

# GEORGIAN MEDICAL NEWS

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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии  
საქართველოს სამედიცინო სიახლენი

# GEORGIAN MEDICAL NEWS

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გამოიცემა თბილისის სახელმწიფო სამედიცინო უნივერსიტეტთან  
თანამშრომლობითა და მისი პატრონაჟით

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ  
ТБИЛИСИ - НЬЮ-ЙОРК

**GMN: Georgian Medical News** is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) since 1994. **GMN** carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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**GMN: Georgian Medical News** – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

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2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.



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## COMPUTED TOMOGRAPHY IN DETECTING FEATURES OF CORONARY ATHEROSCLEROSIS IN DIFFERENT ETHNIC GROUPS OF KAZAKHSTAN POPULATION

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According to a National data of Kazakhstan, mortality from of cardiovascular diseases after the collapse of Soviet Union in early 1990's dramatically increased [1]. With the implementation of National programs since 2008 aimed at controlling modifiable risk factors and development of cardiac centers with catheterization labs and cardiac surgery units, the mortality rate has been drastically decreased by almost 30% [2]. In recent years cardiovascular centers of the country moving towards the prevention of heart events using technology and well-controlled prospective life-style modification studies [3]. Coronary computed tomography (CT) has been widely used in assessment of atherosclerosis burden by the means of quantification and detection of coronary artery calcium (CAC) score and level of stenosis [4]. Nonetheless, there are no works devoted to the assessment of CAC in an association with coronary events in Kazakhstan using CT scanning. According to large prospective studies, CAC score showed a relationship with the risk of future coronary events [5]. CAC score has been shown to be related to the severity of coronary artery disease by one of the biggest studies to date, Multi-Ethnic Study of Atherosclerosis (MESA) [6]. The major drawbacks of using CAC score as a predictor of risk along with the Framingham risk score has been jeopardized by the evidence that there are considerable differences in the extent of CAC among different ethnic groups [7]. Thus, the utmost interest lies in the assessment of structural variability of the coronary artery bed. Currently, no data available to address the prevalence and quantification of CAC score in ethnic groups among Kazakhstani population. It poses an important value to assess the possible ethnic-dependent variations of CAC score due to the fact that Kazakhstan is ethnically very diverse country. About 75% of population are represented by Kazakhs and other Central Asian nations (such as Uigurs, Uzbeks, Tatar's and other), while about 25% account for Russians and other European nationalities [8].

Coronary artery calcification (CAC) score has been proposed as a surrogate method to evaluate coronary atherosclerosis. Multiple studies worldwide defined CAC score and ethnicity association to be valuable in coronary event prognosis along with other established risk-factors. The objectives of this study were to determine the ethnic differences of CAC score in Kazakhstani population with stable chest pain and whether CAC is significantly associated with the traditional cardiovascular risk factors.

**Material and methods.** The study population included medical records of patients who were referred by physicians to undergo CT. Prior to CT scanning, all patients gave informed consents to utilize the collected medical data for research purposes. The study protocol has received an ethical approval from the local Hospital Research Ethics Committee.

935 patient medical records were collected between 2008 to 2018 from Medical Centre Hospital of President's Affairs Administration and National Research Cardiac Surgery Center (NRCS) in Astana, both provide medical care for patients across Kazakhstan. Patients with stable chest pain were included in the study. Patients with history of myocardial infarction, with

cardiomyopathies, previously underwent coronary artery bypass graft (CABG), percutaneous coronary angioplasty or valve replacement procedures and those with chronic rheumatic heart diseases were not included in the study.

CT scanning was conducted on dual-source, Multislice CT scanner ("Somatom Definition AS 64 or Somatom Definition Flash, Siemens, Germany") with prospective cardiac synchronization and reconstruction with 0.6 mm slice thickness. The Agatston calcium score was quantified using commercially available software ("syngo Calcium Scoring, Siemens, Germany"), and calcification was defined as an area  $\geq 1$  of density  $\geq 130$  Hounsfield Units (HU). The summary of all coronary lesion scores represented coronary artery calcification (CAC) score. CT coronary angiography (CTA) data were obtained with injection of contrast agent (Visipaque, 100 ml) intravenously (4 ml/sec). Stenosis level was assessed based on comparison of minimum lumen diameter (MLD) with non-affected arterial segment in closest proximity to the lesion.

Patients were categorized to Kazakh (66.9%), Russian (21.4%) and other (11.7%) ethnicities, which included Tatar, Ukrainian, German, Uzbek, Uygyr, Belarus, Kyrgyz and those who did not specified their ethnicities (3.1%). Additionally, demographic variables (age, gender, body mass index (BMI)) and CHD risk factors (maximally registered systolic (SBP) and diastolic blood pressure (DBP); hypertension, defined as having history of hypertension or SBP  $\geq 140$  mm of Hg or DBP  $\geq 90$  mm of Hg [9]; smoking status (smoker or non-smoker); alcohol use (whether a patient consumed any amount of alcohol drinks for the past year, yes or no); family history of CVD (whether a patient has a first or second-degree relative with CVD) [10]; diabetes mellitus, defined as having a history of diabetes mellitus or glucose  $\geq 7$  mmol/l or Hemoglobin A1c  $\geq 6.5\%$ ; and plasma factors, such as, fibrinogen, creatinine, cholesterol level (total, low-density lipoprotein (LDL) and high-density lipoprotein(HDL)) and triglycerides) were collected from patient medical records. The type of chest pain was categorized to atypical, typical and non-anginal [18].

Continuous variables were summarized as means and standard deviations. When a continuous variable distribution was highly skewed, additionally, median and interquartile range (IQR) were included. To compare demographic characteristics and CHD risk factors' distributions among the ethnic groups, one-way ANOVA test or Kruskal-Wallis test, for categorical independent variables Pearson's chi-square test or Fisher's exact test were utilized.

The outcome variable, CAC score, has extremely right skewed distribution and frequent zero values. Given non-normality of CAC score, relationships between independent variables and continuous CAC score were assessed applying non-parametric tests (Kruskal-Wallis test, Spearman's correlation coefficient, Mann-Whitney U test). In addition, it was decided to dichotomize CAC score (any CAC score and none) to apply multivariate logistic regression analysis examining the association

between ethnicity and CAC score, adjusting for possible confounders and testing for an existence of interactions. After exclusion of all zero values, and log-transformation of the continuous CAC score, similarly, multivariate linear regression analysis was performed. In both modeling approaches, confounder selection was based on statistically significant ( $\alpha=0.20$ ) results from bivariate analyses and previous epidemiological studies [11]. In multivariate analyses, all statistically significant ( $\alpha=0.05$ ) and epidemiologically important covariates were left in the models to compare. All statistical analyses were performed using Stata 13 software [12].

**Results and discussion.** The study population consisted of 935 patients where average age among ethnic groups significantly differed ( $p<0.01$ ); more than half patients in other group were older than 60 years (Table 1). There were statistically significant differences among ethnic groups by BMI ( $p=0.03$ ), type of chest pain ( $p<0.01$ ), use of statins ( $p=0.01$ ) and blood glucose level ( $p<0.01$ ). Russians had the lowest values of percent of statin users (38%) and glucose level ( $5.4\pm 1.0$ ). Kazakhs had the lowest proportion of obese people among three groups (42.0% vs 53.8% and 52.0% in Russian and others, respectively,  $p<0.03$ ).

Table 1. Overall descriptive statistics of participants by ethnicity

Variables	Kazakh n=626	Russian n=200	Other n=109	p-value
Age, (yrs)	58.1 ± 11.0	59.6 ± 11.4	61.9 ± 9.2	<0.01*
Categorical Age (%)				
≤ 50	145 (23.2)	43 (21.5)	11 (10.2)	0.01**
51-60	206 (32.9)	63 (31.5)	33 (30.5)	
61-70	202 (32.3)	58 (29.0)	45 (41.7)	
> 70	73 (11.7)	36 (18.0)	19 (17.6)	
Female	197 (31.5)	78 (39.0)	39 (36.1)	0.13**
Male	429 (68.5)	122 (61)	70 (64.2)	0.15**
BMI Normal (%)	97 (17.5)	29 (15.6)	18 (17.6)	0.03**
BMI Overweight (%)	225 (40.5)	57 (30.6)	31 (30.4)	
BMI Obese (%)	233 (42.0)	100 (53.8)	53 (52.0)	
Systolic BP, mm of Hg	175.2±30.4	181.0±29.8	179.5±25.6	0.07*
Diastolic BP, mm of Hg	97.7±11.9	99.7±11.5	98.6±11.6	0.19*
Hypertension (%)	517 (82.8)	168 (84.4)	98 (89.9)	0.18**
Smoking (%)	119 (19.8)	51 (26.0)	29 (26.8)	0.08**
Alcohol use (%)	65 (10.8)	26 (13.3)	16 (14.8)	0.37**
Family History of CVD (%)	236 (39.5)	84 (42.9)	49 (46.2)	0.33**
Chest pain (%)				
Atypical	175 (29.6)	52 (26.2)	28 (26.2)	<0.01**
Typical	206 (34.8)	92 (46.2)	59 (55.1)	
Non-anginal	211 (35.6)	55 (27.6)	20 (18.7)	
Use of statins (%)	285 (50.3)	70 (38.0)	47 (45.2)	0.01**
Diabetes (%)	166 (26.7)	45 (22.6)	26 (23.8)	0.46**
HbA1C,%	6.9±2.1	5.9±1.2	6.0±1.8	0.06*
Glucose, mmol/l	5.9±1.8	5.4±1.0	5.8±1.7	<0.01*
Fibrinogen, g/l	3.0±0.9	3.0±0.9	3.1±1.0	0.38*
Creatinine, µmol/l	78.7±21.2	81.8±19.8	80.1±17.9	0.20*
Total Cholesterol, mmol/l	5.0±1.2	5.0±1.2	4.9±1.3	0.67*
LDL, mmol/l	3.3±1.1	3.3±1.1	3.3±1.1	0.78*
HDL, mmol/l	1.3±0.5	1.3±0.6	1.3±0.5	0.60*
Triglycerides, mmol/l	1.7±1.2	1.5±0.8	1.7±1.2	0.29*

Percentages are shown in parentheses. Continuous variables are presented as mean ± SD;

\* - One-way ANOVA test or Kruskal-Wallis test when parametric assumptions were violated;

\*\* - Pearson's chi-square test or Fisher's exact test

CAC score, stenosis in coronary arteries and number of vessels with  $\geq 50\%$  stenosis were statistically significantly associated with ethnic descent of the patients (Table 2). Russians had, on average, the highest CAC scores in each of the coronary arteries, and one third of them presented with  $\geq 50\%$  stenosis of

RCA. Kazakhs, on the other hand, had the lowest CAC scores in each of the coronary arteries and suffered less from stenosis of RCA (10.8%). Relatively, lower number of Kazakh patients (11.7%) presented with  $\geq 50\%$  stenosis of two or more vessels in comparison to Russians (16.0%).

Table 2. Characteristics of coronary CT findings by ethnicity

Variables	Kazakh n=626	Russian n=200	Other n=109	p-value
CAC (total)				
mean $\pm$ SD	107.9 $\pm$ 270.4	225.3 $\pm$ 507.5	164.7 $\pm$ 384.2	<0.01*
median (IQR)	7.5 (0-84.1)	17.3 (0-132.3)	28.4 (0-127.1)	
CAC in LAD				
mean $\pm$ SD	48.8 $\pm$ 118.1	95.0 $\pm$ 210.3	71.8 $\pm$ 155.8	0.08*
median (IQR)	0.9 (0-40.3)	3 (0-54.2)	9.8 (0-77.5)	
CAC in LCX				
mean $\pm$ SD	16.4 $\pm$ 49.6	42.2 $\pm$ 149.4	36.6 $\pm$ 84.8	<0.01*
median (IQR)	0 (0-4.8)	0 (0-13.2)	0 (0-25.8)	
CAC in RCA				
mean $\pm$ SD	30.9 $\pm$ 123.5	63.2 $\pm$ 257.8	44.9 $\pm$ 183.1	0.14*
median (IQR)	0 (0-4.4)	0 (0-11.0)	0 (0-9.0)	
CAC in LM				
mean $\pm$ SD	8.2 $\pm$ 47.0	23.6 $\pm$ 88.4	19.4 $\pm$ 65.7	<0.01*
median (IQR)	0 (0-0)	0 (0-6.1)	0 (0-1.2)	
Stenosis of LAD				
None or<50%	444 (73.6)	146 (74.5)	63 (60.0)	<0.01**
$\geq 50\%$	159 (26.4)	50 (25.5)	42 (40.0)	
Stenosis of LCX				
None or<50%	518 (89.8)	174 (88.3)	86 (81.1)	0.04**
$\geq 50\%$	59 (10.2)	23 (11.7)	20 (18.9)	
Stenosis of RCA				
None or<50%	518 (89.2)	135 (69.6)	70 (68.6)	<0.01**
$\geq 50\%$	63 (10.8)	59 (30.4)	32 (31.4)	
Stenosis of LM				
None or<50%	511 (98.8)	149 (100)	76 (100)	0.51**
$\geq 50\%$	6 (1.2)	0 (0)	0 (0)	
Number of vessels with $\geq 50\%$ stenosis				
None	447 (71.4)	113 (56.5)	49 (44.9)	<0.01**
Only one	106 (16.9)	55 (27.5)	35 (32.1)	
Only two	40 (6.4)	19 (9.5)	16 (14.7)	
Three or LMD	33 (5.3)	13 (6.5)	9 (8.3)	
LAD plaque present				
non-calcified	46 (13.3)	7 (6.1)	6 (8.0)	0.24**
low-density, non-calcified	224 (64.7)	79 (68.7)	52 (69.3)	
calcified	76 (22.0)	29 (25.2)	17 (22.7)	
CX plaque present				
non-calcified	32 (14.0)	9 (8.7)	7 (10.6)	0.20**
low-density, non-calcified	117 (51.3)	63 (61.2)	43 (65.2)	
calcified	79 (34.7)	31 (30.1)	16 (24.2)	

RCA plaque present				
non-calcified	39 (15.2)	11 (10.9)	9 (15.0)	0.01**
low-density, non-calcified	146 (57.1)	75 (74.3)	43 (71.7)	
calcified	71 (27.7)	15 (14.8)	8 (13.3)	
LM plaque present				
non-calcified	9 (14.8)	2 (7.2)	1 (7.1)	0.65**
low-density, non-calcified	24 (39.3)	13 (46.4)	8 (57.2)	
calcified	28 (45.9)	13 (46.4)	5 (35.7)	

Percentages are shown in parentheses. Continuous variables are presented as mean  $\pm$  SD and median (IQR) below;  
\* - Kruskal-Wallis test; \*\* - Pearson's chi-square test or Fisher's exact test

CAC score was associated with age ( $p<0.001$ ), gender ( $p<0.001$ ), BMI ( $p<0.05$ ), SBP ( $p<0.01$ ), hypertension ( $p<0.001$ ), use of statins ( $p<0.01$ ), diabetes ( $p<0.001$ ) and creatinine ( $p<0.001$ ) (Table 3). There was a close association between patient age and CAC score (test for trend  $p<0.001$ ). Un-

like continuous CAC, dichotomous CAC score was associated with type of chest pain ( $p=0.04$ ), glucose ( $p<0.01$ ) and triglycerides ( $p<0.01$ ).

According to Bivariate analysis CAC score was strongly associated with coronary CT findings (Table 4).

Table 3. Bivariate analysis for continuous and dichotomous CAC score (CAC score=0 and CAC score > 0) with demographic variables and CV risk factors

Variables	Continuous CAC score	p-value	CAC score=0 (n=355)	CAC score>0 (n=574)	p-value
Age					
$\leq 50$	24.9 $\pm$ 80.9	<0.001*	133 (37.6)	65 (11.3)	<0.001**
51-60	109.3 $\pm$ 364.8		115 (32.5)	186 (32.4)	
61-70	178.0 $\pm$ 354.4		84 (23.7)	219 (38.2)	
More than 70	301.9 $\pm$ 478.5		22 (6.2)	104 (18.1)	
Female	65.2 $\pm$ 188.0	<0.001***	161 (45.6)	152 (26.5)	<0.001**
Male	178.2 $\pm$ 405.3				
Kazakh	107.9 $\pm$ 270.4	<0.01*	256 (72.1)	365 (63.6)	0.03**
Russian	225.3 $\pm$ 507.5		64 (18.0)	135 (23.5)	
Other	164.7 $\pm$ 384.2		35 (9.9)	74 (12.9)	
BMI					
Normal BMI	99.1 $\pm$ 238.1	0.05*	70 (22.2)	73 (14.0)	<0.01**
Overweight	158.0 $\pm$ 404.4		117 (37.2)	193 (37.0)	
Obese	140.4 $\pm$ 343.5		128 (40.6)	256 (49.0)	
SBP	0.14	<0.001****	172.9 $\pm$ 32.4	179.1 $\pm$ 28.1	0.01***
DBP	0.07	0.06****	97.1 $\pm$ 12.7	98.9 $\pm$ 11.3	0.07***
Hypertension					
yes	156.4 $\pm$ 363.9	<0.001***	266 (75.6)	512 (89.2)	<0.001**
no	55.1 $\pm$ 263.7				
Smoking status					
yes	109.5 $\pm$ 312.9	0.43***	78 (22.8)	121 (21.8)	0.71**
no	150.5 $\pm$ 367.1				
Alcohol use					
yes	181.7 $\pm$ 513.3	0.72***	38 (11.0)	69 (12.4)	0.52**
no	135.2 $\pm$ 328.7				
Family history of CHD					
yes	114.8 $\pm$ 275.1	0.41***	138 (40.3)	230 (41.7)	0.68**
no	158.9 $\pm$ 402.8				



Chest pain					
Typical	177.3±436.0	0.21*	128 (37.8)	227 (41.1)	0.04**
Atypical	101.7±242.1		86 (25.4)	166 (30.0)	
Non-anginal	128.7±323.9		125 (36.9)	160 (28.9)	
Use of Statins					
yes	181.4±433.4	<0.01***	123 (38.8)	275 (51.8)	<0.001**
no	107.9±270.6				
Diabetes					
yes	158.8±315.2	<0.001***	66 (18.8)	169 (29.6)	<0.001**
no	133.8±364.2				
HbA1C	0.10	0.32****	6.4±1.5	6.7±2.1	0.65***
Glucose	0.06	0.09****	5.6±1.4	5.9±1.8	<0.01***
Fibrinogen	0.03	0.42****	2.98±0.8	3.08±1.0	0.15***
Creatinine	0.17	<0.001****	75.9±20.0	81.7±20.6	<0.001****
Total Cholesterol	0.04	0.23****	4.9±1.2	5.1±1.2	0.15***
LDL	-0.01	0.70****	3.3±1.1	3.3±1.0	0.90***
HDL	-0.06	0.07****	1.3±0.5	1.3±0.5	0.48***
Triglycerides	0.07	0.06****	1.5±0.8	1.7±1.3	<0.01***

Percentages are shown in parentheses. Continuous variables are presented as mean ± SD;

\* - Kruskal-Wallis test; \*\*Pearson's chi-square test or Fisher's exact test; \*\*\* - Two-sample t-test or Mann-Whitney U-test; \*\*\*\* - Spearman's correlation coefficient

Table 4. Bivariate analysis for continuous and dichotomous CAC score (CAC score=0 and CAC score >0) with coronary CT variables

Variables	Continuous CAC	p-value	CAC=0 (n=355)	CAC>0 (n=574)	p-value
Stenosis of LAD					
None or<50%	53.4±169.6	<0.001***	329 (95.9)	322 (57.9)	<0.001**
≥ 50%	372.6±555.9		14 (4.1)	234 (42.1)	
Stenosis of LCX					
None or<50%	88.7±253.5	<0.001***	334 (98.8)	441 (82.1)	<0.001**
≥ 50%	566.5±657.5		4 (1.2)	96 (17.9)	
Stenosis of RCA					
None or<50%	80.3±242.2	<0.001***	331 (97.1)	389 (73.3)	<0.001**
≥ 50%	434.3±601.9		10 (2.9)	142 (26.7)	
Stenosis of LM					
None or<50%	134.3±359.8	<0.01***	310 (100)	422 (98.6)	0.04**
≥ 50%	394.6±377.3		0 (0)	6 (1.4)	
Number of vessels with stenosis ≥50%					
None	46.7±141.8	<0.001*	329 (92.7)	279 (48.6)	<0.001**
Only one	145.3±360.2		25 (7.0)	168 (29.3)	
Only two	443.4±464.9		0 (0)	73 (12.7)	
Three or LMD	744.9±740.5		1 (0.3)	54 (9.4)	
LAD plaque present					
non-calcified	7.6±20.2	<0.001*	39 (86.7)	20 (4.1)	<0.001**
low-density, non-calcified	319.2±503.1		6 (13.3)	345 (70.8)	
calcified	68.1±142.2		0 (0)	122 (25.1)	
LCX plaque present					

non-calcified	44.5±113.9	<0.001*	24 (85.7)	24 (6.6)	<0.001**
low-density, non-calcified	425.3±589.0		3 (10.7)	217 (59.4)	
calcified	129.1±231.6		1 (3.6)	124 (34.0)	
RCA plaque present					
non-calcified	31.3±82.0	<0.001*	34 (87.2)	24 (6.4)	<0.001**
low-density, non-calcified	383.9±558.7		5 (12.8)	256 (68.5)	
calcified	108.5±178.3		0 (0)	94 (25.1)	
LM plaque present					
non-calcified	101.6±159.1	0.02*	3 (100)	9 (9.1)	<0.01**
low-density, non-calcified	459.2±756.8		0 (0)	44 (44.4)	
calcified	230.2±363.6		0 (0)	46 (46.6)	

Percentages are shown in parentheses. Continuous variables are presented as mean ± SD;

\*- Kruskal-Wallis test when parametric assumptions were violated; \*\* - Pearson's chi-square test or Fisher's exact test;

\*\*\* - Mann-Whitney U test

After adjusting for possible confounders in multivariate analyses, the odds of having positive CAC score increased by 48% (OR=1.48; 95% CI, 0.91 - 2.40) among Russians relatively to Kazakhs. Similarly, in the multivariate linear regression model, CAC score on average increased by 71.4% (p=0.03) between respective ethnic groups among patients with CAC score > 0. The odds of having positive CAC score were almost four times higher (OR=3.87, 95% CI, 2.57-5.84) among males rel-

atively to females in logistic regression model adjusting for covariates. The odds of having positive CAC score and average percent of CAC score increased with older age groups (p<0.001). For example, average CAC was higher 103.5%, 271.0% and 645.6% among 51-60, 61-70 and >70 age groups, respectively, in reference to ≤50 age group. In multivariate analysis, relationships of CAC score with use of statins and SBP were positive.

Table 5. Multivariate linear regression coefficients for independent variables of CAC score among people with CAC score>0

Variable	Coefficient (95% CI) (log of CAC score)	Corresponding percentage change in CAC score (95% CI)	p-value
Kazakh	Reference	Reference	0.03
Russian	0.54 (0.13-0.95)	71.4% (1.4% to 141.3%)	
Other	0.26 (-0.23 to 0.74)	29.4% (-33.0% to 91.9%)	
Female	Reference	Reference	<0.001
Male	1.11 (0.73-1.50)	205.1% (89.6% to 320.6%)	
Age			
≤ 50	Reference	Reference	<0.001
51-60	0.71 (0.06 to 1.36)	103.5% (-28.4% to 235.4%)	
61-70	1.31 (0.67 to 1.96)	271.6% (32.4% to 510.8%)	
>70	2.01 (1.31-2.71)	645.6% (125.9% to 1165.2%)	
Family history of CVD			
no	Reference	Reference	0.02
yes	-0.41 (-0.75 to -0.07)	-33.6% (-56.3% to -10.9%)	
SBP, per 10 mm Hg	0.12 (0.05-0.18)	12.6% (5.3%-19.8%)	<0.001
Total cholesterol, per 10 mmol/l	0.22 (-1.17 to 1.61)	30.9% (-153.0% to 214.8%)	0.71
Use of statins			
no	Reference	Reference	0.02
yes	0.40 (0.06-0.74)	49.8% (-1.0% to 100.5%)	
Diabetes			
non-diabetic	Reference	Reference	0.54
diabetic	-0.11 (-0.48 to 0.25)	-10.7% (-43.3% to 21.9%)	
Intercept	-0.24 (-1.74 to 1.26)		0.76

Table 6. Odds ratio of CAC presence (CAC score>0) by independent variables in multivariate logistic regression

Variable	OR (95% CI)	p-value
Kazakh	1.00 (Reference)	0.28
Russian	1.48 (0.91-2.40)	
Other	1.16 (0.66-2.03)	
Female	1.00 (Reference)	<0.001
Male	3.87 (2.57-5.84)	
Age		
≤ 50	1.00 (Reference)	<0.001
51-60	2.61 (1.49-4.58)	
61-70	5.44 (3.01-9.84)	
>70	8.16 (3.95-16.89)	
Family history of CVD		
no	1.00 (Reference)	0.63
yes	1.14 (0.78-1.68)	
SBP*		
<150 mm Hg	1.00 (Reference)	0.03
150-179 mm Hg	1.04 (0.55-1.94)	
180-199 mm Hg	1.80 (0.93-3.50)	
≥200 mm Hg	1.90 (0.97-3.69)	
Total cholesterol*		
Below 5.2 mmol/l	1.00 (Reference)	0.59
5.2-6.1 mmol/l	0.96 (0.62-1.49)	
6.2 and above	1.26 (0.76-2.10)	
Use of statins		
no	1.00 (Reference)	0.56
yes	1.12 (0.76-1.64)	
Diabetes		
non-diabetic	1.00 (Reference)	0.04
diabetic	1.58 (1.02-2.44)	
Intercept	0.05 (0.01-0.18)	<0.001

\* - Due to violation of the linearity assumption, SBP and total cholesterol were categorized to meet the assumption

In this comparison between different ethnic groups in Kazakhstan with chest pain we have demonstrated that the burden of coronary atherosclerosis, assessed by calcium score, is greater among Russian and other ethnicities than among Kazakhs, even after adjustment for conventional risk factors. To our knowledge there were no previous studies on CAC score in Central Asian population and data about ethnic specificity of CV risk factors in this area are limited. Previous studies have shown that East Asians, including Chinese, Korean, and Japanese subjects, have lower CAD burden measured on CAC compared with Western subjects [13]. The Multi Ethnic Study of Atherosclerosis (MESA) also reported similar observations, whereby Chinese adults had a lower prevalence of CAC compared with Caucasian subjects [14]. Although there is a big difference in eating habit between Chinese and Kazakhs, seemingly lower CAC score is cross-race effect of Asians.

Many studies have shown that CAC score is strongly associated with age in different heterogeneous populations, geography and culture [15,16]. Higher CAC score among Rus-

sians could be attributed with higher prevalence of advanced aged patients in this group, 18% of patients were older than 70 years, in comparison with 11.7% and 17.6% in Kazakh and other ethnicity groups respectively.

Previous studies have shown that BP components have age-dependent roles in the prediction of CAC, and SBP and PP were independent predictors of the presence and quantity of coronary artery calcification in the ≥50 years of age group [17]. In our study, registered maximal systolic blood pressure among Russian population was higher compared to other groups. Systolic blood pressure was strongly associated with higher CAC score, both on Multivariate Linear and logistic regression analysis. Coronary calcium deposition may indicate higher degree of vascular calcification and, thus, impaired vascular compliance and higher blood pressure levels. But more investigations needed to clarify this mechanism.

Russian population had higher BMI and about 53% of Russians enrolled in the study were obese. Whereas, 41.9% of Kazakh population had BMI<30 kg/m<sup>2</sup>. In bivariate analysis BMI showed positive correlation with CAC score, but multi-

variate linear or logistic regression analysis showed no impact of obesity on CAC score. In previous studies higher BMI is independently associated with increased risk of intermediate-term risk of myocardial infarction and abdominal obesity was an independent predictor of CAC progression [18], however, most studies evaluated the association between obesity and CAC in a Western population with conflicting results [19,20].

Several controversial findings were observed. One is character of chest pain which was mostly atypical or non-anginal among Kazakhs, when Russians and other ethnic groups had predominantly typical angina pectoris. One more interesting finding is, that Kazakhs had highest FPG level and multivariate analysis showed strong positive correlation between the presence of diabetes and CAC score. Also, plasma triglyceride levels were higher among Kazakhs compared with Russians and bivariate analysis shows positive correlation of triglyceride level and CAC score.

Several limitations of our study should be acknowledged. First, our study was performed at only two centers, those are located in one city and provides tertiary medical care, which makes it uncertain whether results will be likely generalizable to whole Kazakhstani population. Second, there were no standardized questionnaire to collect CV risk factors. Some of inconsistencies with previous studies results [reference], for example, family history of CVD in multivariate analyses, could be attributed to an absence of standardized approach in data collection. Additionally, there may be other confounders that were not included in adjustment, such as, physical activity, dietary habits and socioeconomic status. Third, this was a cross-sectional study with no prospective follow-up data on the patient management post CT scan and subsequent incidence of MI.

**Conclusion.** As compared with Russians, Kazakhs and other minorities, Kazakhs had significantly lower CAC score. The difference of the CV risk-factor profiles do not explain this finding. This study demonstrated that Russians have a higher atherosclerotic burden than Kazakhs and others, independent of risk-factor differences among patients with stable chest pain. Future longitudinal national and regional population-based studies are, however, warranted.

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## SUMMARY

### COMPUTED TOMOGRAPHY IN DETECTING FEATURES OF CORONARY ATHEROSCLEROSIS IN DIFFERENT ETHNIC GROUPS OF KAZAKHSTAN POPULATION

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The aim of the study was to identify the features of coronary lesions and to determine the correlation between the main risk factors for coronary artery disease according to the SCORE quality of life scale and the calcium index in MSCT in different age and ethnic groups in men and women living in Kazakhstan.

We retrospectively analyzed 935 case histories of patients undergoing MSCT to assess the condition of the coronary arteries. The patients were divided into three groups: Kazakhs (66.9%), Russians (21.4%) and other (11.7%) nationalities. There were statistically significant differences between ethnic groups in BMI ( $p=0.03$ ), type of chest pain ( $p<0.01$ ), statin use ( $p=0.01$ ), and blood glucose ( $p<0.01$ ). The study showed that the prevalence of coronary atherosclerosis is higher among Russians compared to Kazakhs, even after adjusting for traditional risk factors. In multivariate analysis, the calcium index values were significantly higher in the group of the Russian population by 48% (OR=1.48; 95% CI 0.91–2.40) than in the Kazakh population. In the course of the cross-sectional study, statistically significant differences in the nature of coronary lesions were revealed between ethnic groups, mainly males, living in the Republic.

Until now, such studies have not yet been conducted among the inhabitants of Kazakhstan, and data on the ethnic specificity of risk factors for cardiovascular diseases in this geographical region have not been sufficiently studied. Previous studies have shown that East Asians, including Chinese, Koreans, and Japanese, have a lower incidence of coronary artery disease as measured by CI compared to Europeans. A large MESA study also reported observations that study participants of Chinese nationality had a lower CI compared to Europeans. Despite significant differences in dietary habits and living in different climatic conditions between Asians of different countries, lower CI scores appear to be a racial trait of Asians, which was further confirmed by our study.

These results are undoubtedly representative, as patients from different regions of Kazakhstan were treated in two clinics of republican significance. In the future, it is necessary to conduct prospective studies with subsequent follow-up of patients after treatment and in identifying the causes of recurrent coronary events, as was done in the MESA study.

**Keywords:** atherosclerosis, coronary arteries, computed tomography, risk factor, inhabitants of Kazakhstan.

## РЕЗЮМЕ

### КОМПЬЮТЕРНАЯ ТОМОГРАФИЯ В ВЫЯВЛЕНИИ ОСОБЕННОСТЕЙ КОРОНАРНОГО АТЕРОСКЛЕРОЗА У ЖИТЕЛЕЙ РАЗЛИЧНЫХ ЭТНИЧЕСКИХ ГРУПП КАЗАХСТАНА

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Цель исследования - выявление особенностей поражения коронарного русла и определение корреляционной связи основных факторов риска ишемической болезни сердца с показателями кальциевого индекса в различных возрастных и этнических группах у мужчин и женщин, проживающих в Казахстане.

Ретроспективно проведен анализ 935 историй болезни пациентов, которым проведена мультиспиральная компьютерная томография (МСКТ) для оценки состояния коронарных артерий. Пациенты с учетом национальной принадлежности разделены на три группы: казахи (66,9%), русские (21,4%) и другие (11,7%) национальности.

Между этническими группами выявлены статистически значимые различия по индексу массы тела ( $p=0,03$ ), типу боли в груди ( $p<0,01$ ), использованию статинов ( $p=0,01$ ) и уровню глюкозы в крови ( $p<0,01$ ). Исследование показало, что распространенность коронарного атеросклероза выше среди русской национальности в сравнении с казахской, даже после корректировки на традиционные факторы риска. Многофакторный анализ выявил, что показатели кальциевого индекса (КИ) превышают таковые группы русской популяции на 48% (OR=1,48; 95% ДИ 0,91–2,40) в сравнении в казахской. В ходе кросс-секционного исследования выявлены статистически значимые различия



по характеру поражения коронарного русла между этническими группами, преимущественно мужского пола, проживающими в Казахстане.

Авторы исследования считают необходимым проведение проспективных исследований с последующим динамическим наблюдением за пациентами после лечения с целью выявления причин повторных коронарных событий.

#### რეზიუმე

კომპიუტერული ტომოგრაფიის როლი კორონარული ათეროსკლეროზის თავისებურებების გამოვლენაში ყაზახეთში მცხოვრებ სხვადასხვა ეთნიკური ჯგუფის წარმომადგენლებში

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<sup>4</sup> მ.გუტბერღევი, <sup>2,3</sup> დ.მარდენკოვი, <sup>2</sup> ჟ.კოჟახმეტოვა,  
<sup>2,3</sup> ა.სადუაკასოვა

<sup>1</sup> კარდიოქირურგიის ეროვნული სამეცნიერო ცენტრი; <sup>2</sup> ასტანას სამედიცინო უნივერსიტეტი, ნურ-სულტანი; <sup>3</sup> ყაზახეთის რესპუბლიკის პრეზიდენტის ადმინისტრაციული დეპარტამენტის სამედიცინო ცენტრის საავადმყოფო, ნურ-სულტანი, ყაზახეთი; <sup>4</sup> სამედიცინო უნივერსიტეტი, გულის ცენტრი, დიაგნოსტიკისა და ინტერვენციული რადიოლოგიის განყოფილება, ლეიპციგი, გერმანია

კვლევის მიზანს წარმოადგენდა კორონარული სისხლძარღვების დაზიანების თავისებურებების გამოვლენა და გულის იშემიური დაავადების ძირითადი რისკფაქტორების კორელაციური კავშირის განსაზღვრა

კალციუმის ინდექსთან ყაზახეთში მცხოვრებ სხვადასხვა ასაკის და სხვადასხვა ეთნიკური ჯგუფის წარმომადგენელ მამაკაცებსა და ქალებში.

რეტროსპექტულად გაანალიზებულია 935 პაციენტის ავადმყოფობის ისტორია, რომელთაც კორონარული არტერიების მდგომარეობის შეფასების მიზნით ჩაუტარდა მულტისპირალური კომპიუტერული ტომოგრაფია. პაციენტები, ეთნიკური კუთვნილების მიხედვით, დაიყო სამ ჯგუფად: ყაზახები (66,9%), რუსები (21,4%) და სხვა ეროვნების წარმომადგენლები (11,7%). ეთნიკურ ჯგუფებს შორის გამოვლინდა სტატისტიკურად მნიშვნელოვანი განსხვავება სხეულის მასის ინდექსის ( $p=0,03$ ), გულმკერდის მიდამოში ტკივილის ( $p<0,01$ ), სტატინების გამოყენების ( $p=0,01$ ) და სისხლში გლუკოზის დონის ( $p<0,01$ ) მიხედვით.

კვლევის შედეგებმა აჩვენა, რომ კორონარული ათეროსკლეროზის გავრცელება უფრო მაღალია რუსი ეროვნების მოსახლეობაში ყაზახეთთან შედარებით, მათ შორის - ტრადიციული რისკფაქტორების კორექციის შემდეგაც. მრავალფაქტორული ანალიზით გამოვლინდა, რომ რუსულ პოპულაციაში, ყაზახეთთან შედარებით, 48%-ით უფრო მაღალია კალციუმის ინდექსის მაჩვენებლები ( $OR=1,48$ ; 95%-იანი სანდოობის ინტერვალი 0,91–2,40). ქროს-სექციური კვლევით ყაზახეთში მცხოვრებ ეთნიკურ ჯგუფებს შორის, უპირატესად მამაკაცებში, გამოვლინდა სტატისტიკურად სარწმუნო განსხვავება კორონარული სისხლძარღვების დაზიანების ხარისხში.

განმეორებითი კორონარული შემთხვევების მიზეზების გამოსავლენად ავტორებს მიზანშეწონილად მიჩნიათ პროსპექტული კვლევების ჩატარება მკურნალობის შემდეგ პაციენტებზე დაკვირვებით დინამიკაში.

## TRANSFORMING GROWTH FACTOR AND ARTERIAL STIFFNESS IN PATIENTS WITH UNCONTROLLED ARTERIAL HYPERTENSION

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Arterial hypertension (AH) remains the leading cause of premature death and more than 200 million cases of disability worldwide [1]. In hypertensive patients who do not reach the target level of blood pressure (BP), accelerated remodeling of target organs develops [2], which increases the risk of cardiovascular complications. Arterial stiffness is a proven risk factor for cardiovascular complications in hypertension [3]. At the heart of vascular wall damage there are two processes - atherosclerosis and arteriosclerosis [4]. Numerous studies have shown a relationship between the degree of arterial stiffness and the presence of atherosclerotic lesions [5], but the data on the dependence of

arteriosclerosis processes on classical risk factors for atherosclerosis is very contradictory [6,7]. In arteriosclerosis, media is affected: elastin degrades, collagen content increases, hyperplasia and hypertrophy of smooth muscle cells develop, and they are these processes that lead to an increase in arterial stiffness. It is known that transforming growth factor  $\beta 1$  (TGF- $\beta 1$ ), a pleiotropic cytokine, enhances proliferation and growth of smooth muscle cells, as well as the accumulation of extracellular matrix [8], that is, the processes underlying target organ damage (TOD) in hypertension. It is a member of the superfamily of structurally related proteins, which includes at least 40 proteins [9]. Some