CARDIOVASCULAR RISK ASSESSMENT IN THE ADULT (AGED 40-79 YEARS) ROMANIAN POPULATION

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Abstract

Atherosclerotic Cardiovascular Diseases are the leading cause of death worldwide.

Aim. To estimate the prevalence of cardiovascular risk (CVR) categories in the adult population (aged 40-79 years) of Romania.

Design. The present study was part of the epidemiological, cross-sectional PREDATORR study (PREvalence of DiAbeTes mellitus, prediabetes, overweight, Obesity, dyslipidemia, hyperuricemia and chronic kidney disease in Romania).

Subjects and Methods. Exclusion criteria: age <40/ or >79 years old and diagnosis of ischemic vascular disease. The CVR was evaluated using charts developed by the World Health Organization/ International Society of Hypertension (WHO/ISH) available for Europe B (epidemiological sub-region where Romania was included). The CVR was divided into 5 categories: <10%, 10-20%, 20-30%, 30-40%, > 40%.

Results. A total of 1631 subjects (57.0±10.7 years, 45.1% males) were included in the present study.

The age and sex-adjusted prevalence of CVR >40% was 2.9% (95%CI 2.8-3.1%), CVR 30-40% was 1.85% (95%CI 1.8-1.9%), CVR 20-30% was 5.8% (95%CI 5.6-6.0%) and 13.0% (95%CI 12.8-13.3%) of the adult Romanian population has a 10-20% CVR, these CVR categories being more frequent in male and older age. Diabetes, overweight/obesity and smoking were associated with high CVR categories.

Conclusion. Romania is one of the countries with high CVR, requiring CVD prevention measures.

Key words: cardiovascular risk, Romanian population, WHO/ISH charts.

INTRODUCTION

Cardiovascular disease (CVD) is the most common cause of morbidity and the leading cause of death worldwide (1, 2), being a consequence of a wide variety of factors: genetic, socio-economic, environmental and individual (3). Approximately 17.5 million people are estimated to have died in 2012, accounting for 31% of the deaths globally. More than three-quarters of cardiovascular (CV) deaths are recorded in low and middle income countries (1).

In Europe, over 85 million people had CVD in 2015, out of which 11.3 million were new cases. In addition, more than 3.9 million deaths were caused annually by this disease, accounting for over 45% of all deaths (4); in Central and Eastern Europe, the rate of death from ischemic heart disease and stroke is higher, as opposed to Northern, Southern or Western Europe (4).

Romania is still one of the high cardiovascular risk (CVR) European countries according to data from the last European Society of Cardiology guideline for prevention of CVD (5). In our country, more than 62% of deaths are caused by CVD (6), making awareness regarding the prevalence of CVR factors an imperious necessity for the rapid implementation of various prevention strategies to slow the increase in CV mortality. The main causes of death include myocardial infarction, stroke and heart failure, associated with one or more major CVR factors: smoking, hypertension, hypercholesterolemia and diabetes mellitus (DM) (7-9).

Particularly, patients with DM have 2 to 4 fold higher risk of developing CVD compared to

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subjects of the same age and sex, but without DM (10,11). Over time, several diagrams, web applications or calculation methods for CVR have been developed taking into account a maximum number of potential risk factors, so that the contribution of each of these methods is applicable in different regions of the world (5,12–14). Currently, the most common used algorithms for CVR evaluation in daily practice are the SCORE (Systematic COronary Risk Evaluation) risk charts (5) and Framingham score using traditional risk factors (13). The World Health Organization (WHO) and the International Society of Hypertension (ISH) developed in 2007 diagrams for CVR estimation that can be applied in different regions of the world using the best mortality predictors and risk factors (3,12). These charts are based on a series of colored codes recommended by the WHO guidelines for CVD prevention and are available for 14 epidemiological regions worldwide (15, 16).

The aim of this study was to calculate the CVR in the adult population of Romania using the diagrams developed by WHO/ISH, the variant that includes serum cholesterol and the impact of various risk factors on total CVR.

MATERIAL AND METHOD

This study was part of the PREDATORR study (PREvalence of DiABeTes mellitus, prediabetes, overweight, Obesity, dyslipidemia, hyperuricemia and chronic kidney disease in Romania). This was a large cross-sectional, population-based study evaluating the prevalence of DM, prediabetes, overweight and obesity, dyslipidemia, hyperuricemia, and chronic kidney disease in the Romanian adult population. The study was conducted by the Romanian Society of Diabetes, Nutrition and Metabolic Diseases and the Romanian Society of Nephrology, between December 2012 and February 2014 and it was approved by the Romanian National Ethics Committee. Each subject has signed the written informed consent before enrolling into the study. The study design and primary results were previously presented (17).

To calculate the CVR we used, as mentioned above, the diagrams developed by WHO/ISH valid for the Europe B region (epidemiological sub-region where Romania is included), representing the 10 year risk for a major fatal or non-fatal CV event (myocardial infarction or stroke), depending on: age, gender, blood pressure (BP), smoking status, total-cholesterol and diabetes status. There are 5 levels of CVR: <10%, 10-20%, 20-30%, 30-40% and > 40%

(15,16). We excluded subjects younger than 40 years old (age group 20-39 years), as this is the minimum age at which CVR can be calculated with these diagrams. We also excluded subjects with a personal history of ischemic vascular disease (myocardial infarction, cerebrovascular disease -stroke, transient ischemic attack, coronary revascularization and peripheral arterial disease), diagnosed based on self-reported diagnosis, clinical examination or medical records from GPs (electrocardiography, arterial Doppler ultrasound, arteriography, etc.). The remaining eligible subjects were divided into two categories: with and without DM. A subject with DM was defined as a person previously diagnosed with this condition who undergoes anti-diabetic medication, or as the new cases of DM that met WHO diagnostic criteria. For each diabetes category, the CVR was calculated using the corresponding diagram.

Regarding smoking, subjects were divided into smokers (subjects who smoke more than one cigarette, daily or occasionally, or who gave up smoking less than a year before) and non-smokers (never smoked or smokers who have quit smoking for more than a year). The fasting total-cholesterol level was determined using enzymatic method. Hypercholesterolemia was defined as the total-cholesterol value ≥ 5.17 mmol/l and/or current statin treatment, regardless of the total cholesterol level.

BP determination was performed three times, with the patient in the sitting position, after five minutes of rest, with the cuff on the right-arm, at the heart level. The interval between the measurements was at least one minute. The mean of the three measurements was considered for diagnosis. Hypertensive subjects were defined as those with systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg, or if they were on antihypertensive treatment, as well as subjects with a history of diagnosed hypertension. Subjects without hypertension were considered those with SBP < 140mmHg and DBP < 90mmHg without antihypertensive treatment or no personal history of hypertension.

Subjects were weighed using an electronic weighing machine and the height was measured with a tallimeter. The body mass index was calculated as weight in kilograms divided by the square of the height in meters and the weight status was classified according to WHO criteria (18).

As far as the educational level is concerned, the subjects had either a low educational level (primary or secondary school) or high level of education (college,

high school or university).

Regarding the occupation of the subjects, they were: students, employees, farmers, retirees, unemployed with or without social assistance, subjects receiving social assistance and other categories. Marital status was classified as: married, unmarried, divorced, widowed.

Statistical analysis

Confidence interval (CI) for population proportion has been used in order to show the statistical probability that a characteristic is likely to occur within the studied population. We estimated a population proportion (p), using a sample proportion, ($\hat{p}$) plus or minus a margin of error. The result obtained was a CI for the population proportion, p .

Analysis regarding cardiovascular risk prevalence was stratified for gender and age groups. Categorical data were comprised of variables separated into different categories, mutually exclusive from one another. To determine if two variables were associated, we used likelihood ratio chi-square test. $p < 0.05$ was considered significant. We used weighting to exclude bias site selection, adjusting the sample to extrapolate results of targeted population, according to data released since the last census in 2011. Analyses were performed using SPSS software v19.0.

RESULTS

Following the exclusion criteria, there were 1631 eligible subjects: 45.1% men and 54.9% women, which we assigned over decades of age. Most of the subjects were in the 60-69 age group: 36.9% of all women and 35.7% of all men (Table 1).

Among CVD risk factors, prevalence of hypercholesterolemia was the highest, followed by hypertension, smoking and diabetes. The prevalence of hypercholesterolemia was 69.1% (95% CI 66.3% - 71.9%), with no statistically significant gender differences. The percentage of women with a total-cholesterol ≥ 8 mmol/L was 4.7% (95% CI 0% - 10.2%), double compared to that found in men: 2.4% (95% CI 0% - 6.3%).

As shown in Table 1, the prevalence of DM in the study group was 14.9% (95% CI 10.3% - 19.5%), higher in males: 17.4% (95% CI 12.5% - 22.3%) than in females: 12.8% (95% CI 8.6% - 17.1%) ($p = 0.006$). Regarding hypertension, its prevalence was 48.9% (95% CI 45.3% - 52.4%), slightly more frequent among females: 50% (95% CI 46.4% - 53.6%), compared to

males: 47.5% (95% CI, 44% - 51.1%) ($p = \text{NS}$).

Regarding the weight status, more than 75% of the subjects had a BMI above normal: 40.3% (95% CI 36.5% - 44.2%) subjects were overweight (BMI = 25-29.9 kg/m²) and 35.1% (95% CI 31.1% - 39.1%) were obese (BMI > 30kg/m²) (Table 1). Obesity was more common in females: 39.2% (95% CI 35.1% - 43.3%), while almost half of men were overweight: 48.4% (95% CI 44.5% - 52.3%) ($p < 0.001$) (Table 1).

The prevalence of smoking in the studied group was 40.91% (95% CI 37.1% - 44.7%), with the percentage of male smokers 56.1% (95% CI 52.2% - 59.9%) being almost double that of female smokers: 28.3% (95% CI 24.8% - 31.8%) (Table 1).

The CVR calculated using the WHO/ISH diagrams showed that 2.9% (95% CI 2.8% - 3.1%) of the Romanian population aged 40-79 years has a higher than 40% risk of experiencing a major fatal or non-fatal CV event (myocardial infarction or stroke) over the next 10 years while 1.85% (95% CI 1.8% - 1.9%) has a risk of 30-40% (Table 2). The 10 year risk of CV event increased with age, being higher in men than in women (Table 2).

Also, in smokers, the risk was significantly higher than in non-smokers. We observed that 32.8% of smokers had a CVR $\geq 10\%$, while 18% of non-smokers had a CVR $\geq 10\%$ (Table 3). Surprisingly, subjects with hypertension predominated the <10% CVR group, while in the high CVR groups predominated normotensive subjects (Table 3).

As we expected, CVR was higher in subjects with obesity and overweight, compared to subjects with a body mass index within normal range (Table 3). In terms of occupation, both women and men with social assistance had the highest CVR, with 14.3% (95% CI 0% - 40.7%) of women and 33.3% (95% CI 0% - 87.8%) of men belonging to >40% CVR group. The lowest risk (<10%) was observed among all students, unmarried women, women working in agriculture and unemployed men and women with unemployment benefits. Regarding the educational level, it was observed that in both genders the percentage of subjects with CVR > 40% was higher in those with a low educational level compared with those with high educational level, 9.7% (95% CI 2.7% - 16.7%) vs. 3.3% (95% CI 1.9% - 4.7%) in males, respectively 3.6% (95% CI 0.7% - 6.6%) vs. 1.0% (95% CI 0.2% - 1.7%) in females. When we compared the group of subjects with DM with those without this condition, as expected, CVR was higher in subjects with DM, as can be seen in Table 3.

Table 1. Socio-demographic, clinical and biological characteristics by gender

Variable	Women (n=895)	Men (n=736)	p (Women vs. Men)	Total (n=1631)
Age (%)				
40-49 yrs	21.7	23.2	NS	22.4
50-59 yrs	27.7	26.8		27.3
60-69 yrs	36.9	35.7		36.3
70-79 yrs	13.7	14.3		14
Cholesterolemia %; (CI)				
< 5 mmol/L	22.2 (17.8; 26.5)	23.9 (19.4; 28.3)	NS	22.9 (18.6; 27.3)
5-5.99 mmol/L	5.9 (1.5; 10.4)	8.5 (3.2; 13.7)		7.1 (2.3; 11.9)
6-6.99 mmol/L	56.7 (53.3; 59.9)	56.1 (52.8; 59.4)		56.4 (53.1; 59.7)
7-7.99 mmol/L	10.5 (5.6; 15.4)	9.2 (4.6; 13.8)		9.9 (5.2; 14.7)
≥ 8 mmol/L	4.7 (0; 10.2)	2.4 (0; 6.3)		3.6 (0; 8.6)
Smoking %; (CI)	28.3 (24.8; 31.8)	56.1 (52.2; 59.9)	p<0.001	40.9 (37.1; 44.7)
Diabetes %; (CI)	12.8 (8.6; 17.1)	17.4 (12.5; 22.3)	NS	14.9 (10.3; 19.5)
Systolic blood pressure %; (CI)				
< 140 mmHg	63.1 (59.9; 66.2)	52.1 (48.8; 55.4)	p<0.001	58.1 (54.9; 61.4)
140-159 mmHg	26.1 (22.0; 30.3)	31.6 (27.2; 35.9)		28.6 (24.3; 32.8)
160-179 mmHg	8.6 (4.2; 13.1)	12.0 (6.9; 17.1)		10.2 (5.4; 14.9)
>180 mmHg	2.2 (0; 6.3)	4.3 (0; 10.1)		3.1 (0; 8.1)
Body mass index %; (CI)				
< 25.0 kg/m ²	27.0 (22.6; 31.5)	21.5 (17.4; 25.6)	p<0.001	24.5 (20.2; 28.8)
25-29.9 kg/m ²	33.7 (30.1; 37.4)	48.4 (44.5; 52.3)		40.3 (36.5; 44.2)
≥ 30 kg/m ²	39.2 (35.1; 43.3)	30.2 (26.3; 34.0)		35.1 (31.1; 39.1)
Marital Status %; (CI)				
Widowed	20.4 (14.9; 25.9)	4.6 (1.8; 7.5)	p<0.001	13.3 (8.7; 17.9)
Divorced	7.8 (2.7; 13.0)	5.4 (1.1; 9.8)		6.8 (2.0; 11.6)
Unmarried	3.9 (0; 9.3)	2.3 (0; 6.5)		3.2 (0; 8.1)
Married	67.8 (65.2; 70.5)	87.6 (85.7; 89.5)		76.8 (74.4; 79.1)
Educational Level %; (CI)				
Low Educational Level	18.5 (13.5; 23.6)	9.8 (6.0; 13.7)	p<0.001	14.6 (10.0; 19.2)
High Educational Level	81.5 (79.4; 83.6)	90.2 (88.6; 91.8)		85.4 (83.5; 87.3)
Occupation %; (CI)				
Employed	31.2 (27.2; 35.1)	40.9 (36.7; 45.2)	p<0.001	35.5 (31.4; 39.7)
Student	0.2 (0; 5.9)	0.1 (0; 4.6)		0.2 (0; 5.3)
Social aid	0.8 (0; 6.6)	0.4 (0; 4.6)		0.7 (0; 5.8)
Unemployed	2.3 (0; 5.9)	3.6 (0; 7.8)		2.9 (0; 6.6)
Pensioner	56.4 (52.9; 59.9)	48.5 (45; 52.1)		52.9 (49.3; 56.4)
Farmer	0.5 (0; 4.6)	1 (0; 7.1)		0.7 (0; 5.8)
Other	8.6 (3.2; 13.9)	5.3 (1.0; 9.6)		7.1 (2.1; 12.0)

Table 2. WHO/ISH Cardiovascular Risk Score Category according to gender and age group

		CVR < 10%	CVR 10 - 20%	CVR 20 - 30%	CVR 30 - 40%	CVR > 40%
Total	40 - 49 years	96.7 (94.8; 98.6)	2.2 (0.7; 3.7)	0.8 (0.0; 1.8)	0.0 (0.0; 0.0)	0.3 (0.0; 0.8)
	50 - 59 years	88.8 (85.8; 91.8)	5.8 (3.6; 8.1)	2.9 (1.3; 4.5)	0.7 (0.0; 1.4)	1.8 (0.5; 3.1)
	60 - 69 years	74.2 (70.6; 77.8)	13.2 (10.4; 15.9)	6.7 (4.7; 8.8)	2.2 (1.0; 3.4)	3.7 (2.2; 5.3)
	70 - 79 years	45.2 (38.6; 51.8)	32.9 (26.7; 39.1)	12.3 (7.9; 16.6)	4.4 (1.7; 7.1)	5.3 (2.3; 8.2)
	Overall	76.3 (76.1; 76.6)	13.0 (12.8; 13.3)	5.8 (5.6; 6.0)	1.85 (1.8; 1.9)	2.9 (2.8; 3.1)
Women	40 - 49 years	97.9 (95.9; 100.0)	1.5 (0.0; 3.3)	0.5 (0.0; 1.5)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
	50 - 59 years	93.1 (89.9; 96.4)	4.4 (1.8; 7.1)	1.6 (0.0; 3.2)	0.0 (0.0; 0.0)	0.8 (0.0; 1.9)
	60 - 69 years	84.2 (80.2; 88.3)	7.6 (4.7; 10.5)	5.8 (3.2; 8.3)	0.0 (0.0; 0.0)	2.4 (0.7; 4.1)
	70 - 79 years	63.4 (54.7; 72.1)	26.0 (18.1; 33.9)	6.5 (2.1; 11.0)	0.8 (0.0; 2.4)	3.3 (0.1; 6.5)
	Overall	86.8(84.6;89.1)	7.9(6.1;9.7)	3.6(2.3;4.8)	0.1(0.0;0.3)	1.6(0.7;2.4)
Men	40 - 49 years	95.3 (92.1; 98.6)	2.9 (0.3; 5.5)	1.2 (0.0; 2.8)	0.0 (0.0; 0.0)	0.6 (0.1; 1.8)
	50 - 59 years	83.2 (77.9; 88.6)	7.6 (3.8; 11.4)	4.6 (1.6; 7.5)	1.5 (0.0; 3.3)	3.0 (0.6; 5.5)
	60 - 69 years	61.6 (55.6; 67.6)	20.2 (15.2; 25.1)	8.0 (4.6; 11.3)	4.9 (2.3; 7.6)	5.3 (2.6; 8.1)
	70 - 79 years	23.8 (15.5; 32.1)	41.0 (31.4; 50.6)	19.0 (11.4; 26.7)	8.6 (3.1; 14.0)	7.6 (2.4; 12.8)
	Overall	69.8(66.5;73.2)	15.8(13.1;18.4)	7.1(5.2;9.0)	3.4(2.1;4.7)	3.9(2.5;5.4)

Table 3. Distribution of projected WHO/ISH 10 years risk category (percentage with 95% CI) by metabolic traits and smoking

		CVR <10%	CVR 10-20%	CVR 20-30%	CVR 30-40%	CVR > 40%
BMI	Normal weight	85.9 (81.7; 90.1)	7.6 (4.4; 10.8)	3.4 (1.2; 5.6)	1.1 (0.0; 2.4)	1.9 (0.2; 3.6)
	Overweight	76.8 (73.1; 80.5)	15.5 (12.3; 18.7)	4.8 (2.9; 6.7)	1.8 (1.0; 2.6)	2.2 (0.9; 3.5)
	Obesity	74.8 (70.7; 78.9)	5.4 (3.2; 7.6)	5.2 (3.1; 7.3)	1.9 (0.6; 3.2)	2.6 (1.1; 4.1)
Diabetes	Yes	51.9 (45.4; 58.3)	23.0 (17.6; 28.4)	12.8 (8.5; 17.0)	4.5 (1.9; 7.2)	7.8 (4.4; 11.3)
	No	83.9 (82.0; 85.9)	9.4 (7.9; 11.0)	3.8 (2.8; 4.8)	1.1 (0.5; 1.6)	1.7 (1.0; 2.4)
Hypertension	Yes	77.4 (77.0; 77.7)	12.6 (12.3; 12.9)	5.6 (5.4; 5.8)	1.6 (1.5; 1.7)	2.8 (2.7; 3.0)
	No	74.6 (74.1; 75.0)	13.9 (13.5; 14.3)	6.1 (5.8; 6.4)	2.3 (2.1; 2.5)	3.1 (2.9; 3.3)
Smoking	Yes	67.2 (66.7; 67.7)	16.4 (16.0; 16.8)	9.3 (9.0; 9.6)	3.3 (3.1; 3.5)	3.8 (3.6; 4.0)
	No	82.0 (81.7; 82.3)	10.9 (10.6; 11.2)	3.7 (3.5; 3.8)	1.0 (0.9; 1.1)	2.5 (2.3; 2.6)

DISCUSSION

Although the most commonly used CVR estimation method is represented by the SCORE diagrams, we used the WHO/ISH diagrams because they take into account the presence or absence of diabetes.

Data from this study have shown that although the prevalence of modifiable CVR factors (hypercholesterolemia, hypertension, smoking, diabetes) is increased, most subjects were within the < 10% CVR group.

As we mentioned above, the prevalence of DM in our study was 14.9% (95% CI 10.3% - 19.5%), while in the whole population of the PREDATORR study, the DM prevalence in the adult population in Romania was 11.6% (95% CI 9.6% - 13.6%) (17), the difference from this analysis being due to the fact that in our study we excluded the 20-39 age group according to the CVR calculation criteria.

Also, the prevalence of hypercholesterolemia in our study was 69.1% (95% CI 66.3% - 71.9%). For comparison, it should be mentioned that in the SEPHAR I study (Study for the Evaluation of Prevalence of Hypertension and Cardiovascular Risk among the Adult Population of Romania), performed in our country in 2005, the prevalence of hypercholesterolemia in the analyzed group was 40% (19), similar with the prevalence reported by Cinteza M *et al.* in a population aged 18-85 years from 8 EURO-regions of Romania (20). The difference in percentages could be due to the fact that in the mentioned studies subjects enrolled were between 18 and 85 years while our study included subjects over 40 years old.

The prevalence of hypertension in our study was 48.9% (95% CI 45.3% - 52.4%). It should be mentioned that in the SEPHAR II study (performed in our country in 2011) the prevalence of hypertension was 40.4% (21,22) while in SEPHAR I study the hypertension was found in 44.9% of subjects (21),

slightly lower than in our study, the difference in the percentages between studies being attributed to the older age inclusion criteria used in our study. In addition, SEPHAR II was performed in 2011 and SEPHAR I in 2005, approximately 3 years, respectively 9 years before PREDATORR study, so a genuine increase in prevalence cannot be excluded. In both studies, hypertension prevalence was found to be more common among females (22).

In the present study, both the prevalence of obesity and overweight were higher than those recorded in the original PREDATORR study, where the prevalence of obesity in the Romanian adult population (aged 20-79) was 31.90% (95% CI 30.44% - 33.36%) and also higher than the prevalence reported by Roman G *et al.* and Mihalache L *et al.* in the Romanian population older than 18 years (23-25). Also the prevalence of overweight was 34.70% (95% CI 33.24% - 36.16%) in PREDATORR study (23) and 21.3% in the study performed by Roman G *et al.* (24), the differences being justified by the same arguments as those mentioned in the case of hypertension and DM.

Regarding the estimation of the CVR using the diagrams developed by WHO and ISH, our country is included in the Europe-B (EUR-B) sub-region with countries such as Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Georgia, Kyrgyzstan, Poland, Serbia and Montenegro, Slovakia, Tajikistan, the former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Uzbekistan (16).

Mendis *et al.* published a study that analyzed estimated CVR using WHO/ISH charts in eight low- and middle-income countries from eight different WHO epidemiological sub-regions (26). In Georgia, a country included in the same sub-region as Romania, the percentages obtained in CVR estimation were quite similar to those obtained in our study (26). Thus, 83.1% of the subjects had a <10% CVR, while 16.9% of the subjects were in the > 10% risk groups in Georgia,

compared to our country where 76.3% of the subjects had a low risk (<10%) and over 23% had a $\geq 10\%$ risk (26). In each of the eight analyzed countries from this study, less than 10% of the subjects included had a $> 20\%$ risk (China: 1.1%, Iran: 1.6%, Sri Lanka: 2.3%, Cuba: 2.9% 3.3%, Nigeria: 5%, Georgia: 9.6% and Pakistan 10%), while in Romania 10.55% of the subjects had an $> 20\%$ of estimated CVR, higher than in all the countries mentioned above (26), which emphasizes that CVR is influenced by many factors, not just by the income.

A similar percentage to ours was recorded in a rural Bangladeshi population study where 11% of the subjects had a CVR of $\geq 20\%$, while in 89% of subjects enrolled the risk was under 10 %. Also this study showed that men had a higher CVR than women (27).

Another study, conducted this time in Jamaica, estimated that 89.6% of enrolled subjects had a <10% risk of developing a major CV event, while over 10% of subjects had a risk of over 10% (28). These results are similar to ours, with no significant difference between males and females.

Also, in a recent study developed in Nepal, 86.4% of subjects had a CVR below 10%, and over 13% of subjects had a risk higher than 10%, a higher percentage than ours (29).

Two other studies developed in India showed alarming results. Thus, a study conducted on a rural population in Northern India showed that 55.6% of subjects were in the <10% risk group, while 44.4% had a $\geq 10\%$ CVR, almost four times higher than in our country (30). Also in a rural population, this time in South India, a study by Norman *et al.* showed that a percentage of over 15% of subjects had $\geq 30\%$ CVR to have a fatal or non-fatal myocardial infarction or stroke within 10 years (31), three times higher than in our study.

Overall our study indicated a prevalence of CVR $\geq 10\%$ in Romanian population aged 20-79 years lower than the prevalence of high CVR (SCORE $\geq 5\%$ in non DM, non CVD) reported by Bunescu D in a population aged 25-65 years from the north area of Romania (32).

These CVR variations may be due to different geographical areas, genetic variability, ethnic differences, culture, and the socio-economic level of each country.

As we mentioned above, in our study, hypertensive subjects predominated in the <10% CVR group, while normotensive subjects had a higher CVR.

There are several possible explanations for this result: the CVR was calculated based on the BP value at the time of the study visit so that treated hypertensive subjects could have a therapeutically corrected BP value at the time of the study visit. On the other hand, hypertensive subjects may become more compliant with treatment of other comorbidities, including hypercholesterolemia so that their cholesterol level at the time of the visit could have been therapeutically corrected. Finally, once diagnosed with hypertension, patients may change their lifestyle, as shown by the SEPHAR II study (21), contributing to the decrease in the CVR.

The WHO/ISH prediction charts identify those at highest risk for a CV event that would include both coronary disease and stroke. In a recent WHO report, the number of subjects with CVD in 2015 in our country was over 2 million in both genders. Also, the number of subjects with ischemic heart disease was over 510,000 in men and over 370,000 in women, while the number of subjects with stroke was over 113,000 in men and over 139,000 in women (4).

Strengths of our study: the first study that examines the CVR in subjects with and without DM in the adult population of Romania; all data were measured directly, not obtained through questionnaires; all biological explorations were performed at the same certified laboratory.

The study had some limitations: the CVR score cannot assess the dynamics of CVR, being only a surrogate that indicates the CVR of a subject at the time of analysis, without providing the opportunity to capture the influence of risk factors variations on the CVR.

In conclusion, with the exception of the SEPHAR Studies as we cited above (who estimated CVR using SCORE charts), no other studies have reported CVR among the Romanian population (using the WHO/ISH tool or other risk scoring system).

This is the first study from Romania on prediction of fatal/non-fatal CVD events using the WHO/ISH algorithm. In our study, CVR was associated with age and male gender, which are unchangeable risk factors and also with the presence of DM. Our study shows that Romania is a country with high CVR and we believe that the results presented by our study are important for current medical practice.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the Romanian National Ethics Committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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