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Research Article

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Age and Ethnic Peculiarities of Atherosclerotic Changes of Carotid Arteries According to the Data of Medical Sonography in Women with Metabolic Syndrome of the Republic of Khakassia

Nikolai V. Khanarin, Oksana Iu. Kilina, Tatiana S. Kulakova,

Svetlana V. Dutova and Iuliia V. Saranchina

Katanov Khakass State University (KhSU)

coluria@mail.ru

ABSTRACT

The urgency of the problem under investigation is due to an increase in the incidence of atherosclerosis (ASVD) in patients of young and middle age [2, 10-12]. This adds to the increase of cardiovascular and cerebrovascular disease among the able-bodied population, reduces the quality of life and is the main factor of mortality [23]. Therefore, studies aimed at the prevention and early diagnosis of atherosclerotic vascular lesions are up-to-date and in high demand. The aim of the paper present was to identify the age and ethnic characteristics of atherosclerotic changes in carotid arteries. A total of 113 women with metabolic syndrome (MS) and 50 women of the control group aged 25 to 65 years were examined. All patients were divided into 2 ethnic groups: the incoming population (Caucasian) and the native population (Khakass). To detect the MS, the body mass index (BMI) was determined, the fat tissue topography in the abdominal region was examined, the intima-media thickness (IMT) was measured, and the biochemical blood indices were determined. The detection of atherosclerotic changes in blood vessels was performed using ultrasonography. The obtained results showed a regular increase in the index of IMT with age. The mean values of IMT in patients with MS exceed the threshold both in the incoming population and in the native population group, despite the fact that the severity of visceral obesity in the native group is statistically significantly lower. Statistically significantly higher values of the IMT indicator in patients with MS were established, related to the native population in comparison with the incoming population. The revealed differences are among the reasons for developing personalized approaches for the diagnosis, prevention and treatment of MS in women in Khakassia.

Keywords*:* atherosclerosis, intima-media complex, age features, metabolic syndrome, Khakass

INTRODUCTION

Atherosclerosis (ASVD) is a pathological change in the arterial wall, resulting from the accumulation of lipids, complex carbohydrates, fibrous tissue, blood components and from the deposition of calcium salts on the intima with subsequent changes in the media [1]. Currently, atherosclerotic lesions in the aorta and carotid arteries with stenoses are detected in young and middle-aged people in 60% and 50% of cases, respectively [2, 10-12]. These vascular changes progress with age, resulting in an increase in the number of cardiovascular and cerebrovascular diseases in the older able-bodied group, compared with young people - 40.6% and 7.6% under the age of 30 compared with 46.8%-49.4% and 16.9%-14.4% from 30 to 44 years (in men and women, respectively). At the age of over 44 years, the percentage of cardiovascular and cerebrovascular diseases in men remains practically unchanged, while in women it exceeds 60% and 16.8%, respectively. Deaths from the diseases of the circulatory system (myocardial infarction, stroke) take the leading place in the mortality rate of the adult population in Russia - 55% of the total number of deaths [4].

The steady growth of these pathologies requires timely diagnosis. The most accessible and informative method for detecting vascular pathology in the early stages of ASVD development (stages associated with the asymptomatic period of disease formation) is ultrasonography [5, 15-17]. It should be taken into account that the risk factors for vascular diseases may also become indirect causes of death. The main ones are those which in total constitute the metabolic syndrome (MS), in particular abdominal obesity, characterized by excess fat in the abdomen and upper body and leading to type 2 diabetes, arterial hypertension, myocardial infarction and strokes [4]. The simplest and most affordable method for assessing the degree of obesity is the determination of the body mass index (BMI), yet it does not always adequately reflect the level and localization of body fat. Therefore, for visual examination of adipose tissue, computed tomography (CT), magnetic resonance imaging (MRI) or ultrasonography are used. In this regard, studies aimed at developing methods for early diagnosis of the risk of ASVD development are of obvious interest. In addition, the identification of the relationship between the severity of visceral obesity and atherosclerotic vascular changes is necessary for understanding the development mechanisms of pathological processes. Ethnic peculiarities of MS development and atherosclerotic vascular changes are actual direction of research worldwide [23]; thus, the present study focused on the age and ethnic characteristics of atherosclerotic changes in carotid arteries in women with metabolic syndrome in Khakassia.

MATERIALS AND METHODS

The study was conducted on the basis of the State Budgetary Healthcare Institution of the Republic of Khakassia 'Remishevskaya Republican Clinical Hospital' in the city of Abakan and in accordance with the WMA Declaration of Helsinki. It included 113 women with MS and 50 women in the control group aged 25 to 65 years. The patients were grouped as representatives of the native and incoming population, since the indigenous inhabitants of the Republic of Khakassia (Khakass) belong to the Asian race (Table 1).

Table 1: Distribution of patients by age in the research groups

Indicators	Patients with MS (n=113)		Control group (n=50)
Number of observations	Native n=65 (57,5,5%)	Incoming n=48	Native n=50 (100%)
Average age	49,5 (45-53)		41 (34-49)
	49 (43-53)	50 (47-53)	

The Khakass women belonging to the native group had no mixed marriages in the previous three generations, and the women of other nationalities were Caucasians living in the territory of Khakassia.

MS was diagnosed according to the criteria proposed by the International Diabetes Federation (IDF, 2005). Anthropometric parameters were determined: height, body weight, waist circumference and hips; the body mass index (BMI) was calculated. Body weight was determined with an accuracy of 0.1 kg; height was estimated using a height rod, without shoes and outer clothing, with an accuracy of 1 cm. BMI (Quetelet index) was calculated as the ratio of body weight (kg) to the square of body height (m^2). BMI values of 18.5-25kg/m^2 were considered normal. With BMI values of 25.0-29.9 kg/m^2, excess body weight was diagnosed, with BMI values of 30.0 and more kg/ m^2

obesity was diagnosed: first degree at 30-35 kg/m^2, second degree at 35-40 kg/m^2, third degree at 40 kg/m^2 and more. The waist circumference (WC) was measured in the standing position with no outer clothing. The measurement was performed with a centimeter tape at the midpoint of the distance between the costal arches and the crests of the iliac bones. All patients underwent medical ultrasound of the brachiocephalic region arteries, which included color duplex scanning of common carotid arteries and areas of bifurcation with the aim of revealing atherosclerotic changes. The increase in IMT at standard points of the common carotid arteries was measured according to the international classifications. *The* ultrasound scan *was* performed on Philips En Visor (Philips, The Netherlands) with multifrequency linear sensor (5-10 MHz). Women also underwent a CT scan of fat tissue topography in the abdominal area. Computed tomography was performed on the Aquilion 16 device (Toshiba, Japan). The standard protocol for examining the abdominal cavity was used – the patient was lying on the table on her back, hands behind the head; on the control panel, the program 'ABDOMEN' was selected. After this, a topographic scan of the abdominal region was performed to determine the zone of interest. Afterwards, a layered spiral tomography was performed within the following technical parameters: the tube voltage of 120 kV, electric current of 220 mA, the layer thickness of 3 mm. All patients underwent a biochemical blood test, including the determination of total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoproteins (LDL), triglyceride (TG), and the **glycemic** index (on an empty stomach). Calculation of LDL was performed according to **The Friedewald formula**: TC LDL, mmol/L = TC, mmol/L – TC HDL, mmol/L – TG, mmol/L x 0.45. Statistical processing was carried out in the package of applied programs Statistica 8.0. Nonparametric methods were used. The data are presented as median (Me) and interquartile range (25th and 75th percentile). The reliability of the differences was estimated by the Mann-Whitney criterion. The relationship between the signs was estimated by Spearman's rank correlation method (R).

RESULTS

The average age of patients with MS was 49.5 (45-53) years and was significantly higher than the age of patients in the control group - 41 (34-49) (Table 1). The anthropometric indicators of patients in the research groups were statistically significantly different in the WC and BMI (these indicators were significantly higher in the group of patients with MS). Incoming MS patients had higher visceral obesity based on higher values of WC and BMI (Table 2).

Table 2 Anthropometric indicators in the research groups

Indicators	Patients with MS		P	Control group	P_1
	Native	Incoming		Native	
1	2	3	4	5	6
WC, cm	98,5 (91,0-104,0)	110,0 (103,5-118,5)	<0,001	75,0 (67,0-80)	<0,001
BMI, kg/m^2	29,1 (27,0-32,9)	35,6 (32,0-41,8)	<0,001	27,5 (24,8-30,5)	0,006

Legend:

P – the level of statistical significance of the differences between the indicators of incoming and native women with MS;

P_1– the level of statistical significance of the differences between the parameters of the Khakass women with MS and the control group.

The values of TC LDL, TG and glucose in patients with MS were statistically higher than in the control group (Table 3). The data obtained coincided with the data from literature sources [24, 25].

Table 3 Indicators of laboratory diagnostic methods in the research groups

Indicators	Patients with MS		P	Control group	P_1
	Native	Incoming		Native	
1	2	3	4	5	6
HDL, mmol/L	1,3 (0,14-1,5)	1,27 (1-1,65)	0,97	1,36 (1,19-1,54)	0,39
LDL, mmol/L	3,38 (2,77-4,31)	3,8 (2,33-4,47)	0,79	2,46 (2,11-3,02)	<0,001
TG, mmol/L	2,04 (1,66-3,05)	1,71 (1,18-2,35)	0,07	0,8 (0,64-1,07)	<0,001
Glucose, mmol/L	5,23 (5-6)	5,75 (5,16-7,5)	0,12	4,92 (4,3-5,24)	<0,001

Legend:

P – the level of statistical significance of the differences between the indicators of incoming and native women with MS;

P_1– the level of statistical significance of the differences between the parameters of the Khakass women with MS and the control group.

The frequency of individual components of MS in native and incoming groups differed statistically insignificantly (Table 4).

Table 4 :The frequency of individual components of MS in native and incoming women of the Republic of Khakassia

Indicators	Native women with MS	Incoming women with MS	P
1	2	3	4
TG > 1,7 mmol/L	15/20 (75%)	23/42 (55%)	0,13
TC HDL <1,3 mmol/L	11/20 (55%)	21/42 (50%)	0,72
TC LDL >3,0 mmol/L	12/19 (63%)	30/41 (73%)	0,44
Glucose ≥ 5,6 mmol/L	11/34 (32%)	25/46 (54%)	0,052
2 components of MS	4/24 (17%)	12/25(48%)	0,02
3 components of MS	8/32 (25%)	15/40(38%)	0,258
4 and more components of MS	2/34 (6%)	5/45 (11%)	0,428

Legend:

P – the level of statistical significance of the differences between the indicators of incoming and native patients with MS.

Incidence analysis of the combinations of 2 or more MS components revealed that multicomponent MS prevailed in both groups, and cases of MS with a combination of two components in the native group were statistically significantly less common than in the incoming group. When analyzing the anthropometric parameters and the results of the biochemical blood test, a statistically significant positive correlation between BMI and TG level was revealed. Statistically significant correlation was found between WC and all the parameters of biochemical blood analysis, except for TC HDL (Table 5).

Table 5: Correlation analysis between anthropometric indicators and the results of the biochemical blood test for native women

Indicators	Glucose	TC HDL	TC LDL	TG
BMI	r= 0,13 p=0,246	r=0,045 p=0,716	r= 0,119 p=0,332	r=0,281 p=0,019
WC	r=0,314 p=0,005	r= -0,1 p=0,418	r= 0,43 p<0,001	r=0,593 p<0,001

Legend:

r – correlation coefficient;

p – level of statistical significance.

All the patients with MS and native residents of the Republic of Khakassia included in the control group underwent color duplex scanning of carotid arteries (Table 6).

Table 6 : Results of carotid arteries ultrasound of the research groups

Indicators	Patients with MS		P_1	Control group	P_2
	Native	Incoming		Native	
1	2	3	4	5	6
IMT (right)	1,03 (0,85-1,13)	0,87 (0,75-1,04)	0,008	0,71 (0,62-0,91)	p<0,001
IMT (left)	1,04 (0,87-1,17)	0,92 (0,76-1,06)	0,002	0,75 (0,66-0,86)	p<0,001

Legend:

P_1 – the level of statistical significance of the differences between the indicators of incoming and native patients with MS;

P_2 – the level of statistical significance of the differences between the parameters of the Khakass women with MS and the control group.

It was revealed that the average values of IMT in patients with MS (both in the incoming and the native groups) exceeded the threshold of 0.9 mm. This indicator in Khakass MS patients is statistically significantly higher than in the control group (<0.001). Statistically significantly higher values of the IMT indicator in native patients with MS in comparison with the incoming population representatives were established. It is known that the intima-media thickness x increases with age [18]; in the present study similar patterns was established in all the research groups of women. At the same time, in patients with MS in all the age groups the parameters of IMT were statistically significantly higher than in the control group. An important fact that the authors managed to establish is the presence of higher IMT in the group of Khakass patients with MS compared to the women of the incoming population in the analyzed age groups (Table 7), despite the fact that the severity of visceral obesity in the native group is statistically significantly lower.

Table 7 : Age dependence of IMT in the research groups

Age, yrs	Native patients with MS	Incoming patients with MS	Native, control	P_1	P_2
1	2	3	4	5	6
20-29 right/left	0,85 (0,85-0,85) / 0,82 (0,82-0,82)	------	0,61 (0,59-0,66) / 0,66 (0,63-0,68)	*	*
30-39 right/left	0,83 (0,8-0,95) / 0,82 (0,76-0,99)	0,79 (0,68-0,86) / 0,73 (0,73-0,74)	0,68 (0,61-0,81) / 0,73 (0,62-0,81)	0,23/ 0,05	0,007/ 0,02
40-49 right/left	0,9 (0,8-1,03) / 0,96 (0,84-1,06)	0,83 (0,73-1,05) / 0,83 (0,75-1,03)	0,71 (0,66-0,89) / 0,81 (0,7-0,86)	0,55/ 0,11	0,007/ 0,001
50-59 right/left	1,07 (1,03-1,17) / 1,07 (1,03-0,22)	0,9 (0,8-1,03) / 0,97 (0,81-1,06)	0,95 (0,78-1,01) / 0,91 (0,86-0,96)	0,001 / 0,003	0,003/ 0,002
60-65 right/left	1,19 (0,99-1,39)/ 1,11 (1,01-1,21)	1,16 (1,16-1,16)/ 1,12 (1,12-1,12)	------	*	*

Legend:
P_1 – the level of statistical significance of the differences between the indicators of incoming and native patients with MS;
P_2 – the level of statistical significance of the differences between the parameters of the Khakass women with MS and the control group;
* – calculating statistical significance (p) is impossible due to the insufficient number of subjects surveyed in subgroups.

In addition, the results of Khakass patients of the control group were compared with the published data on IMT in Caucasians. It was established that the average value of IMT in the Khakass group significantly exceeds that of Caucasians according to the Carotid Atherosclerosis Progression Study [9]. The range of difference varies from 0.04 mm at a young age to 0.23 mm in the older age group (Fig. 1).

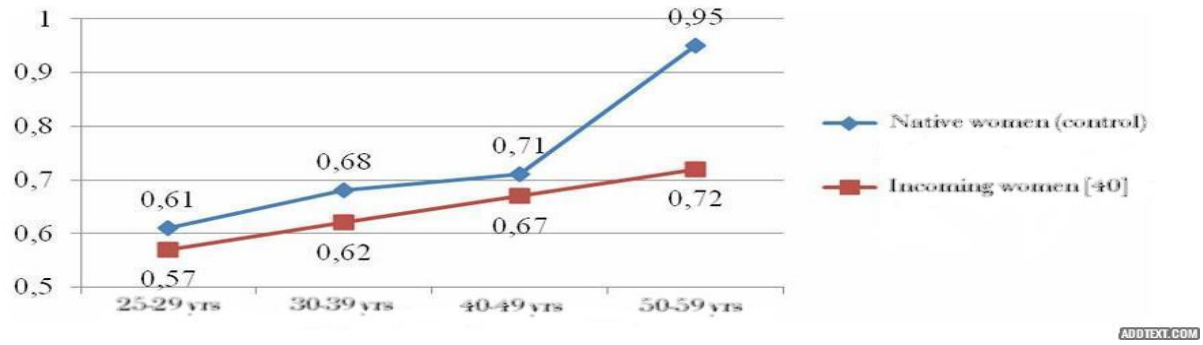

Figure 1. Age dependence of IMT in the research groups

The incidence of IMT, atheroma and stenosis among native and incoming patients with MS was statistically insignificant (Table 8).

Table 8 : Frequency of increase in IMT, atheroma and stenosis of carotid arteries (obtained by *ultrasonography)*

Indicators	Native patients with MS	Incoming patients with MS	P
IMT increase	45/65 (69,2%)	27/48 (56,3%)	0,16
Atheroma	11/65 (16,9%)	9/48 (18,8%)	0,81
Stenosis	10/65 (15,4%)	6/48 (12,5%)	0,8

Legend:
P – the level of statistical significance of the differences between the indicators of incoming and native patients with MS.

When assessing the results of the correlation analysis between the components of MS and IMT in patients of the research groups, it was found that such components of MS as elevated glucose, LDL and TG are combined with increase in IMT, except for the HDL cholesterol index (Table 9).

Table 9: Data of the correlation analysis between the results of the biochemical blood test, anthropometric indices and IMT in the native population

Показатели	**Glucose**	**TC HDL**	**TC LDL**	**TG**
IMT right	r=0,22 p=0,048	r= - 0,056 p=0,65	r= 0,18 p=0,13	r=0,34 p=0,005
IMT left	r=0,23 p=0,043	r= - 0,04 p=0,74	r=0,29 p=0,015	r=0,37 p=0,003

Legend:
r – correlation coefficient;
p – level of statistical significance.

As mentioned above, the native and incoming women of Khakassia have differences in mean values of IMT, which indicates a higher risk of myocardial infarction. One of the reasons for these differences may be the topography of adipose tissue in the abdominal area. To assess the effect of visceral obesity on the increase of IMT in a part of native patients, a CT scan of adipose tissue topography in the abdominal area was performed; iIn total 48 women were examined in this way (45 from the control

group and 3 from the MS group). A strong statistically significant correlation between the IMT level and the volume and area of the visceral adipose tissue (VAT) and a statistically insignificant correlation between IMT and the volume and area of the subcutaneous adipose tissue (SAT) were established (Table 10).

Table 10: Results of correlation analysis between CT scans of adipose tissue in the abdominal area and IMT in native patients

Indicators	SAT volume	SAT area	VAT volume	VAT area
1	2	3	4	5
IMT right	r=0,19 p=0,2	r=0,19 p=0,2	r=0,62 p<0,001	r=0,62 p<0,001
1	2	3	4	5
IMT left	r=0,21 p= 0,16	r=0,21 p=0,16	r=0,55 p<0,001	r=0,55 p<0,001

Legend:

r – correlation coefficient;

p – level of statistical significance.

It is known the values of visceral adipose tissue area exceeding 130 cm² are regarded as a criterion for visceral obesity [19, 20]. The present study revealed that among Khakass females the area of visceral adipose tissue exceeding 130 cm² was observed in all the women with MS and in 6 women of the control group, and the area of visceral adipose tissue less than 130 cm² was observed only in the patients of the control group (39 women). Since the control group included women with WC less than 80 cm, the revealed fact allows considering that in the female Khakass population the criterion of the waist circumference does not always suggest visceral obesity. The group of indigenous women with a visceral obesity area exceeding 130 cm² included both MS patients and healthy women, but nevertheless their IMT indicators were statistically significantly different from those of native women from the group with visceral obesity of less than 130 cm² (Table 11).

Table 11: IMT parameters in patients of the research groups

Indicators	Native women		P_1
	VAT ≥ 130 см^2	VAT < 130 см^2	
IMT right	1,12 (0,81-1,19)	0,68 (0,61-0,89)	0,00 3
IMT left	1,13 (0,82-1,21)	0,74 (0,66-0,86)	0,01 3

Legend:

P1 – the level of statistical significance of the difference between IMT indicators among native women with VAT≥130 and VAT <130.

DISCUSSION

The results can be interpreted as follows: when analyzing the biochemical composition of blood it was found that despite the high level of visceral obesity in the incoming population, there were no statistically significant differences in lipid spectrum and glucose levels. Perhaps, this fact is a reflection of the ethnic polymorphism of the MS. The results obtained are consistent with the literature data [21-23]. The established relationship between WC (characterizing the visceral type of obesity) and all indicators of biochemical blood analysis proves its role in the formation of MS. Thus, the results obtained indicate that the amount of visceral adipose tissue is clinically significant for assessing the risk of MS manifestations. A more pronounced increase in IMT in the native women refers to another manifestation of the ethnic polymorphism of MS. It is known that an increase in total IMT is associated with a high risk of vascular accidents, especially ischemic stroke [6]. Therefore, it can be assumed that Khakass patients with MS run a higher risk of developing cardiovascular diseases. According to data from large multicenter studies, the IMT difference of 0.1 mm is associated with an increased risk of myocardial infarction – from

10% to 15% [7, 8]. According to the data obtained by the authors, the difference in mean values of IMT among native and incoming women in Khakassia is 0.1 mm, which indicates a higher risk of myocardial infarction in the group of native women with MS. Thus, additional information indicating the existence of ethnic polymorphism of MS in the inhabitants of Khakassia was received. The most important are the data on the arterial vessels changes (increase in IMT), leading to the development of vascular complications.

CONCLUSION

In all studied groups of women residents of the Republic of Khakassia a natural increase in IMT with age is observed, correlating with the severity of MS manifestations. Native women suffering from MS have a statistically significantly higher IMT compared to Caucasian women and women of the control group (with less visceral obesity). Native women of the control group are characterized by higher values of IMT compared to data from multicenter European studies. Indigenous women have a strong statistically significant correlation between the level of IMT and the amount of visceral adipose tissue. The differences identified are one of the reasons for developing personalized approaches for the diagnosis, prevention and treatment of MS and ASVD in women of different ethnic groups.

RECOMMENDATIONS

Using non-invasive instrument markers greatly enhances the physician’s ability to diagnose ASVD and to stratify the risk of developing cardiovascular events.

To this end, the ultrasonic evaluation of IMT can be used in the practical healthcare for early diagnosis of ASVD, especially in patients suffering from MS. In connection with the ethnic characteristics of IMT and visceral obesity in the native women of the Republic of Khakassia, the authors recommend that practitioners pay special attention to assessing the risk of coronary artery disease and its consequences in the Asian race.

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