Prevalence of Early Ischemic Heart Disease and Its Associations with Risk Factors and Socioeconomic Variables in the 25–44-year Age Group in Western Siberia

Yuliya I. Ragino
IIPM - Branch of IC&G SB RAS
Natalya A. Kuzminykh
IIPM - Branch of IC&G SB RAS
Liliia V. Shcherbakova
IIPM - Branch of IC&G SB RAS
Viktoriya Shramko (Nosova@211.ru)
Naucno-issledovatel'skij institut terapii i profilakticeskoj mediciny SO RAMN https://orcid.org/0000-0002-0436-2549
Diana V. Denisova
IIPM - Branch of IC&G SB RAS

Research article

Keywords: epidemiological study, definite ischemic heart disease, 25-44-year-old population, risk factors, socioeconomic factors, smoking

DOI: https://doi.org/10.21203/rs.3.rs-39561/v1

Abstract

The aim of this study was to investigate the prevalence of early ischemic heart disease (IHD) in accordance with standardized epidemiological criteria in the 25–44-year age group in Novosibirsk (Russia) and to identify associations with some risk factors and socioeconomic factors.

Materials and methods. A cross-sectional populational medical examination was conducted on a random sample of the 25–44-year age group in Novosibirsk. A total of 1457 people were analyzed (653 males and 804 females). Epidemiological IHD diagnosis was made according to validated epidemiological (cardiological Rose questionnaire) and functional criteria (recording of an ECG interpreted via the Minnesota Code). The “definite IHD” diagnosis was made in the presence of the following criteria: a history of large-focal myocardial infarction (ECG), tension angina pectoris (Rose questionnaire), ischemic changes on ECG without left ventricular hypertrophy (ECG). Further, the diagnosis of "definite IHD" was confirmed by conducting an ECG test with physical activity. The evaluated IHD modifiable risk factors were cigarette smoking, elevated body mass index, elevated waist circumference, the presence of arterial hypertension, low physical activity, and elevated blood levels of low-density lipoprotein cholesterol, non–high-density lipoprotein cholesterol, and triglycerides. Socioeconomic factors were assessed too: marital status, occupation type, education, health self-rating, and economic status.

Results. The prevalence of definite IHD in the study population was found to be 3.36% (49 subjects): 2.8% (18 subjects) among males and 3.9% (31 subjects) among females. All quantitative data on IHD risk factors were higher in males than in females. The prevalence of IHD risk factors (except for elevated waist circumference) was higher among males than females. The prevalence of IHD risk factors (except for cigarette smoking) was not different between IHD and no-IHD groups in the study population. Smoker prevalence was 1.66-fold higher ($p = 0.031$) in the no-IHD group than in the IHD group. Multivariate logistic regression analysis uncovered an inverse association of cigarette smoking (independently of age, sex, and other risk factors) with the relative risk of early IHD in the study population. Furthermore, in males, the relative risk of definite IHD (regardless of age) directly correlated with heavy manual labor (odds ratio [OR] = 3.495, confidence interval [CI] 1.306–9.353, $p = 0.013$) and unfavorable marital status (divorced or widowed; OR = 4.976, CI 0.944–26.228, $p = 0.058$). Meanwhile, these two factors inversely correlated with cigarette smoking (OR = 0.202, CI 0.060–0.672, $p = 0.009$).

Conclusion. In males aged 25–44 years in Novosibirsk, the relative risk of early IHD is directly associated with heavy manual labor or unfavorable marital status, and these factors are inversely associated with smoking. This correlation needs further research.

The medical-examination–based screening was performed within the framework of a government-funded research topic in State Assignment No. AAAA-A17-117112850280-2. The biochemical and functional analyses were financially supported by a Russian Federation President grant for leading scientific schools, No. НШ-2595.2020.7.

Introduction

According to data from the World Health Organization (WHO), ischemic heart disease (IHD) continues to be the leading cause of morbidity and mortality in industrially developed and developing countries and is responsible for ~[illegible] of all deaths among people older than 35 years [1, 2].

The IHD is considered early or premature if it develops before age 55 years in males and before age 65 in females [3]. Other terminology may be used in various studies (IHD at a young age, IHD at a very young age, or premature development of IHD), whereas the age limit of the study population varies from 35 to 65 years, thus complicating comparisons of the findings [4–7].

In recent years, IHD prevalence among the young has been increasing, and this is an important socioeconomic problem because of early disability and early deaths. Patients presenting with IHD at a younger age differ from elderly IHD patients in the structure of risk factors (RFs), clinical manifestations, and in the prognosis. Virtually all young patients with IHD have at least one traditional RF of this disease [8, 9].

The present study was aimed at investigating the prevalence of IHD according to standardized epidemiological criteria in the age group of 25–44-year-oldsin Novosibirsk and at identifying associations of IHD with some of its RFs.

Material And Methods

Ethics approval and consent to participate

The study protocol was approved by the local Ethics Committee of the Institute of Internal and Preventive Medicine (a branch of the Institute of Cytology and Genetics, the Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia). All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent to the medical examination and analysis of personal data was obtained from each patient.

Selection and Description of Participants

During 2014–2015, a cross-sectional populational medical examination was conducted on a random sample of people from a typical borough of Novosibirsk, which is a capital of Western Siberia. To compile the population sample, we used a database of the Novosibirsk Territorial Fund of mandatory health insurance, from which (by means of a random number generator) 2500 subjects of both sexes aged 25–44 years were selected. It is known that young age groups are among the least responsive to invitations to a medical examination; therefore, methods of gradual epidemiological stimulation were employed: postal invitations, telephone calls, and announcements in mass media. The response rate was 58.3%. At our Screening Center, 1457 people underwent the medical examination: 653 males (45%) and 804 females (55%). All the participates provided informed consent to the medical examination and analysis of personal data. The screening was carried out by a team of physicians, who had been trained in standardized epidemiological methods of medical-examination–based screenings.

The medical-examination program included collection of demographic and social data, questions about cigarette-smoking and alcohol-drinking habits, a socioeconomic questionnaire, nutritional survey, collection of chronic-disease and medication history, the cardiological Rose questionnaire, anthropometric-data collection, three-time measurement of arterial blood pressure (BP), spirometry, ECG recording with interpretation in accordance with the Minnesota Code (MC), and assessment of other parameters.

The BP measurement was performed thrice with a 2 min interval on the right arm in a sitting position after a 5 min rest by means of a digital BP monitor, and the average of the three measurements was recorded. The body mass index (BMI) was determined via the following formula: body weight (kg) divided by the height squared (m^2). Participants were assumed to be smokers if they smoked at least one cigarette a day.

One-time blood collection from the medial cubital vein was carried out in the morning after a 12 h fast. Indicators of lipid metabolism were measured by the enzymatic method using standard reagents from TermoFisher on a KoneLab 30i automatic biochemical analyzer (Finland).

The following socioeconomic factors were evaluated: marital status (married, single, divorced, or widowed), the occupation type (sedentary job, standing work, manual labor, or heavy manual labor), education level (grammar school, a high school diploma, or a college degree), health self-rating (good, fair, or bad), and economic status (employed, student, or unemployed).

Age, gender and heredity (IHD family history) were assessed as unmodifiable risk factors. The following IHD modifiable RFs were assessed [10]: cigarette smoking, elevated BMI(> 25 kg/m^2), waist circumference (WC) ≥ 94 cm in males or ≥ 80 cm in females, arterial hypertension (AH; ≥140/≥90 mmHg), low physical activity(<3.5 h/week), an elevated blood level of low-density lipoprotein cholesterol(LDL-C; ≥116 mg/dL or ≥ 3 mM), an elevated blood level of non–high-density lipoprotein cholesterol(non-HDL-C; ≥130 mg/dL or ≥ 3.4 mM), and elevated blood concentration of triglycerides (TGs; ≥150 mg/dL or ≥ 1.7 mM).

The epidemiological diagnosis of IHD was made via validated epidemiological (using the Rose questionnaire) and functional criteria (ECG recording with interpretation using the MC). The diagnosis of “definite IHD” was made in the presence of the following criteria: a history of large-focal myocardial infarction (MI) (ECG with MC), tension angina pectoris (Rose questionnaire), ischemic changes on ECG without left ventricular hypertrophy (ECG with MC). Further, the diagnosis of "definite IHD" was confirmed by conducting an ECG test with physical activity.

Statistics

Statistical analysis was carried out in the SPSS software for Windows (version 17) with evaluation (for each variable) of the mean, median, standard deviation, confidence intervals (CIs), and lower and upper quartiles. The following methods of group comparison were used: the Mann–Whitney *U* test for a comparison of medians, Wilcoxon's test, one-way ANOVA with Dunnett's test for a multigroup comparison, calculation of the odds ratio (OR) by means of contingency tables, OR calculation in a logistical regression model, the χ^2test, and *t*-test. The 95% level of statistical significance was assumed.

Results

The prevalence of definite IHD in the study population (25–44-year-olds) was 3.36% (49 subjects). Among 653males, IHD was detected in 18 subjects (2.8%), and among 804 females, in 31 subjects (3.9%). No significant difference in IHD prevalence was found between males and females (p=0.247). No statistically significant association of the IHD family history with the presence of early IHD was found (p = 0.229).

As shown in Table 1, there were no significant differences in age between the males and females. All quantitative data on the analyzed IHD modifiable RFs were higher in males than in females.

Table 1
Quantitative data on RFs of IHD among 25–44-year-olds in Novosibirsk

Variable	Whole study population (n = 1457)		Males(n = 653)		Females(n = 804)		p value, males/ females
	M	SD	M	SD	M	SD	
	Me	(25%; 75%)	Me	(25%; 75%)	Me	(25%; 75%)	
Age, years	36.7	6.0	36.5	6.0	36.8	6.1	0.259
	37.0	(31.6; 41.7)	36.7	(31.5; 41.4)	37.2	(31.7; 41.9)	
BMI, kg/m^2	26.1	5.5	26.7	4.9	25.6	5.9	< 0.001
	25.2	(22.1; 29.1)	26.3	(23.3; 29.3)	24.3	(21.4; 28.6)	
WC, cm	86.4	14.0	92.8	12.4	81.2	13.1	< 0.001
	85.4	(76.0; 95.6)	91.6	(84.0; 100.0)	79.0	(71.1; 88.5)	
Systolic BP, mmHg	120.6	15.5	126.6	13.9	115.6	15.0	< 0.001
	119.0	(110.0; 129.0)	125.0	(117.0; 134.0)	113.5	(106.0; 122.5)	
Diastolic BP, mmHg	79.1	11.2	83.4	10.3	75.6	10.7	< 0.001
	78.0	(71.5; 86.0)	82.5	(76.0; 90.0)	74.5	(68.5; 81.5)	
Physical activity, h/week	2.0	4.6	2.5	5.4	1.6	3.7	< 0.001
	0	(0; 3.0)	1.0	(0; 3.25)	0	(0; 2.0)	
LDL-C, mg/dL	121.7	33.8	126.5	35.2	117.5	31.9	< 0.001
	120.2	(97.0; 143.0)	125.2	(102.0; 147.4)	115.8	(95.2; 138.9)	
Non-HDL-C, mg/dL	142.3	40.0	151.0	42.8	134.8	35.7	< 0.001
	139.0	(113.0; 166.0)	147.0	(123.0; 176.0)	133.0	(108.2; 156.0)	
TGs, mg/dL	103.4	72.2	123.5	88.9	86.4	47.8	< 0.001
	83.0	(60.0; 122.0)	98.0	(68.0; 150.0)	74.0	(54.0; 103.0)	

BMI - body mass index; BP - arterial blood pressure; LDL-C - low-density lipoprotein cholesterol; M - mean; Me - median; non-HDL-C - non–high-density lipoprotein cholesterol; SD - standard deviation; TG – triglyceride; WC - waist circumference

As depicted in Table 2, the prevalence of the studied IHD modifiable RFs (except for elevated WC) was higher among males than among females.

Table 2
The prevalence of IHD RFs among 25–44-year-olds in Novosibirsk depending on sex

Variable	Males (n = 653)	Females (n = 804)	p value
Smoking	44.5%	24.6%	<0.001
BMI > 25 kg/m^2	60.2%	44.3%	<0.001
WC ≥ 94 cm in males, ≥ 80 cm in females	42.1%	44.8%	0.163
AH ≥ 140/≥90 mmHg	28.1%	10.4%	<0.001
Physical activity<3.5 h/week	75.0%	84.5%	<0.001
LDL-C ≥ 116 mg/dL	61.0%	49.9%	<0.001
Non-HDL-C ≥ 130 mg/dL	68.6%	53.3%	<0.001
TGs ≥ 150 mg/dL	25.2%	9.7%	<0.001

AH - arterial hypertension; BMI - body mass index; LDL-C - low-density lipoprotein cholesterol; non-HDL-C - non–high-density lipoprotein cholesterol; TG – triglyceride; WC - waist circumference

We analyzed quantitative data on the studied RFs depending on the presence of IHD in the study population (25–44-year-olds in Novosibirsk; Table 3). Significant differences between the two groups (with and without IHD) were not found. There were no significant differences in the quantitative data on the analyzed RFs depending on the presence of IHD either in the male subpopulation or in the female subpopulation.

Table 3
Quantitative data on RFs depending on the presence of definite IHD in 25–44-year-olds in Novosibirsk

Variable	Absence of definite IHD (n = 1408)		Presence of definite IHD (n = 49)		p value
	M	SD	M	SD	
	Me	(25%; 75%)	Me	(25%; 75%)	
Age, years	36.6	6.0	38.0	6.3	0.107
	37.0	(31.6; 41.7)	39.0	(32.2; 43.1)	
BMI, kg/m^2	26.0	5.4	26.2	6.3	0.853
	25.2	(22.1; 29.1)	24.9	(22.2; 28.4)	
WC, cm	86.4	13.9	85.7	15.9	0.718
	85.5	(76.0; 95.9)	84.0	(75.2; 95.0)	
Systolic BP, mmHg	120.5	15.3	121.2	20.0	0.759
	119.0	(110.5; 129.0)	119.5	(105.7; 133.7)	
Diastolic BP, mmHg	79.1	11.2	78.6	12.5	0.744
	78.0	(71.5; 86.0)	78.0	(70.0; 85.7)	
Physical activity, h/week	2.0	4.6	2.1	3.3	0.838
	0	(0, 3.0)	1.0	(0; 2.0)	
LDL-C, mg/dL	121.4	33.2	129.3	47.2	0.117
	120.0	(96.8; 143.0)	124.0	(107.2; 140.2)	
Non-HDL-C, mg/dL	142.0	39.4	149.2	53.9	0.223
	139.0	(113.0; 166.0)	144.0	(120.0; 172.0)	
TGs, mg/dL	103.6	71.6	99.9	87.9	0.731
	84.0	(61.0; 123.0)	74.0	(54.0; 112.0)	

BMI - body mass index; BP - arterial blood pressure; IHD - ischemic heart disease; LDL-C - low-density lipoprotein cholesterol; M - mean; Me - median; non-HDL-C - non–high-density lipoprotein cholesterol; SD - standard deviation; TG – triglyceride; WC - waist circumference

As presented in Table 4, in the study population, the prevalence of the studied IHD RFs (except for cigarette smoking) was not different between the subjects with and without IHD. The prevalence of smokers was 1.66-fold higher (p = 0.031) in the group without IHD than in the group with IHD. Having analyzed this result, we found that in the male population (653 subjects), the prevalence of smoking was 1.6-fold higher (without significance, p = 0.113) among people without IHD (635 subjects) than among those with IHD (18 subjects), whereas in the female population (773 subjects), the prevalence of smoking was 1.55-fold higher (without significance, p = 0.184) among people without IHD (773subjects) than among those with IHD (31subjects). Thus, the prevalence of smokers among males and females with IHD, albeit statistically insignificantly, was somewhat lower than that in the groups without IHD.

Table 4
The prevalence of RFs depending on the presence of definite IHD in the Novosibirsk population of 25–44-year-olds

Variable	**Absence of definite IHD** **(n = 1408)**	**Presence of definite IHD** **(n = 49)**	**p value**
Smoking	34.0%	20.4%	**0.031**
BMI > 25 kg/m^2	51.5%	49.0%	0.420
WC ≥ 94 cm in males, ≥ 80 cm in females	43.4%	49.0%	0.265
AH ≥ 140/≥90 mmHg	18.2%	22.4%	0.276
Physical activity<3.5 h/week	80.2%	81.6%	0.489
LDL-C ≥ 116 mg/dL	54.7%	61.7%	0.214
Non-HDL-C ≥ 130 mg/dL	60.1%	66.0%	0.260
TGs ≥ 150 mg/dL	17.0%	12.8%	0.297
AH - arterial hypertension; BMI - body mass index; IHD - ischemic heart disease; LDL-C - low-density lipoprotein cholesterol; non-HDL-C - non–high-density lipoprotein cholesterol; TG – triglyceride; WC - waist circumference			

Subsequent multivariate logistical regression analysis identified an inverse association of smoking (independent of age, sex, and other analyzed RFs) with the relative risk of definite IHD in the study population (25–44-year-olds in Novosibirsk; Table 5). This “paradoxical result” can be explained by an above-mentioned finding (Table 4) that it was the IHD group where the prevalence of smoking was statistically significantly lower 1.66-fold relative to the no-IHD group.

Table 5
The relative risk of definite IHD in relation to the RFs of IHD, among 25–44-year-olds in Novosibirsk

Variables and IHD RFs	**OR**	**95% CI**		**p value**
		lower limit	**upper limit**	
Age	1.036	0.986	1.088	0.157
Sex	1.141	0.617	2.110	0.674
Smoking	0.432	0.203	0.921	**0.030**
BMI, kg/m^2	1.207	0.571	2.168	0.530
WC, cm	1.201	0.670	2.153	0.539
AH	1.117	0.477	2.265	0.647
Physical activity	0.983	0.463	2.086	0.965
LDL-C, mg/dL	1.284	0.699	2.361	0.420
Non-HDL-C, mg/dL	1.239	0.658	2.332	0.506
TGs, mg/dL	1.206	0.765	2.389	0.542

AH - arterial hypertension; BMI - body mass index; CI - confidence interval; IHD - ischemic heart disease; LDL-C - low-density lipoprotein cholesterol; non-HDL-C - non–high-density lipoprotein cholesterol; OR - odds ratio; RF - risk factor; TG – triglyceride; WC - waist circumference

Because none of the analyzed RFs (except for smoking) manifested an evident correlation with the relative risk of IHD, and because cigarette-smoking analysis yielded the "paradoxical" result, next we studied the relation of IHD with socioeconomic factors. The multivariate logistical regression analysis of socioeconomic factors was performed in relation to the risk of definite IHD in the study population (25–44-year-olds in Novosibirsk) and in its male and female subpopulations. Statistically significant results were obtained only in the male population. We noted age-independent correlations of the occupation type and of marital status (which are associated with cigarette smoking: OR = 0.202, CI 0.060–0.672, p=0.009) with the relative risk of definite IHD among 25–44-year-old males. For instance, among divorced non-smoking males, the probability of IHD presence was 5-fold higher (OR = 4.976, CI 0.944–26.228, p=0.058), whereas among non-smoking males occupationally engaged in heavy manual labor, it was 3.5-fold higher (OR = 3.495, CI 1.306–9.353, p=0.013).

Therefore, among 25–44-year-old males in Novosibirsk, the relative risk of IHD (namely, early IHD, manifesting itself before 45 years of age) is directly associated with heavy manual labor and unfavorable marital status but inversely correlates with smoking.

Discussion

There is evidence of high prevalence of IHD (according to epidemiological criteria) and its RFs in the population of Novosibirsk, a capital of Western Siberia. In this city, a young population (25–44 years of age) was last analyzed during the WHO project MONICA in the1990s [11–13].

Our results were obtained via a medical examination of the 25–44-year-old age group in Novosibirsk during 2014–2015. The results showed that at present, the prevalence of definite IHD in the study population (3.36%) and in its male (2.8%) and female (3.9%) subpopulations is not high.

It is known that more than half of young adults even at the age of 18–24 years have at least one RF of IHD [14].

We studied quantitative data on IHD RFs and data on the prevalence of IHD RFs, such as smoking, elevated BMI, elevated WC, AH presence, low physical activity, and elevated blood levels of LDL-C, non-HDL-C, and TG sin older subjects: 25–44 years. The prevalence of the aforementioned RFs in the study population ranged from 25–85%. All quantitative data on the analyzed RFs of IHD were higher in males than in females. In addition, the prevalence of the studied IHD RFs turned out to be higher among males than females, except for the "elevated WC" RF (indicating abdominal obesity), whose prevalence was not significantly different between males (42%) and females (45%). As for the excess body weight in general, it was found to be 1.3-fold higher among males than among females.

While discussing this result, we should point out that obesity occurs more often among patients with early development of IHD and is an independent predictor of coronary atherosclerosis at a young age, as revealed in some studies. In particular, this pattern was demonstrated in a comparison of the prevalence of RFs among patients hospitalized with acute MI at age younger and older than 50, in a registry containing 1199 patients [15]. The link of obesity with atherosclerosis at a young age was demonstrated in a study on autopsies of 3 000 subjects aged 15–34 years who died of non-cardiological causes [16]. In the Framingham study, it was shown that the contribution of obesity to the development of IHD in middle-aged people may be as high as 23% of the cases among males and 15% of the cases among females [17].

In our study population, the prevalence of the analyzed IHD RFs (except for cigarette smoking) was found to be not different between the groups with and without IHD. The prevalence of smokers was 1.7-fold higher in the no-IHD group than in the group with IHD. Our multivariate logistical regression analysis also uncovered an inverse association of smoking (independent of age, sex, and other analyzed RFs) with the relative risk of definite IHD in the study population (25–44-year-olds in Novosibirsk). We explain this finding, which contradicts known classical data, by the insufficient number of IHD cases (a total of 49 subjects, 18 males and 31 females) in our study.

Indeed, all the data from the international literature point to a rather significant role of smoking in IHD development and complications. It is believed that smoking is the most prevalent RF of early IHD. According to Cole J.H. and coworkers, the number of smokers among IHD patients under 45 years ranges from 60%to 90%, whereas among patients older than 45 years, from 24%to 56% [18].

In a meta-analysis including 14 international randomized studies on IHD, among76716 MI patients with ST segment elevation, 35527 patients with unstable angina pectoris/MI without ST segment elevation, and 10215 patients who underwent percutaneous coronary interventions, researchers analyzed the prevalence of 4 RFs (smoking, diabetes mellitus, AH, and hyperlipidemia) depending on sex and age. In the majority of younger patients, at least one RF was noted, with the most frequent one being smoking: 72% frequency among subjects younger than 45 years, both in males and in females [8].

In a study on a registry intended for observation of 892 patients with acute MI with ST segment elevation who underwent their first percutaneous coronary intervention, there were 78% of smokers among the patients aged 18 to 34 years, and 23% of smokers in the whole study population; the percentage of smokers decreased with the increasing age at MI diagnosis [19].

Kafadar D. and colleagues have examined 235 patients with coronary-angiography–verified coronary atherosclerosis. Active smokers showed the highest mean levels of TGs in the blood, whereas nonsmokers were reported to have the highest mean HDL-C concentrations [20].

Christus T. and coworkers have examined 200 males younger than 35 years with IHD diagnosed by coronary angiography and concluded that the main RFin this population is cigarette smoking [5].

As compared with the total number of publications about the adverse impact of cigarette smoking on the development of CVDs in the world literature, there are only a few papers where the results defy the traditional findings, for example, the study by Li G. and colleagues [21]. They examined a Chinese population aged 20–80 years (1248 subjects) and concluded that sex- and age-adjusted BP is lower in smokers than in nonsmokers or former smokers. There was no significant dose-dependent influence of smoking on sex- and age-adjusted BP. Furthermore, smoking cessation was significantly associated with a higher risk of hypertension.

Because none of the RFs analyzed by us, except for smoking, manifested an apparent association with the relative risk of IHD, and because the cigarette smoking analysis yielded the “paradoxical” result, we then investigated the link of IHD with socioeconomic factors whose influence on IHD development has been actively discussed in the last decades [22].

We performed a multivariate logistical regression analysis of the socioeconomic factors in relation to the risk of definite IHD in our study population (25–44-year-olds in Novosibirsk) and in its male and female subpopulations. Statistically significant results were obtained only in the male subpopulation. We identified age-independent associations of the occupation type and marital status (which correlated with smoking), with the relative risk of early IHD in males aged 25–44 years. It was found that among divorced males aged 25–44 years, the probability of the presence of early IHD is 5-fold higher, whereas among males occupationally engaged in heavy manual labor, it is 3.5-fold higher.

Our results are consistent with data from other studies. For example, the influence of marital status on the frequency of CVDs and prognosis after CVD was assessed in a meta-analysis of 34 studies involving more than 2 million participants. In comparison with married participants, the absence of marriage (never married, divorced, or widowed) correlated with a higher risk of CVDs, IHD, death from IHD, and death from stroke. Divorce was associated with a higher risk of IHD both in males and in females [23].

Leisure time physical activity is a widely recognized protective factor against cardiovascular mortality. Participants of a prospective epidemiological study on MI (PRIME; n = 9758; age 50 to 59 years), who did not have IHD at the beginning of the study, were observed for 5 years: the researchers registered 167 cases of severe IHD and 154 cases of tension angina pectoris. A beneficial effect of leisure time physical activity was noted among the subjects who did not report high-intensity activity, in France and Northern Ireland. By contrast, increasing the level of leisure time physical activity was associated with a higher risk of tension angina pectoris in both countries [24].

In the CORDIS study, investigators analyzed the influence of leisure time physical activity and of heavy physical activity associated with one's job (occupational heavy manual labor) on cardiovascular mortality among males (4819 subjects) during 22-year prospective observation. It was occupational heavy manual labor that posed the highest risk of death, including IHD-related mortality. Those authors concluded that heavy manual labor at one's job is bad for health [25].

Thus, our data suggest that among 25–44-year-old males in Novosibirsk, the relative risk of IHD (namely, early IHD, manifesting itself before 45 years of age) directly correlates with occupational heavy manual labor and unfavorable marital status but is inversely associated with smoking. In our opinion, these results undoubtedly require further research.

Conclusion

Early detection of IHD, especially early IHD, presenting before 45 years of age, is highly important for programs on secondary prevention of IHD. Nevertheless, earlier detection of IHD RFs is even more important for programs on the primary prevention of this disease. In a young population at 25–44 years of age, owing to the high employment rate at this age, there is insufficient self-rating of health and not enough effort aimed at the risk assessment and prevention of IHD. Consequently, it is crucial to motivate the young population to undergo timely screening (medical exam) to prevent CVDs and their RFs, i.e., mostly conventional RFs, such as the social ones.

Abbreviations

AH: arterial hypertension

BMI: body mass index

BP: arterial blood pressure

CI: confidence interval

CVD: cardiovascular disease

ECG: electrocardiogram

HDL-C: high-density lipoprotein cholesterol

IHD: ischemic heart disease

LDL-C: low-density lipoprotein cholesterol

MC: Minnesota Code

MI: myocardial infarction

non-HDL-C: non–high-density lipoprotein cholesterol

OR: odds ratio

RF: risk factor

TG: triglyceride

WC: waist circumference

WHO: World Health Organization

Declarations

Ethics approval and consent to participate

The study protocol was approved by the local Ethics Committee of the Institute of Internal and Preventive Medicine (a branch of the Institute of Cytology and Genetics, the Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia). All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent to the medical examination and analysis of personal data was obtained from each patient.

Consent for publication

All the authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval to the version to be published.

Availability of data and material

The datasets before and after analysis in this study are available from the corresponding author on reasonable request.

Funding

The medical-examination–based screening was performed within the framework of a government-funded research topic in State Assignment No. AAAA-A17-117112850280-2. The biochemical and functional analyses were financially supported by a Russian Federation President grant for leading scientific schools, No. НШ-2595.2020.7.

Competing interests

The authors declare that they have no conflicts of interest associated with publication of this article.

Authors' contributions

Yuliya I. Ragino: study conception and design and critical revision of the manuscript

Natalya A. Kuzminykh: wrote the main manuscript text, collection of the clinical data, drafting of the manuscript

Liliia V. Shcherbakova: statistical analysis

Viktoriya S. Shramko: analysis and interpretation of the biochemical data, participation in discussion

Diana V. Denisova: collection of the clinical data, revision of the manuscript and participation in discussion

Acknowledgements

The English language was corrected and certified by shevchuk-editing.com. The authors thank the patients for participation in this study.

References

1. Organization WH. WHO Mortality Database. WHO. http://www.who.int/healthinfo/ mortality_data / en /. Published 2015. Accessed May 25, 2016.
2. Townsend N., Wilson L., Bhatnagar P. et al. Cardiovascular disease in Europe: Epidemiological update 2016. Eur Heart J 2016; 37 (42): 3232–3245. DOI:10.1093/eurheartj/ehw334.

3. Piepoli M.F., Hoes A.W., Agewall S. et al. European Guidelines on Cardiovascular Disease Prevention in Clinical Practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). European Heart Journal 2016; 37: 2315–2381. DOI:10.1093/eurheartj/ehw106.
4. Carr J.J., Jacobs D.R., Terry J.G. et al. Association of coronary artery calcium in adults aged 32 to 46 years with incident coronary heart disease and death. JAMA Cardiol 2017; 2 (4): 391–399. DOI:10.1001/jamacardio.2016.5493.
5. Christus T., Shukkur A.M., Rashdan I. et al. Coronary Artery Disease in Patients Aged 35 or less – A Different Beast? Heart Views 2011; 12 (1): 7–11. DOI:10.4103/1995- 705X.81550.
6. Wilmot K.A., O'Flaherty M., Capewell S. et al. Coronary heart disease mortality declines in the United States from 1979 through 2011: Evidence for stagnation in young adults, especially women. Circulation 2015; 132 (11): 997–1002. DOI:10.1161/CIRCULATIONAHA. 115.015293.
7. Otaki Y., Gransar H., Berman D.S. et al. Impact of family history of coronary artery disease in young individuals (from the CONFIRM registry). Am J Cardiol 2013; 111 (8): 1081–1086. DOI:10.1016 /j.amjcard. 2012.12.042.
8. Khot U.N., Khot M.B., Bajzer C.T. et al. Prevalence of conventional risk factors in patients with coronary heart disease. JAMA 2003; 290 (7): 898–904. DOI:10.1001/jama.290.7.898.
9. Celik T., Iyisoy A. Premature coronary artery disease in young patients: An uncommon but growing entity. Int J Cardiol 2010; 144 (1): 131–132. DOI:10.1016/j.ijcard.2008.12.150.
10. Authors/Task Force Members; ESC Committee for Practice Guidelines (CPG); ESC National Cardiac Societies. 2019 ESC/EASguidelines for the management of dyslipidaemias: Lipidmodification to reducecardiovascularrisk. Atherosclerosis 2019; 290: 140-205. DOI:10.1016/j.atherosclerosis.2019.08.014.
11. MONICA, monograph, and multimedia sourcebook: World's largest study of heart disease, stroke, risk factors, and population trends 1979-2002 / edited by Hugh Tunstall-Pedoe; prepared by Hugh Tunstall-Pedoe (et al.) with 64 other contributors for the WHO MONICA Project. - Geneva : WHO, cop. 2003. - xix, 244 p.
12. Malyutina S., Bobak M., Simonova G., et al. Education, marital status, and total and cardiovascular mortality in Novosibirsk, Russia: a prospective cohort study. Ann Epidemiol 2004; 14 (4): 244-249. DOI:1016/S1047-2797(03)00133-9.
13. Vikhireva O., Pajak A., Broda G., et al. SCORE performance in Central and Eastern Europe and former Soviet Union: MONICA and HAPIEE results. Eur Heart J 2014; 35 (9): 571-577. DOI:10.1093/eurheartj/eht189.
14. Arts J., Fernandez M.L., Lofgren I.E. Coronary heart disease risk factors in college students. Adv Nutr 2014; 5 (2): 177-187. DOI:10.3945/an.113.005447.

15. Matsis K., Holley A., Al-Sinan A. et al. Differing Clinical Characteristics Between Young and Older Patients Presenting with Myocardial Infarction. Hear Lung Circ 2017; 26 (6): 566–571. DOI:10.1016/j.hlc. 2016.09.007.
16. McGill H.C., McMahan C.A., Herderick E.E. et al. Obesity accelerates the progression of coronary atherosclerosis in young men. Circulation 2002; 105 (23): 2712–2718. DOI:10.1161/01.CIR.0000018121.67607.CE.
17. Turpie A.G., Bauer K.A., Eriksson B.I., et al. Overweight and obesity as determinants of cardiovascular risk: The Framingham experience. Arch Intern Med 2002; 162 (16): 1867–1872. DOI:10.1001/archinte.162.16.1867.
18. Cole J.H., Miller J.I., Sperling L.S., et al. Long-term follow-up of coronary artery disease presenting in young adults. J Am Coll Cardiol 2003; 41 (4): 521–528. DOI:10.1016/S0735–1097(02) 02862–0.
19. Larsen G.K., Seth M., Gurm H.S. The ongoing importance of smoking as a powerful risk factor for ST-segment elevation myocardial infarction in young patients. JAMA Intern Med 2013; 173 (13): 1261–1262. DOI:10.1001/jamainternmed.2013.6075.
20. Kafadar D., Dogan F.G., Oren M.M., et al. Association of sociodemographic profile, dyslipidemias, and obesity in smoker, former smoker, and nonsmoker patients with coronary artery disease. Niger J Clin 2018; 21 (9): 1190-1197. DOI:10.4103/njcp.njcp_171_17.
21. Li G., Wang H., Wang K., et al. The association between smoking and blood pressure in men: a cross-sectional study. BMC Public Health 2017; 17 (1): 797. DOI:10.1186/s12889- 017-4802-x.
22. Albus C. Psychological and socialfactors in coronary heart disease. Ann Med 2010; 42 (7): 487-494. DOI:10.3109/07853890.2010.515605.
23. Wong C.W., Kwok C.S., Narain A., et al. Marital status and risk of cardiovascular diseases: a systematic review and meta-analysis. Heart. 2018; 104 (23): 1937-1948. DOI:10.1136/heartjnl-2018-313005.
24. Wagner A., Simon C., Evans A., et al. Physical activity and coronary event incidence in Northern Ireland and France: the Prospective Epidemiological Study of Myocardial Infarction (PRIME). Circulation 2002; 105 (19): 2247-2252. DOI:1161/01.cir.0000016345.58696.4f.
25. Harari G., Green M.S., Zelber -Sagi S. Combined association of occupational and leisure-time physical activity with all-cause and coronaryheartdisease mortality among a cohort of men followed-up for 22 years. Occup Environ Med 2015; 72 (9): 617-624. DOI:10.1136/oemed-2014-102613.