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LEADING ARTICLE

Association of CVD risk factors and probability of fatal cardiovascular events development with the amount of consumed alcohol in 42–44 years old patients

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Objective

To estimate cardiovascular disease (CVD) risk factors (RF) association and the probability of fatal cardiovascular events development with the amount of consumed alcohol in 42-44 years old males.

Materials and methods

This study is the part of 32-years long prospective cohort observation of males starting from the childhood. 303 (30,1%) males have been observed. Observation included: obtaining patient's and family history, information about RF, bad habits, blood pressure (BP) changes, anthropometric characteristics, blood lipid profile, C-reactive protein (CRP), ureic acid, glucose, and insulin levels in blood serum. Males have been classified into three categories depending on alcohol consumption: nondrinkers, moderate drinkers, heavy drinkers. Then the total risk of CVD for the next 10 years has been estimated.

Results

The majority of observed men consume alcohol relatively rarely but in the amount exceeding the safe levels. Linear correlation between the frequency of abdominal obesity, arterial hypertension (AH), elevated total cholesterol (TC) and low density lipids (LDL) cholesterol levels and the amount of consumed alcohol. Systolic blood pressure (SBP), diastolic blood pressure (DBP), TC, ApoA1, ureic acid and glucose in heavy and excessively drinking males were higher comparing with nondrinkers, and the difference in waist circumference (WC), high density lipids (HDL) cholesterol, LDL cholesterol, ApoB and HOMA-IR were observed only between nondrinkers and heavy drinkers. Heavy drinkers have the highest risk of CVD development. SBP impact on total risk is higher in heavy drinkers, and TC has stronger impact on total risk in moderate and heavy drinkers. The impact of smoking on total risk does not correlate with the amount of consumed alcohol. The probability of AH development in drinkers is 2,6 times higher than in nondrinkers.

Conclusion

The majority of males of 42–44 years consume alcohol, 40% of them consume dangerous for health amount of alcohol. The frequency of abdominal obesity, AH and atherogenic changes of blood lipid profile goes along with increased alcohol consumption. Alcohol has direct influence on SBP and DBP levels, TC, ApoA1, uric acid and glucose concentration. The value of total risk of CVD is mostly determined by other CVD RF like TC levels and smoking.

Keywords

Alcohol, middle-aged men, risk factors, cardiovascular diseases, total cardiovascular risk.

Excessive alcohol consumption is an important problem for the Russian federation and world population in general. Experts demonstrate increased alcohol consumption in all age groups starting from children and ending with older groups of able-bodied population. Beer and vodka forms of alcohol abuse become more spread, deviant behavior, somatic disorders and alcohol-dependent mortality become more common [1]. According with the study of World Health Organization "Global Status Report on Alcohol and Health", in 2014 per capita alcohol consumption in Russia reached 15,76 L in people above 15 years old [2]. This is one of the highest results in the world. According with the major cohort study, that had been performed in Russia in 2012, estimated number of deaths related to alcohol consumption was 231 900 (161100 for males and 70800 for females) per year and the number of years lost due to acquired disability (disability-adjusted life year, DALY index) was 13295000 (9625000 for males and 3 670 000 for females) [3].

33,4% of deaths related to alcohol consumption (6% of total amount of lethal cases in the world) are caused by cardiovascular diseases (CVD) and diabetes mellitus (DM) [4]. Impact of alcoholic beverages on cardiovascular mortality depends on two factors: amount of consumed alcohol and the pattern of alcohol consumption [5].

Excessive alcohol consumption has significant impact on several CVD risk factors (RF).Toxic doses of alcohol lead to essential hypertension development (EH), hypercholesterolemia, obesity (Ob), particularly in males, food behavior deviations, smoking [6–11].

Alcohol consumption in toxic doses is more typical for males than females. Percentage of lethal cases related to alcohol in the world between males is

7,6% of total death cases comparing with the 4% in females. Average total amount of consumed alcohol per capita measured as absolute alcohol volume between males and females in 2010 was >12,5 L and 8,9 L, respectively [12]. This difference can be considered significant.

At the same time, cardioprotective effects of alcohol in small amounts and their influence on antiatherogenic parameters of blood lipid spectrum are widely discussed in literature [13-15]. However the questions of impact of consumed alcohol amount on CVD RF and probability of fatal cardiovascular events (CVE) development in males still remain open.

The objective of this study was to estimate cardiovascular disease (CVD) risk factors (RF) association and the probability of fatal CVE development with the amount of consumed alcohol in 42-43 years old males.

Materials and methods

This study is the part of 32-years long prospective cohort observation of 1005 males starting from the childhood age (11-12 year). This study involved 303 males (30,1% of initial population sample).

This study has been performed according with the ethic regulations of Helsinki's Declaration and the National Standard of the Russian Federation "Good Clinical Practice (GCP)", State Standard R2379-2005.

This study included a survey according with the standard form (passport information, education, social position, personal and family history, information about physical activity (PA) and bad habits (smoking, alcohol consumption); triple blood pressure (BP) measurement, pulse estimation, body height (BH) and body weight (BW) estimation, abdominal skinfold (ASF), subscapular skinfold (SSF) and triceps skinfold (TSF) thickness, waist and thighs circumference (WC and ThC), total cholesterol (TC), high density lipids cholesterol (HDL Ch), triglycerides (TG), Apo-A1 and Apo-B lipoprotein (Apo-A1 and Apo-B, respectively), lipoprotein (a) (LPa), C-reactive protein (CRP), ureic acid (UA), glucose and insulin levels in blood serum. We used body mass index (BM) to estimate interrelation between BW and BH using the formula $BMI=BW(kg)/BH^2(m^2)$. Low density lipids cholesterol (LDL Ch) concentration was determined using formula LDL Ch=Ch – (HDL Ch+VLDL Ch), where VLDL Ch – very low density lipids cholesterol levels. TyG index was estimated using interrelation between TG (mg/dL) and glucose (mg/dL) concentration in blood serum. HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) index of insulin resistance was quantified using the following formula (Matthews D.R. and coauthors, 1985): HOMA-IR=fasting glucose levels (mmol/L)* fasting insulin levels (μU/mL)/22,5. All measurement were performed using standardized methods with regular quality control.

Arterial hypertension (AH) group included persons with BP levels ⩾ 140/90 mm Hg. BMI ⩾ 25 and 30 kg/m^2 was considered as eBW and Ob, respectively. The group of abdominal (central) Ob included persons with WC>94 cm. Categories of blood lipid spectrum were formed according with the classification presented in the third report of the group of experts of the National Cholesterol Education Program (NCEP) for detection, estimation and therapy of high Ch levels in adults – Adult Treatment Panel III (ATP III). We used International Physical Activity Questionnaires (IPAQ) to estimate PA of participants [16]. PA categories were formed according with the IPAQ guidelines [17]. Men who smoked at least one cigarette per day were considered smokers. All men independently on their attitude to alcohol were classified into three categories: the first group (n=59) – non-drinkers, the second group (n=126) – moderate drinkers (consuming not more than 84 g of conventional absolute alcohol per week); the third group (n=118) of heavy drinkers consuming >84 g of conventional absolute alcohol per week [18].

Estimation of total fatal CVE development risk during the next 10 years was performed according with the SCORE (Systematic Coronary Risk Evaluation) scale for countries with the high risk of CVD, that include Russia. Total risk of fatal CVE development was classified as low (<1%), moderate (1-5%) and high (>5%) [19].

We used average value and median as the measure of central trend to describe obtained results, and we took standard deviation and quartile deviation as the measure of variability. Kolmogorov-Smirnov test was used for distribution normality testing in order to select statistical data for further analysis. Evaluation of connection between CVD Rf and the amount of consumed alcohol was performed using Pearson's chi-squared test (χ^2) for linear trend. We used Z-test with Bonferroni's correction for multiple comparisons for paired comparisons of proportions. To estimate the dependence of studied characteristics on the levels of alcohol consumption we used Kruskal-Wallis ANOVA dispersion analysis. Paired group comparisons for variables with not-normal distribution were made using Mann-Whitney U test with Bonferroni's

p-value correction for multiple comparison. Critical level of significance was set up for 95% for all statistical parameters (p<0,05). To describe power and direction of correlation between characteristics we used gamma(γ) coefficient of Goodman-Kruskall (Goodman-Kruskall's gamma). The size of the effect of consumed alcohol levels on investigated characteristics was made using eta-squared (η^2) values for non-parametrical Kruskal-Wallis test [20]: η^2=[H/(n–1)], where H is the value of Kruskal-Wallis test, n – number of observations. The size of the effect of consumed alcohol levels was estimated using the criteria suggested by Cohen (Cohen, 1988): small (η^2 = 0.01); medium (η^2 = 0.06) and big (η^2 = 0.14) effect [21]. Relative risk of AH development in the group of persons consuming alcohol was evaluated using logistic regression analysis. We quantified the odds ratio (OR) with 95% confidence interval (CI) and included non-drinker (OR=1.0) in the group of comparison.

Statistical processing of results was performed using IBM SPSS Statistics (Version 23.0) software.

Results

This analysis includes the results of observation of 303 male participants aged 42-44 years. The majority of examined men were married with specialized secondary or higher education (Figure 1). 74.6% of men had children. Divorced men consumed higher amounts of alcohol — 201.7±47.9 g per week comparing with married ones — 118.8±13.5 g per week and single ones — 141.2±46.2 g per week (p=0.012).

General characteristic of examined population sample is present in the Table 1. Average value of BMI exceeded common eBW criteria and average WC was higher than abdominal Ob criteria. Value of ASF and SSF indicate the excess of subcutane-

Table 1. **General characteristic of examined male patients**

Characteristic	M ± SD
Age, years	42.9 ± 0.5
Length of alcohol consumption	24.6 ± 0.2
BMI, kg/m^2	27.6 ± 4.8
WC, cm	94.2 ± 13.3
WC/ThC	0.93 ± 0.08
WC/BH	0.53 ± 0.07
ASF (left), mm	29.9 ± 9.4
SSF (left), mm	25.1 ± 9.8
TSF (left), mm	14.4 ± 6.9
SBP, mm Hg	122 ± 15
DBP, mm Hg	82 ± 11
Pulse, beats per minute	74 ± 10
TC, mmol/L	5.7 ± 1.2
HDL Ch, mmol/L	1.0 ± 0.3
TG, mmol/L	1.4 ± 0.9
LDL Ch, mmol/L	4.1 ± 1.2
Apo-A1, mg/dL	163.6 ± 30.6
Apo-B, mg/dL	103.1 ± 25.3
LP (a), mg/dL	29.6 ± 42.8
CRP, mg/dL	3.9 ± 3.8
UA, mg/dL	6.4 ± 1.4
Glucose, mmol/L	5.2 ± 1.2
TyG-index	8.5 ± 0.6
Insulin, μU/mL	9.0 ± 5.8
HOMA-IR index	2.13 ± 1.58
Total risk of fatal CVE (SCORE), %	1.2 ± 0.7
SBP impact on total risk, %	2.7 ± 11.9
TC impact on total risk, %	47.6 ± 44.2
Smoking impact on total risk, %	33.7 ± 41.3
Frequency of compromised family history of coronary heart disease, n (%)	22 (7.3)
eBW frequency, n (%)	117 (38.6)
OB frequency (based on BMI), n (%)	87 (28.7)
Abdominal OB frequency (WC>94 cm), n (%)	138 (45.5)

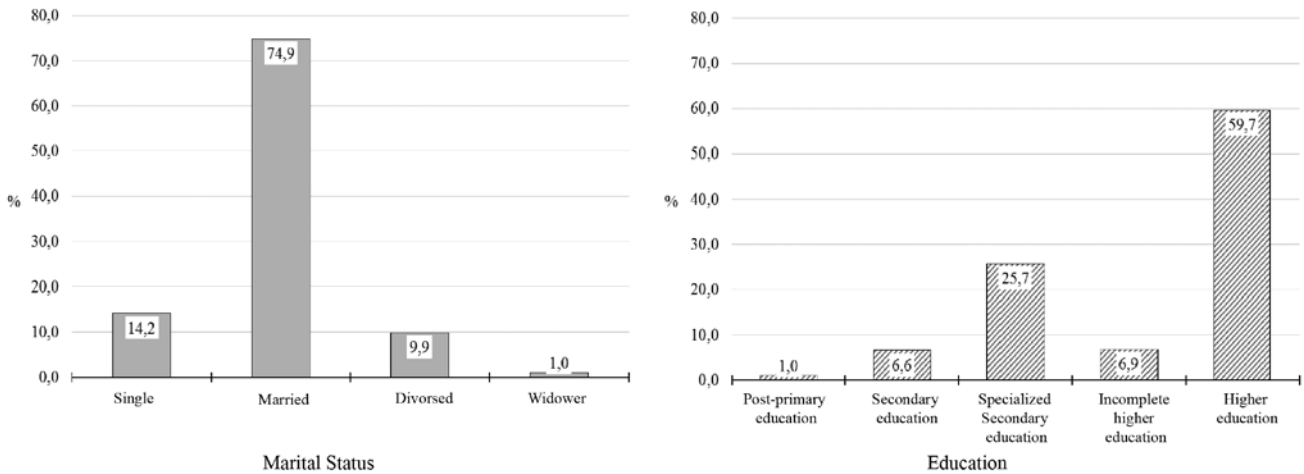

Figure 1. Marital status and education of patients

Table 1

Characteristic	M ± SD
Abdominal OB frequency (WC>102 cm), n (%)	87 (28.7)
AH frequency, n (%)	70 (23.1)
Hyper-TC frequency, n (%)	99 (32.7)
Hypo-HDL Ch frequency, n (%)	197 (65.0)
Hyper-TG frequency, n (%)	46 (15.2)
Hyper-LDL Ch frequency, n (%)	129 (42.6)
Smoking frequency, n (%)	128 (42.3)
Low PA frequency, n (%)	79 (26.1)

ous body fat deposits. 67.3% of examined men have eBW and Ob and more than the half of them have abdominal Ob. Average tC and LDL Ch levels reflect atherogenic trend of lipid blood spectrum. More than 40% of participants have dyslipoproteinemia (DLP). Average LP(a) levels in investigated population demonstrate prognostic potential corresponding to the low risk of CVD development and CRP levels in these males go along with high probability to develop CVD and their complications. 37.3% of male participants smoke regularly. 65% of examined people had ⩾2 RF. Average total risk of fatal CVE estimated with SCORE scale was moderate. TC and smoking have the biggest impact on total risk of CVE.

Almost all participants of this study, apart from the small exception, consumed alcohol with 30 days preceding this investigation (Table 2), mostly vodka and beer. The majority of them consumes alcohol enough rarely but in the amounts exceeding safe ones. Around 38,9% of people abuse alcohol (Figure 2).

Table 2. **Quantity and frequency of alcoholic beverages consumption by male patients during the last 30 days preceding the examination**

Characteristic	Value
Age of start of alcohol consumption, years; M (95% CI)	18.3 (15.0–24.0)
Did you consume alcoholic beverages during the last month, n (%):	
yes	246 (92.1)
not	21 (7.9)
Beer consumption frequency, n (%):	
every day	7 (3.7)
4 times for week	13 (6.8)
2 times for week	41 (21.6)
Once for week	42 (22.1)
2 times during last 30 days	34 (17.9)
Once during last 30 days	53 (27.9)
Total	190 (100.0)
Volume of beer normally consumed at once (mL), M (95% CI)	1025.7 (330.0–2500.0)
Volume of beer normally consumed per week (mL), M (95% CI)	1537.6 (116.7–5600.0)

Table 2

Characteristic	Value
Dry wine consumption frequency, n (%):	
every day	2 (1.5)
4 times for week	1 (0.7)
2 times for week	22 (16.1)
Once for week	26 (19.0)
2 times during last 30 days	28 (20.4)
Once during last 30 days	58 (42.3)
Total	137 (100.0)
Volume of dry wine normally consumed at once (mL), M (95% CI)	380.2 (100.0–750.0)
Volume of dry wine normally consumed per week (mL), M (95% CI)	692.5 (35.0–3733.3)
Fortified wine consumption frequency	
every day	0
4 times for week	0
2 times for week	1 (2.9)
Once for week	3 (8.8)
2 times during last 30 days	6 (17.6)
Once during last 30 days	24 (70.6)
Total	34 (100.0)
Volume of fortified wine normally consumed at once (mL), M (95% CI)	289.7 (50.0–1000.0)
Volume of fortified wine normally consumed per week (mL), M (95% CI)	113.9 (23.3–233.3)
Vodka consumption frequency	
every day	2 (1.0)
4 times for week	5 (2.5)
2 times for week	31 (15.7)
Once for week	37 (18.7)
2 times during last 30 days	53 (26.8)
Once during last 30 days	70 (35.4)
Total	208 (100.0)
Volume of vodka normally consumed at once (mL), M (95% CI)	263.6 (50.0–500.0)
Volume of vodka normally consumed per week (mL), M (95% CI)	242.1 (23.3–933.3)
Other alcoholic beverages consumption frequency	
every day	7 (3.7)
4 times for week	13 (6.8)
2 times for week	41 (21.6)
Once for week	42 (22.1)
2 times during last 30 days	34 (17.9)
Once during last 30 days	53 (27.9)
Total	190 (100.0)
Volume of other alcoholic beverages normally consumed at once (mL), M (95% CI)	1025.7 (330.0–2500.0)
Total volume of alcohol (in terms of absolute ethanol) consumed per week (g), M (95% CI)	162.6 (10.4–626.4)
Total volume of alcohol (in terms of absolute ethanol) consumed per week (g), (units UK), M (95% CI)	20.3 (1.3–78.3)
Total volume of alcohol (in terms of absolute ethanol) consumed per week (g), (units USA), M (95% CI)	11.6 (0.7–44.7)

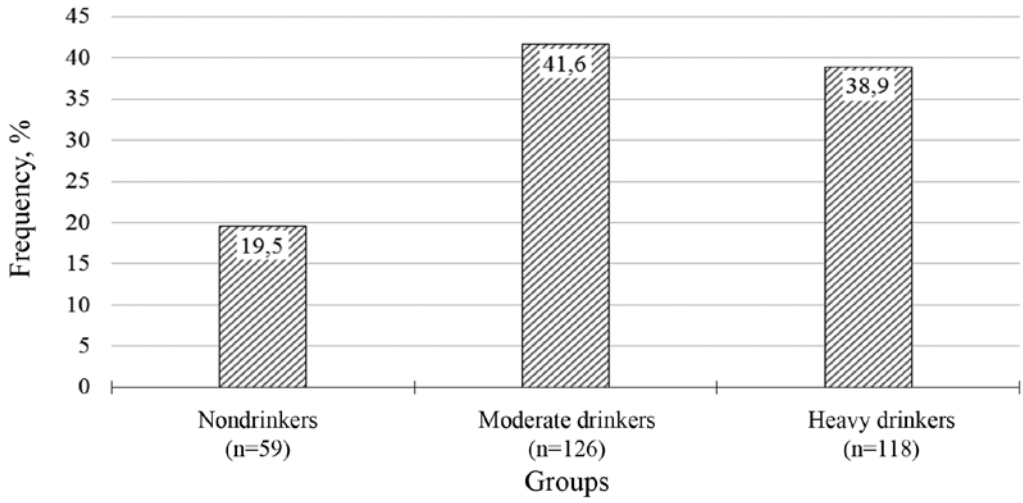

Figure 2. Distribution of patients according with the amount of consumed alcohol (n=303)

Results of χ^2 Pearson's test for linear trend (Table 3) evidence the presence of linear correlation between the frequency of abdominal Ob, AH, hypercholesterolemia (hyper-Ch), hyper-LDL-Ch and the levels of alcohol consumption. The percentage of people with abdominal Ob, AH, hyper-Ch and hyper-LDL-Ch goes up with the increase of alcohol consumption. Abdominal Ob, AH and hyper-Ch are more frequent in the group of heavy drinkers comparing with non-drinkers and/or moderate drinkers. There is a direct correlation between the increase of frequency of mentioned RF and the increase of consumed alcohol amount, it is proved by highly significant coefficients of Goodman-Kruskall' gamma rank correlation. The frequency of hyper-LDL-Ch is connected with increased alcohol consumption levels, but this correlation is weaker comparing with abdominal Ob, AH and hyper-Ch. Unidirectional trend between the frequency of smoking and amount of consumed alcohol was not found. The biggest number of smokers was present in the groups of moderate drinkers.

Table 3. **CVD RF frequency in groups of male patients with different levels of alcohol consumption**

RF	Groups			γ Goodman-Kruskal	χ^2 for linear trend
	Non-drinkers (1)	Moderate drinkers (2)	Heavy drinkers (3)		
Frequency of compromised family history of coronary heart disease, n (%)	4 (6.8)	9 (7.1)	9 (7.6)	0.040 p=0.829	χ^2=0.046 p=0.830
eBW, n (%)	17 (28.8)	51 (40.5)	49 (41.5)	0.138 p=0.158	χ^2=2.159 p=0.142
OB frequency (based on BMI), n (%)	16 (27.1)	33 (26.2)	38 (32.2)	0.098 p=0.360	χ^2=0.753 p=0.385
Abdominal OB frequency (WC>94 cm), n (%)	22 (37.3)	50 (39.7)	66 (55.9) [2]	0.264 p=0.005	χ^2=7.124 p=0.008
AH, n (%)	7 (11.9)	27 (21.4)	36 (30.5) [1]	0.325 P=0.003	χ^2=8.007 p=0.005
Hyper-TC, n (%)	9 (15.3)	41 (32.5) [1]	49 (41.5) [1]	0.345 p<0.001	χ^2=11.756 p=0.001
Hypo-HDL Ch, n (%)	46 (78.0)	78 (61.9)	73 (61.9)	−0.175 p=0.075	χ^2=3.417 p=0.065
Hyper-TG, n (%)	4 (6.8)	22 (17.5)	20 (16.9)	0.194 p=0.127	χ^2=2.320 p=0.128
Hyper-LDL Ch, n (%)	19 (32.2)	52 (41.3)	58 (49.2)	0.211 p=0.028	χ^2=4.746 p=0.029
Smoking, n (%)	30 (50.8) [2]	37 (29.4)	61 (51.7) [2]	0.121 p=0.218	χ^2=0.911 p=0.340
Low PA, n (%)	15 (25.4)	26 (20.6)	38 (32.2)	0.161 p=0.151	χ^2=1.813 p=0.178

Comment: Results of multiple comparison are based on two-sided tests with significance level of 0.05. For each significant pair number of group with smaller percentage of column is put into the group with higher percentage of column. For each pair comparison p-values were corrected according with Bonferroni method. Size of alcohol consumption levels' effect: a — big, b — medium, c — small.

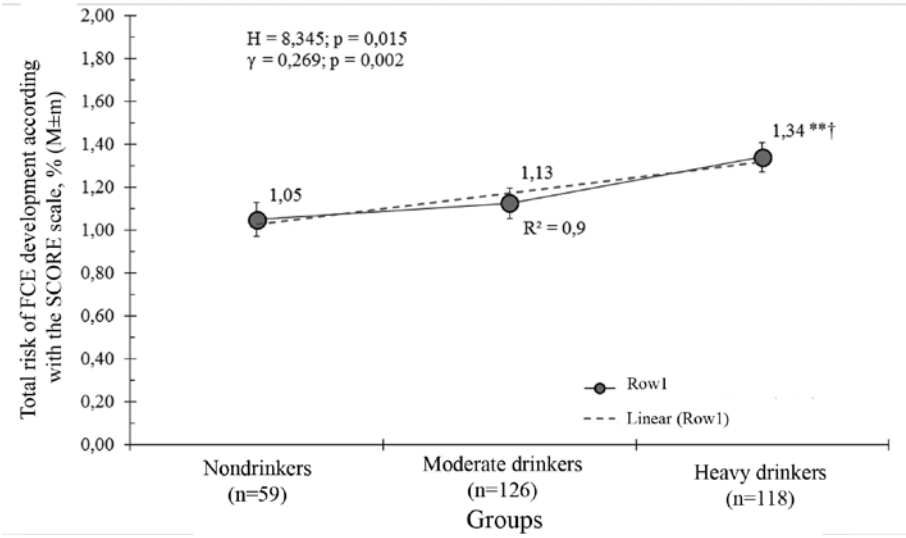

Figure 3. Total risk of FCE development during next 10 years in groups of male patients with different levels of alcohol consumption
Comment: R2 – coefficient of approximation significance, ** - p=0,008 vs the group of non-drinkers; † - p=0,017 vs the group of moderate drinkers; H – Kruskal-Wallis test; g – Goodman and Kruskal's rank correlation coefficient; paired comparisons have been performed using Mann-Whitney U-test (only the differences corresponding with the new critical level of significance corrected with the number of compared pairs 0,05/3=0,017 are shown).

Alcohol consumption length has the same duration independently on the levels of consumed alcohol. During analysis we paid attention not only on the fact of existence of differences between several groups, but also on the direction of changes in average RF levels (increase or decrease) moving from one group to another. Non-parametrical dispersion analysis (Kruskal-Wallis test) allowed detecting statistically highly significant differences of systolic BP (SBP), diastolic BP (DBP), TC, Apo-A1, UA, glucose, WC, HDL Ch, LDL Ch, Apo-B, HOMA-IR levels between the groups that proved the influence of the factor (in this case – the level of alcohol consumption) on dependent variables (mentioned above). At the same time we identified the growth of all mentioned characteristics' medians moving from the group of non-drinkers to the groups with the increased levels of alcohol consumption. Paired comparison revealed that SBP, DBP, TC, Apo-A1, UA and glucose levels in the groups of moderate and heavy drinkers were significantly higher than in the group of non-drinkers, and statistically significant differences in TC, HDL Ch, LDL Ch, ApoB and HOMA-IR existed only between the groups of non-drinkers and heavy drinkers. Statistically significant positive Goodman-Kruskal gammas also demonstrate the contingency of the majority of studied characteristics presented in the Table 4, excluding BH, ThC, pulse, LP(a) and CRP, with alcohol consumption levels. Alcohol influences many parameters listed in the Table 4, but alcohol have the biggest effect of moderate intensity on SBP, glucose and UA levels in blood.

Also the results of Kruskal-Wallis test demonstrate (Figure 3) that there are the differences of the value of total risk of fatal CVE between the groups ordered according with the increase of alcohol consumption levels. The highest total risk of fatal CVE development was present in the group of heavy drinkers comparing with the groups of non-drinkers and moderate drinkers. Linear trend line describes well enough the relation between total risk of fatal CVE and the levels of alcohol consumption. R^2 value = 0.9 indicates that the curve corresponds well with the obtained data. The higher probability of fatal CVE development in men with alcohol abuse comparing with non-drinkers and moderate drinkers can be proved with statistically significant Goodman-Kruskal gamma rank correlation coefficient. SBP impact on total risk of fatal CVE (Figure 4) is higher in the group of heavy drinkers comparing with non-drinkers and moderate drinkers, and the impact of TC on total CVE risk is higher in the groups of moderate and heavy drinkers comparing with non-drinkers, so it is not connected with the amount of consumed alcohol. The probability of AH development in male subjects consuming alcohol is 2,6 times higher than in non-drinkers (OR=2.6; 95% CI 1.1-5.9; p=0.029).

Discussion

In our study daily and weekly amount of consumed alcohol goes beyond the standard safe quantities of all alcoholic beverages [22-24]. Obtained results go along with the previously published data demonstrating that Russia is characterized with prevailed intake

Table 4. **Statistical average values of investigated characteristics in groups of male patients with different levels of alcohol consumption**

Characteristic	Statistical parameters	Groups			Gamma correlation	Kruskal-Wallis test	Multiple comparisons *
		Non-drinkers	Moderate drinkers	Heavy drinkers			
		(1)	(2)	(3)			
Age, years	M (SD)	43.1 (0.4)	42.9 (0.5)	42.9 (0.5)	— 0.109; p=0.041	H=8.204; p=0.017	p_{1-2}=0.009; p_{1-3}=0.009
	Me [25%-75%]	43.0 [42.8–43.3]	42.9 [42.6–43.2]	42.8 [42.6–43.2]			
Length of alcohol consumption	M (SD)	—	24.6 (3.4)	24.6 (2.8)	— 0.056; p=0.452	H=0.563; p=0.453	
	Me [25%-75%]	—	25.2 [23.4–26.6]	24.9 [23.0–26.4]			
BMI, kg/m^2	M (SD)	26.8 (5.0)	27.5 (4.7)	28.2 (4.7)	0.117; p=0.042	H=4.314; p=0.116	
	Me [25%-75%]	25.7 [23.5–31.6]	27.1 [24.0–30.2]	27.5 [24.8–31.3]			
WC, cm	M (SD)	91.9 (13.7)	93.2 (13.2)	96.5 (12.9)	0.148; p=0.010	H=6.806; [c] p=0.033	
	Me [25%-75%]	88.0 [83.0–106.5]	92.0 [84.0–102.0]	96.0 [87.0–104.0]			
WC/ThC	M (SD)	0.92 (0.08)	0.92 (0.09)	0.94 (0.07)	0.142; p=0.009	H=6.795; [c] p=0.033	p_{1-3}=0.016
	Me [25%-75%]	0.91 [0.86–0.97]	0.91 [0.87–0.99]	0.94 [0.89–1.0]			
WC/BH	M (SD)	0.51 (0.08)	0.52 (0.07)	0.54 (0.07)	0.149; p=0.008	H=6.996; [c] p=0.030	p_{1-3}=0.012
	Me [25%-75%]	0.50 [0.45–0.55]	0.52 [0.47–0.57]	0.54 [0.48–0.58]			
ASF, mm	M (SD)	28.3 (9.4)	29.2 (9.4)	31.4 (9.1)	0.144; p=0.012	H=6.290; [c] p=0.043	
	Me [25%-75%]	30.0 [20.6–37.0]	30.2 [23.0–38.4]	33.6 [26.0–40.0]			
SSF, mm	M (SD)	22.9 (10.0)	25.4 (9.7)	26.0 (9.7)	0.100; p=0.081	H=4.084; p=0.130	
	Me [25%-75%]	22.1 [14.3–29.7]	25.4 [17.4–32.1]	26.8 [18.4–33.7]			
TSF, mm	M (SD)	13.2 (6.8)	14.6 (6.9)	14.8 (6.9)	0.083; p=0.140	H=3.628; p=0.163	
	Me [25%-75%]	11.7 [8.0–17.1]	13.9 [10.0–17.8]	13.1 [10.3–18.0]			
SBP, mm Hg.	M (SD)	117 (12)	120 (14)	127 (16)	0.250; p<0.001	H=19.930; [b] p<0.001	p_{1-3}<0.001; p_{1-3}=0.001;
	Me [25%-75%]	117 [110.0–122.0]	119 [111.0–127.0]	124 [116.0–136.0]			
DBP, mm Hg.	M (SD)	79 (9)	81 (11)	85 (12)	0.204; p<0.001	H=13.737; [c] p=0.001	p_{1-3}<0.001; p_{1-3}=0.003;
	Me [25%-75%]	78 [74.0–84.0]	79 [73.0–87.0]	82 [77.0–91.0]			
Pulse, beats per minute	M (SD)	75 (9)	73 (10)	75 (10)	0.036; p=0.533	H=2.934; p=0.231	
	Me [25%-75%]	74 [68.0–88.0]	72 [68.0–80.0]	74 [68.0–82.0]			
TC, mmol/L	M (SD)	5.2 (1.0)	5.7 (1.1)	6.0 (1.4)	0.227; p<0.001	H=16.932; [c] p<0.001	p_{1-3}<0.001
	Me [25%-75%]	5.2 [4.4–5.7]	5.7 [4.8–6.5]	5.8 [5.1–6.7]			
HDL Ch, mmol/L	M (SD)	0.9 (0.3)	1.0 (0.3)	1.0 (0.3)	0.134; p=0.017	H=8.006; [c] p=0.018	p_{1-3}=0.006
	Me [25%-75%]	0.9 [0.7–1.0]	0.9 [0.8–1.2]	0.9 [0.8–1.2]			
LDL Ch, mmol/L	M (SD)	3.8 (1.0)	4.0 (1.1)	4.3 (1.3)	0.155; p=0.005	H=7.607; [c] p=0.022	p_{1-3}=0.010
	Me [25%-75%]	3.7 [3.1–4.4]	4.1 [3.3–4.7]	4.1 [3.4–5.1]			
TG, mmol/L	M (SD)	1.2 (0.7)	1.5 (1.0)	1.5 (1.0)	0.113; p=0.027	H=4.352; p=0.113	
	Me [25%-75%]	1.1 [0.8–1.5]	1.2 [0.7–1.9]	1.3 [0.9–1.7]			
Apo-A1, mg/dL	M (SD)	152.0 (22.4)	161.8 (26.6)	171.3 (35.8)	0.222; p<0.001	H=16.096; [c] p<0.001	p_{1-3}<0.001
	Me [25%-75%]	149.0 [136.0–163.0]	157.5 [143.0–178.0]	167.0 [149.0–190.2]			
Apo-B, mg/dL	M (SD)	98.8 (25.7)	100.9 (25.3)	107.7 (24.7)	0.166; p=0.002	H=9.094; [c] p=0.011	p_{1-3}=0.007; p_{1-3}=0.017;
	Me [25%-75%]	95.3 [83.0–111.0]	97.0 [84.8–116.0]	109.0 [91.0–124.3]			
LP (a), mg/dL	M (SD)	24.9 (35.1)	22.8 (32.7)	39.0 (53.0)	0.049; p=0.400	H=1.358; p=0.507	
	Me [25%-75%]	9.2 [5.3–21.9]	9.5 [5.4–21.4]	10.1 [4.9–64.1]			
CRP, mg/L	M (SD)	3.4 (3.2)	3.8 (3.7)	4.2 (4.1)	0.104; p=0.078	H=3.488; p=0.175	
	Me [25%-75%]	2.1 [1.6–4.8]	2.6 [1.9–4.2]	3.0 [2.1–4.5]			
UA, mg/dL	M (SD)	5.9 (1.2)	6.3 (1.4)	6.8 (1.3)	0.248; p<0.001	H=18.838; [b] p<0.001	p_{1-3}<0.001; p_{1-3}=0.003;
	Me [25%-75%]	5.9 [5.0–6.6]	6.1 [5.5–7.1]	6.8 [6.0–7.6]			
Glucose, mmol/L	M (SD)	4.8 (0.4)	5.2 (1.4)	5.4 (1.2)	0.305; p<0.001	H=27.166; [b] p<0.001	p_{1-3}<0.001; p_{1-3}=0.001;
	Me [25%-75%]	4.8 [4.6–5.2]	4.9 [4.7–5.3]	5.2 [4.9–5.7]			
TyG-index	M (SD)	8.3 (0.5)	8.5 (0.7)	8.6 (0.6)	0.161; p=0.001	H=8.672; [c] p=0.013	p_{1-3}=0.003
	Me [25%-75%]	8.4 [8.0–8.6]	8.5 [8.0–9.0]	8.6 [8.2–8.9]			
Insulin, μE/mL	M (SD)	8.2 (4.8)	8.6 (5.1)	9.9 (6.8)	0.118; p=0.039	H=4.296; p=0.117	
	Me [25%-75%]	6.9 [5.0–10.6]	7.2 [5.5–10.4]	8.1 [5.7–11.7]			
HOMA-IR	M (SD)	1.77 (1.11)	2.04 (1.39)	2.41 (1.91)	0.160; p=0.004	H=8.061; [c] p=0.018	p_{1-3}=0.008
	Me [25%-75%]	1.46 [1.05–2.17]	1.56 [1.16–2.50]	1.89 [1.37–2.71]			

Comment: * — Paired comparison was performed using Mann-Whitney test with p-values correction for multiple comparisons using Bonferroni method. Results of multiple comparison are based on two-sided tests with the new critical level of significance: 0.05/3=0.017. Size of alcohol consumption levels' effect: a — big, b — medium, c— small.

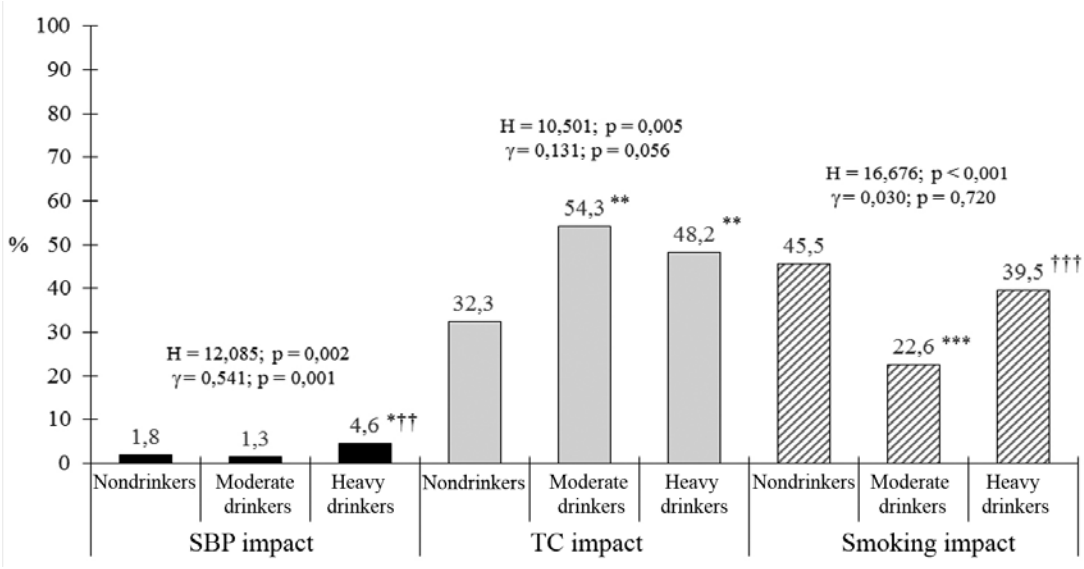

Figure 4. SBP, TC and smoking impact on total risk of FCE in groups of male patients with different levels of alcohol consumption. Comment: * - p=0,015 vs the group of non-drinkers; ** - p<0,01 vs the group of non-drinkers; *** - p<0,001 vs the group of non-drinkers; †† - p<0,01 vs the group of moderate drinkers; ††† - p<0,001 vs the group of moderate drinkers; H – Kruskal-Wallis test; g – Goodman and Kruskal's rank correlation coefficient; paired comparisons have been performed using Mann-Whitney U-test (only the differences corresponding with the new critical level of significance corrected with the number of compared pairs 0,05/3=0,017 are shown).

of strong alcohol drinks and beer – rarely but in big quantities [23, 24]. This fact is reflected in the results of big prospective study that had been performed in Russia during the last decade. It demonstrated that the major cause of premature death of adult RF population in the category of mortality due to external causes is the excessive alcohol consumption, vodka in particular [25].

It is interesting to mention the fact that the group of moderate drinkers in our study has the biggest number of smokers and the smallest levels of PA. Other works demonstrated that smoking becomes more intense and frequent according with the increase of amount of consumed alcohol [7]. This fact should be studied more precisely.

There is the correlation of AH frequency and hyper-Ch with alcohol consumption levels. These results are proved with international studies. The only difference is related to the fact, that several studies pointed out the positive influence of regular intake of small amounts of alcohol on TG and TC levels and that these works did not demonstrate the relation between DLP and amount of consumed alcohol drinks [6, 7, 15, 26].

Numerous studies demonstrate that there is the strong direct correlation between the patterns of alcohol consumption with WC and Ob, and this linkage is present particularly in males. The strongest correlation was identified for beer and strong alcohol drinks, whereas this correlation with wine has not been identified. There are some contradictory results demonstrating how different doses of alcohol influence the characteristics of carbohydrate metabolism, metabolic syndrome and DM 2 type development. The majority of the researchers agree that high doses of alcohol increase basal and postprandial glucose and insulin levels and also UA concentration, unlike the lower doses which can prevent DM 2 type development [7, 8, 27-29].

Impact of alcohol consumption on AH development is widely discussed in scientific literature. All works with no exception demonstrate correlation between AH and the mode of alcohol drinks consumption. Systematic alcohol drinks consumption in toxic doses causes the change of metabolic processes occurring in liver and oxidative stress that triggers a complicated cascade of reactions leading to liver cirrhosis, pancreatitis and HB. In particular, it is typical for young men [9-11, 30-32).

Talking about total risk of fatal CVE development, the majority of studies indicate that heavy drinkers have higher risk of CVD and non-infection diseases related mortality comparing with non-drinkers and moderate drinkers [5, 33-38]. This risk goes up along with the increase of consumed alcohol drinks amount, and hard periodic drinking does not increase total mortality, but it influences just the mortality due to alcohol-related causes and just in males [5] Excessive alcohol consumption influences mortality in males aged 70-89 years [34]. More than that, reduction of alcohol consumption by 18g of absolute ethanol per day allows decreasing mortality rate by 43%, and the higher was the initial amount of alcohol

consumption the more effective and useful for mortality rate reduction would be the effect of decreased alcoholic beverages intake [35,37].

Some studies demonstrate also the threshold amount of alcohol consumed per day (24 g) after exceeding which mortality risk starts to increase [18]. It is worth to mention that there are the studies that suggest that heavy drinkers have less mortality rate comparing with non-drinkers [38]. In our population average total risk of fatal CVE development increases along with the increase of amount of consumed alcohol drinks (from 1,1 to 1,4%). This risk had the smallest value in the group of non-drinkers and the highest value in the group of heavy drinkers (Figure 3).

During the last 30 years the question of cardioprotective effect of regular intake of alcohol in small amounts is widely discussed in literature. Numerous studies demonstrated inverse relation between moderate alcohol beverages consumption and the risk of fatal CVE development [5, 13-15, 36, 39-41]. In this study we identified also lower risk of fatal CVE (Figure 3) in the group of moderate drinkers comparing with the group of heavy drinkers.

As it has been previously shown, SBP, TC and smoking have the biggest impact on fatal CVE development. In the current study TC and smoking have the strongest impact on CVD mortality risk. In non-drinkers smoking had the strongest influence and TC had the least impact. The situation in moderate drinkers was directly opposite. Difference between these two groups is statistically significant. Although SBP has a small impact on fatal CVE risk formation in general, heavy drinkers are the most likely to develop fatal CVE due to increased SBP (Figure 3).

Conclusion

Results of this study demonstrated that the majority of male patients aged 42-44 years consume alcohol, at the same time around 40% of participants take alcohol beverages in quantities dangerous for health. It has been shown that the frequency of abdominal Ob, AH and blood lipid spectrum goes up with the increase of alcohol consumption. It has been identified that in males with the same length of alcohol consumption amount of consumed alcohol influences directly SBP, DBP, TC, ApoA1, UA and blood glucose levels. Alcohol has the most prominent effect on SBP, UA and glucose blood levels (medium level of effect). Though total risk of fatal CVE development is linked with the amount of consumed alcohol, its value depends more on other CVD RF like TC levels and smoking.

Conflict of interest: None declared

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