wave in leads V1, V2, V3 and inverted T wave in leads V1-V6 old anterior-septum myocardial infarction and anterior lateral ischemia



Figure 3. Xanthelasma at a young woman 34 years hypertensive and with dyslipidemia



Figure 4. Xanthelasma at a young woman 34 years hypertensive and with dyslipidemia



Figure 5. Lipomatosis on the left arm at young patient of 30 years



Figure 6. Lipomatosis of the left arm at young patient of 30 years



Figure 7. Lipomatosis at young patient of 31 years



Figure 8. Lipomatosis at young patient of 31 years



Figure 9. Lipoma at a young obese woman 28 years old



Figure 10. Lipoma at a young woman 30 years old

DISCUSSION

Hypertriglyceridemia is the most common abnormality among young people with hypertension dyslipidemia frequently associated with impaired glucose tolerance and the presence of LDL cholesterol. A strong correlation exists between total cholesterol and LDL cholesterol, lipid deposits and extension of fibrous plaques in the arteries, as was demonstrated pathologic. Mixed dyslipidemia are also commonly found in the young history of hypertension, with high LDL and high triglycerides. There are young people under 35 who have a risk factor for hypertension and familial hypercholesterolemia. In young patients under 35 years, the value of LDL cholesterol was found that suggestive for early predictor of atherosclerosis, risk of heart attack and hypertension. In 1908, Fremont-Smith (Fremont-Smith, 1908) published a literature review on atherosclerosis in youngsters, reporting that various authors had found the disease in autopsies of adolescents and young adults who had died from acute infectious processes, thus establishing a relationship between acute infection and arterial disease (4). In 1930, Zeek (1930) in a review of the literature on juvenile atherosclerosis observed that the first mention of this condition in children was that of Hodgson in 1815 (13). The author selected 98 well-defined cases of atherosclerosis in subjects up to 20 years of age and concluded that atherosclerosis can occur at any age level from birth onwards, without differences due to sex (13). Enos *et al.* (1953) found grossly visible atherosclerosis in the coronary arteries of 77.3% of 300 American soldiers aged between 18 and 48 years, killed in the Korean War (2). The study called attention to atherosclerosis in young people (2). Holman *et al.* (1958) in necropsy studies on 526 individuals aged from 1 to 40 years noted the appearance of fatty streaks from the first year of life on, and that the percentage of the arterial surface involved increased slowly until the age of 8 years, but afterwards progressed more rapidly (5). Fibrous plaques appeared in the second decade of life, increased until the third so that after the age of 30, 90% of the aortas had showed some degree of fibrous plaques. (5) The conversion of streaks to fibrous plaques took approximately 15 years, and at 40 years about 20% of the area covered by the streaks had changed into fibrous plaques (5). The Caucasian race was most affected, as was the abdominal segment of the aorta (Holman *et al.*, 1958) (5). The International Atherosclerosis Project, an extensive study about the geographic distribution of this disease involving 14 nations including the USA, Chile,

Colombia, Puerto Rico, Costa Rica, Brazil, Guatemala, and South Africa, in 1968 published results of necropsies performed in 4,737 individuals of both sexes, aged between 10 and 39 years (7). The sequence of fat deposition occurred in the following manner in these subjects. The aorta was the first structure involved starting at infancy with the formation of fatty streaks, and peaking at puberty (8). In the coronaries, fatty streaks began at puberty, increasing significantly in the third decade of life, showing inclusively an evolution towards fibrous plaques (8). The carotids started to become involved at the same age range as the aorta; cerebral arteries were affected simultaneously with the coronaries (McGill *et al.*, 1968; McGill, 1968; Strong and McGill, 1969) (7,8,12). In 1974, Oliver wrote a landmark paper titled "Ischaemic heart disease in young women." (Oliver, 1974) (11). He subsequently located and studied 150 women under the age of 45 with coronary heart disease (11). Ten years later, McCready and colleagues reported on 47 patients under age 40 who were seen over the course of 15 years with atherosclerotic vascular disease; there were 12 women in the group. (McCready *et al.*, 1984) (6). The title of the paper is interesting: "Atherosclerosis in the young: a virulent disease." (McCready *et al.*, 1984) (6). Most recently, Cole *et al* reviewed 843 patients seen between 1975 and 1985 who had atherosclerosis prior to age 40 (1). There were 94 women in the group (Cole *et al.*, 2003) (1). Elevated glycohemoglobin levels were associated with a substantial excess of fatty streaks and raised lesions in the right coronary artery and a lesser excess of raised lesions in the aorta (McGill *et al.*, 1995) (9). A small number of cases from the Bogalusa Heart Study showed associations of atherosclerosis with serum lipoprotein levels and blood pressure (Newman *et al.*, 1986; Freedman *et al.*, 1988) (3, 10). The real prevention of atherosclerosis must begin as early as possible, in adolescence as or better than that in childhood period. The research remain open on this topic in the future to find also other predictive markers of early atherosclerosis in the young people that can be used as a screening test, except those known in present.

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