

Cardiovascular risk in an urban population in Ukraine

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On behalf of the Working Group of the Ukraine-Russia study of 20 risk factors in Dnepropetrovsk**

Abstract

Aim

To conduct a large-scale study of cardiovascular risk in an urban population in Ukraine following current recommendations of the European Society of Cardiology (ESC).

Materials and Methods

The study protocol included identification and assessment of 20 cardiovascular risk factors in an urban population of Dnepropetrovsk (Ukraine), involving 1,000 respondents (468 men and 532 women) living in five districts of Dnepropetrovsk, aged 30-69 years. It also included determination of the prevalence of very high risk using all variations of the Systematic COronary Risk Evaluation (SCORE) scale, recommended by the ESC.

Results

According to the results of this Ukrainian-Russian study, conducted between 2009 and 2013, cardiovascular risk factors were identified which can be merged into three main groups according to prevalence among the adult population.

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The most prevalent group of risk factors in this population, found in approximately 70% of cases, in descending order, were: abdominal obesity (by ESC criteria); overweight and obesity (by BMI); hypercholesterolemia and increased low density lipoprotein (LDL) cholesterol.

The second most common group of risk factors, found in approximately 40–45% of the cases, in descending order, were: abdominal obesity (by the criteria of the Adult Treatment Panel (ATP) III (2001); hypertension; hyperinsulinemia and insulin resistance (IR) by the homeostatic model assessment (HOMA) index.

The third most common risk factors, found in up to 30% of the population, in descending order, were: hypertriglyceridemia; impaired glucose tolerance (IGT); smoking; decreased HDL cholesterol; hyperuricemia and diabetes.

Conclusion

According to results of the analysis on the prevalence of risk factors and calculations of cardiovascular risk in urban population in Ukraine, using recommendations of the ESC (2012) and all three versions of the SCORE risk scale, a prevalence of very high risk involving cardiovascular complications was found in 30% of the adult population. These findings should serve as a basis for further multicenter epidemiological studies and prompt long-term prevention programmes.

Keywords

Risk factors, cardiovascular disease, urban population

According to the *World Health Organization* (WHO), cardiovascular disease (CVD) is the main cause of death worldwide. The latest estimates have shown that in 2008 17.3 million people died from CVD and, of that number, 7.3 million people died from coronary (ischemic) heart disease and 6.2 million died from stroke. This problem mostly affects low-income and middle-income countries and it is predicted that by 2030 global mortality from CVD will reach 23.3 million people per year [9].

The peculiarity of the European Region is that, along with a decrease of overall mortality in recent years, which in 2010 reached an age-standardized mortality rate of 813 per 100,000 of population, there are still wide differences between countries. For example, according to *WHO*, the age-specific structure in 15 countries that joined the European Union (EU) before 2004 is characterized by an increase in mortality in older age groups by two times, and in 12 other countries that joined the EU after May 2004 and in the CIS countries, it increased by more than three times. On average about 50% of all deaths in Europe occur due to CVD, and of all deaths in the age group to 75 years old, 42% related are related to CVD in women and 38% in men [5].

Some decrease in age-standardized mortality rates from CVD was observed in the period from 1970s and 1990s, which was most pronounced in rich developed countries, demonstrating the potential for preventive measures to avoid premature death and to extend healthy life expectancy. The results of the international research project MONICA (Multinational MONItoring of trends and determi-

nants in Cardiovascular disease) were quite demonstrative, and was conducted in 21 countries on four continents over the period 1976–1996 to monitor the trends and determinants of CVD under the aegis of *WHO*. The following risk factors were explored: smoking, cholesterol, systolic blood pressure and body mass index (BMI). The following dynamics were noted: the reduction of smoking in men, along with an increase in women; some tendency to lower cholesterol, which, however, significantly affected the CVD risk; a tendency to decrease blood pressure, along with a tendency to increase the body mass index, in half of women and two thirds of men.

Also, within the framework of the WHO MONICA project, from mid 1980s to mid 1990s, there was monitoring of the frequency of coronary heart disease (CHD), risk factors and treatment of coronary patients among selected populations in order to obtain an accurate picture of the levels and trends associated with CVD. The most significant reduction in the incidence of CHD in men occurred in three populations in northern Europe: North Karelia and Kuopio in Finland, and in Northern Sweden. An increase in the frequency of CHD was also observed among both male and female population in the countries of Eastern Europe.

The importance and effectiveness of a multifactorial approach to solving this problem was clearly demonstrated by the example of the North Karelia project in Finland. Thus, during the period from 1972 to 2007, the total cholesterol in men in North Karelia decreased from 6.9 mmol/L to 5.4 mmol/L (i.e., 1.5 mmol/L), diastolic blood pressure decreased from 92.6 mmHg to 83.9 mmHg (i.e. by 8.7 mmHg) and the prevalence of

smoking decreased from 51% to 30% (i.e. by 21%). As a result, based on the reduction in diastolic pressure, cholesterol and smoking, overall risk fell by 60%. At the same time, observed mortality from CHD decreased in the same geographical area by 80%.

In 2012, the *European Atherosclerosis Society* (EAS) once again highlighted the importance of risk factor modification using the results of a meta-analysis of 18 studies involving more than 250,000 men and women aged 55 years and older [7]. It was found that in individuals with optimal profile of risk factors (non-smoking, non-diabetic, with optimal level of cholesterol and blood pressure) enjoyed a more than 3 times reduced risk of major cardiovascular events, more than 6 times reduction in death from CVD, and more than 10 times reduction in the risk of developing CHD. None of the most advanced medical technologies, including interventional and surgical methods of treatment, has this degree of influence on cardiovascular risk.

In Ukraine, according to the latest official statistics, more than 440,000 people died from cardiovascular diseases in 2011, which represents 66.3% of all causes of death, and this figure continues to be one of the highest in the structure of mortality in Europe. Along with the available data on the prevalence in Ukraine of five traditional risk factors, including smoking, hypertension, obesity, dyslipidemia and lack of physical activity, there is no analysis of the new predictors of CVD, the importance of which is emphasized in policy documents published by the *European Society of Cardiology* (ESC) and the *EAS*. Firstly, the problems associated with carbohydrate metabolism and especially the prevalence of type 2 diabetes, a recognized equivalent of CHD; visceral fat distribution, not only overweight; hyperuricemia; level of C-reactive protein; thyroid disease, especially due to the accident at the Chernobyl Nuclear Power Plant and a number of other factors.

To solve this problem in 2009 the *M.D. Strazhesko Institute of Cardiology*, Kiev, Ukraine; the *Dnepropetrovsk State Medical Academy*, Dnepropetrovsk, Ukraine, and the *National Research Centre for Preventive Medicine*, Moscow, Russia started a joint Ukraine-Russia project to study 20 risk factors in an urban population of Dnepropetrovsk attending its five polyclinics. It should be noted that a similar protocol study was initiated in Russia in 2007 in multi-centres across five regions of the country. At present, the completed part of the study involves 20 risk factors in the urban population of the city of Cheboksary, the Chuvash Republic of the Russian Federation.

The study protocol included identification and assessment of the following parameters in 1,000 respondents (468 men and 532 women), living in five districts of Dnepropetrovsk, aged 30–69 years:

1. Anthropometric data (height, weight, BMI);
2. Definition of abdominal obesity (waist circumference, hip circumference, and their ratio);
3. Systolic (SBP) and diastolic blood pressure (DBP), a history of hypertension and its treatment;
4. Lipid profile (total (T) cholesterol, LDL cholesterol, cholesterol, very low density lipoprotein (VLDL) cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, atherogenic index);
5. Smoking status;
6. Glycemic status (levels of fasting glucose and insulin, insulin sensitivity by the homeostatic model assessment (HOMA) index, history of diabetes);
7. Alcohol intake;
8. Social status (education, marital status);
9. Family history (hypertension, obesity, diabetes, CHD (including angina), stroke, heart attack in immediate family);
10. presence of CHD (Rose questionnaire, Minnesota code for electrocardiogram (ECG), including data on left ventricular hypertrophy, myocardial infarction);
11. Presence of cardiac arrhythmias and conduction abnormalities (extrasystole, atrial fibrillation);
12. Presence of heart failure;
13. Level of physical activity;
14. Eating pattern;
15. Levels of anxiety, depression and stress;
16. C-reactive protein level;
17. Uric acid level and urolithiasis history;
18. Presence of comorbidity on the thyroid gland, liver, and kidneys;
19. Presence of menopause in women;
20. Presence of peripheral vascular disease (atherosclerosis of the carotid arteries, atherosclerosis of the lower limbs and / or presence of varicose veins of the lower limbs).

There was a high response from the participants who took part in this project (72%). Consent to examination was given by 1,000 residents of Dnepropetrovsk from 1,388 people initially involved in the survey, which indicates a representative sample. Analysis of the data was conducted by the *National Research Centre for Preventive Medicine* in Moscow, in accordance with the standards of medical statistics involving the following methods of standardization:

- direct by age in accordance with the WHO MONICA project [11];

- regression – in general linear models (using SAS PROC GLM) [8].

According to the data obtained, we were able to analyze a number of epidemiological characteristics.

Hypertension

To analyze the prevalence of hypertension, data on blood pressure exceeding SBP \geq 140 mmHg and/or DBP \geq 90 mmHg were taken into account by measuring blood pressure 2 times: on the 1st and 2nd minute of the examination. The existing history of hypertension was also considered, including information on prescriptions for antihypertensive drugs. At the time of the survey, hypertension was diagnosed in 457 respondents (45.7%), including in 16 respondents (1.6%) for whom it was revealed for the first time. Sex distribution of hypertension was found in 37.6% of men and 52.8% of women. A progressive increase in the prevalence with age was noted. Hypertension was found in 31.5% of cases (29.5% men and 34.0% women) in the age group of 30–39 years, 29.8% (28.5% men and 31.5% women) in the age group of 40–49 years, 55.6% (43.6% men and 64.8% women) – followed by almost two-fold increase in the age group of 50–59 years, and 68.6% in the age group of 60–69 years (66.0% men and 69.7% women). A distinctive feature of our data is not only an increase in the overall percentage of hypertension prevalence in general population (45.7% vs. 29.3%) and in relevant age groups compared with the epidemiological data obtained earlier, but also a significant prevalence of hypertension among women in all age groups, not previously detected [1,2].

Dyslipidemias

Taking into account a need for a full lipid analysis of the surveyed respondents, as well as the fact that most prognostically significant levels of LDL cholesterol in Ukraine are determined by calculation based on the Friedewald formula, we analyzed the levels of total cholesterol >5.0 mmol/L in accordance with the recommendations of the ESC (2007), the *Ukrainian Society of Cardiology*, (2011) [3], and the *International Atherosclerosis Society* (2013) [6]. It was found that the prevalence of hypercholesterolemia in this urban population is on average 69.4% (62.3% men and 71.8% women), with prevalence increasing with age. An increased prevalence of hypercholesterolemia in men was observed from 56.8% in the age group of 30–39, to 69.8% in the age group of 50–59 years. There is a reduced prevalence of up to 54.3% in the prevalence of hypercholesterolemia in the age group of 60–69 years in men. It would be nice to believe that this did not happen due to the exclusion from the analysis of respon-

dents due to increased mortality from CHD in men with hypercholesterolemia in the age range of 50–70 years, however it is not possible to exclude this possibility. There is a steady increase in the prevalence of hypercholesterolemia in women from 45.2% in the age group of 30–39 years to 86.0% in the age group of 60–69 years.

The prevalence of low HDL cholesterol (<1.0 mmol/L for men and <1.3 mmol/L for women) was not a very specific characteristic for the studied population. Only 18.3% of respondents (10.4% men and 24.6% women) had an average risk factor for CVD in the form of lower HDL cholesterol levels, but for both men and women there was a slight increase of this risk factor with age: from 10.7% to 11.9% in men and from 22.0% to 24.0% in women.

Hypertriglyceridemia (>1.7 mmol/L) was found on average in 31.7% of respondents (35.6% men and 26.2% women). For both men and women there was an increase of hypertriglyceridemia with age from 29.0% to 33.8% in men and more rapid in women, from 13.0% to 39.7%.

The prevalence of a high level of the most prognostically significant LDL cholesterol (>3.0 mmol/L) in the studied population was 68.1% (68.1% in men and 66.0% in women), and largely repeated the trend of hypercholesterolemia, which was certainly due to the calculation method. With regard to age, an increase was noted in the prevalence of this risk factor from 65.9% in the age group of 30–39 years to 71.9% in the age group of 50–59 years in men, with some reduction to 64.8% in the age group of 60–69 years. In women, by contrast, there was a steady increase in the prevalence of this risk factor from 43.6% to 75.8% in older age groups.

Smoking

The prevalence of smoking in the studied population averaged 24.2% (36.8% men and 13.1% women). There was a decrease of this risk factor with age, from 47.3% in the age group of 30–39 years to 18.1% in the age group of 60–69 years in men and from 20.5% to 5.03% in women. There was a big surprise for researchers to find such high prevalence (5.03%) of smoking in older age group of women (60–69 years), which is associated with the highest risk of CVD in this contingent.

Overweight and obesity

According to our data, normal weight with a BMI <25 kg/m² (or 18.5–24.9 kg/m²) in the studied population represented only 29.3% of the sample, while the total share of overweight and obesity was 70.1%

(69.6% men and 71.0% women). Moreover, in the population, according to BMI definition, overweight (25–29.9 kg/m²) was detected in 42.3% men and 36.4% women, while classes I, II and III obesity was revealed in 20.0%, 6.3% and 1.0% men and 23.4%, 8.7% and 1.4% women, respectively.

In previously conducted epidemiological studies in Ukraine there are no data on the prevalence of abdominal type of obesity, measured by waist circumference. This risk factor is one of a cluster of factors called the metabolic syndrome, and received its mathematical interpretation in the *Adult Treatment Panel (ATP) III*, 2001 [10] as following measurements of waist circumference: >102 cm for men and >88 cm for women. Nevertheless, the recommendations of the *International Diabetes Federation* and recommendations for the prevention of CVD of the *ESC* (2012) [5] have more strict criteria for abdominal obesity as following measurements of waist circumference: >94 cm for men and >80 cm for women. We conducted an analysis using both the first and second values of the measurement. According to the less strict measurement, *ATP-III* (2001), abdominal obesity was found in 46.8% of the respondents (37.0% men and 56.6% women), while according to the more strict measurement, supported by the *ESC* (2012), abdominal obesity was found in 72.8% of respondents (62.3% men and 77.3% women). This represents an extremely high prevalence of cardiovascular and cardiometabolic risk not only for CVD, but also the manifestation of diabetes and a variety of metabolic disorders.

Type 2 diabetes mellitus, impaired glucose tolerance (IGT), insulin resistance (IR)

Data on the prevalence of diabetes, IGT and IR have not yet been presented in statistical reports in Ukraine. Taking into account the fact that diabetes is recognized throughout the world of cardiology as a CHD equivalent, i.e. this cohort of patients belongs to a group with very high cardiovascular risk, we analyzed glucose and fasting insulin levels, and also the HOMA index for IR in all respondents.

According to the results, the prevalence of all cases of diabetes, including first time identified diabetes, was 8% of the population – about the same proportion among men (7.9%) and women (8.1%). Interesting data was also discovered on the prevalence of IGT and IR. IGT was revealed in nearly one third of all respondents (28.0%), with clear predominance in the male cohort (38.9% vs. 19.1% women). This relationship was observed in all age groups. Thus, in the age group 30–39 years, it was found in 40.1% of men and only in 14.6% of women. With increasing age, the prevalence of IGT in men remained

almost constant, whereas in women it increased up to 21.4% in the age group of 60–69 years due to lower estrogen, which has a strong antidiabetic effect. At the same time, the prevalence of hyperinsulinemia (>11 µU/kg) and IR, determined by the HOMA index, >2.77, was found in over one third of respondents (41.2%) with a primary detection in women (44.8%) compared with men (37.8%). This predominance was maintained in all age groups. Hyperinsulinemia, observed in the age group 30–39 years (31.9% men and 46.8% women) achieved a prevalence of 46.7% in men and 54.8% in women aged 60–69 years. This fact, together with the high prevalence of abdominal type of obesity in this urban population (46.8% according to the *ATP-III* (2001) criteria and 72.8% according the *ESC* (2012) criteria) suggests that the problem of the insulin resistance syndrome or metabolic syndrome, as well as all its associated cardiometabolic disorders, is highly relevant to Ukraine, which may not be fully appreciated by cardiologists.

Thyropathies

Thyroid dysfunction has first place in the structure of endocrinopathies in Ukraine. We did not carry out an additional screening of respondents' hormonal status, only information about previously diagnosed thyroid disease was analyzed. On average in this population, thyropathies had been diagnosed in 8.9% of cases (2.4% men and 14.5% women). This pathology should be considered in clinical and epidemiological developments, firstly, because of the close connection between hypothyroidism and atherogenic dyslipidemia; and, secondly, because of the significant increase in thyroid disorders after the Chernobyl accident.

Hyperuricemia

Elevated levels of uric acid in the blood are due to the consumption of foods rich in purines or chronic issues with a diet associated with consuming high calorie and fat foods. Increased levels of uric acid raise the predisposition toward gout and (at a very high level) renal insufficiency, and is also observed in the insulin resistance syndrome. The maximum values for a normal level are 360 µmol/L for women and 400 µmol/L for men. In the studied population, hyperuricemia was observed on average in 17.3% of cases with twice the predominance in the male population (23.0%) compared with female (11.5%).

Conclusion

It is difficult to analyze the prevalence of all 20 investigated risk factors in one article. However, as we touched on some of the traditional and identified new

predictors of CVD, we can try to characterize the profile of the main cardiovascular risk factors of this urban population in Ukraine (Figure 1). As shown in the diagram, the risk factors analyzed in this publication can be assigned to three main groups according to their degree of prevalence in the adult population. First, the most widespread group of risk factors in the population, represented in about 70% of cases, comprising, in decreasing order: abdominal obesity according to the ESC (2012) criteria; overweight and obesity according to BMI; hypercholesterolemia; and increased LDL cholesterol. The second most common group of risk factors (about 40–45% of the population) comprised: abdominal obesity, identified by the ATP-III (2001) criteria; hypertension; hyperinsulinemia and IR determined by the HOMA index. The third group of CVD risk factors (30% or less in the population), in descending order, comprised: hypertriglyceridemia; IGT; smoking; decreased HDL cholesterol; hyperuricemia and diabetes.

At the final stage of the study, in accordance with the recommendations of the ESC (2012), we tried to determine the prevalence of very high cardiovascular risk in this urban population in Ukraine using all three variations of the Systematic COronary Risk Evaluation (SCORE) scale, presented on-line on the ESC web page, using the scale for high-risk countries like Ukraine: <https://escoll.org/heartscore/calc.aspx?model=europehigh>

Initially, calculating the number of respondents suffering from CHD (using only objective criteria like electrocardiogram (ECG), myocardial infarction, revascularization in anamnesis), as well as the number

of respondents additionally identified with type 2 diabetes without history of coronary artery disease (CAD), which, in accordance with the ESC recommendations, is the equivalent of CAD, we discovered a group of 224 respondents with established very high risk.

During the next step, using the first SCORE1 scale, for which it is necessary to take into account the date of birth, sex, SBP, cholesterol, and smoking status, we further identified an additional 26 respondents. Consequently, using in addition the SCORE1 scale, we identified in the population $224+26=250$ respondents at a very high risk.

Using the second SCORE2 scale to determine the risk according to which, in addition to all of the above, it is necessary to consider the level of HDL cholesterol, we got a slight decrease in the high-risk group, compared with the SCORE1 scale, identified in addition to CAD and diabetes, namely, the reduction of HDL cholesterol was noted only in 9 respondents. As we have already mentioned, this risk factor is not the lead in the Ukrainian urban population. Therefore, using the SCORE2 scale, we identified a group at a very high risk only in $224+9=233$ respondents.

Using the third SCORE3 scale, to determine the risk in which, besides the date of birth and sex of a respondent, were used the parameters of height and weight to determine their BMI, and smoking status, we identified a further 67 respondents in addition to those with CAD and diabetes. Therefore, in total, using the SCORE3 scale we found a very high risk in $224+67=291$ respondents.

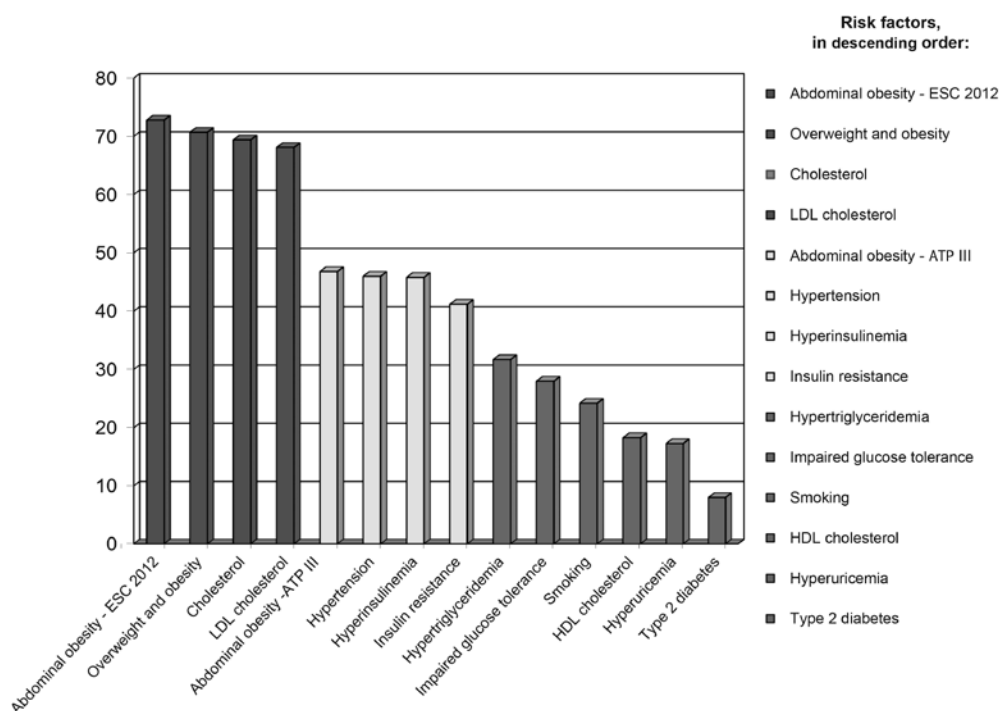


Figure 1. Prevalence of cardiovascular risk factors in an urban population in Ukraine

Attempting to determine the maximum cohort at a very high risk, we analyzed the possibility of defining this parameter, using all scales simultaneously, i.e. using every opportunity to determine the cohort threatened by the emergence of fatal CVD or SCOREmax, which was 71 respondents. Therefore, when using any possibility to determining SCORE more than 10%, which corresponds to a very high risk, we found it in total in 224+71=295 respondents. That is at the maximum consideration of all possible predictors in an adult urban population in Ukraine at the age of 30–69 years, the cohort with a very high risk of fatal complications comprised about 30% of the population, which, perhaps, is reflected in government statistics on the incidence and mortality of the *Ministry of Health* of Ukraine.

The results of this research allows us to conclude that there is a serious epidemiological situation with the prevalence of cardiovascular risk factors in the urban population in Ukraine. This may include about 30% of population aged 30–69 years being categorized at a very high risk.

This data should serve as an incentive for large-scale multicenter epidemiological studies, with the support of government organizations, to follow the example of Western countries. This would include a full assessment of the entire population and study of the population aged from 18 to 70 years living in industrialized regions and cities, deprived of large industrial enterprises, to evaluate the situation objectively and carry out appropriate preventive measures.

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