MINISTRY OF HEALTH OF THE REPUBLIC OF MOLDOVA
STATE UNIVERSITY OF MEDICINE AND PHARMACY
"NICOLAE TESTEMITANU"
DEPARTMENT OF INTERNAL MEDICINE,
MEDICAL CLINICS N. 3,
DISCIPLINE OF CARDIOLOGY

SIGNIFICANCE OF THE RISK FACTORS IN CARDIOVASCULAR DISEASE

DEVELOPMENT METHODOLOGY

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Chişinău 2017

Elaboration of Methodology was approved and recommended by the Board methodical editing of the Internal Medicine Department of the University of Medicine and Pharmacy „Nicolae Testemitanu" No. ... in 2017 _____.

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S U M M A R Y

ABBREVIATIONS AND ACRONYMS

- BMI – body mass index
- BP – blood pressure
- AC – the abdominal circumference
- DCM – dilatative cardiomyopathy
- CVD – cardiovascular disease
- CVR – cardiovascular risc
- CVRF – cardiovascular risk factors
- IHD – ischemic heart disease
- DM – diabetes miellitus
- EGFR estimated glomerular filtration rate
- Hcys – Homocysteine
- HDL – high density lipoproteins
- HDL-C – HDL-colesterol
- HT – Hypertension
- hs-CRP – high-sensitivity C-reactive protein
- LDL – low density lipoproteins
- LDL-C – LDL-colesterol
- Lp (A)– lipoprotein A
- HF- heart failure
- IMT – intima-media thickness
- PAI-1 – plasminogen activator inhibitor 1
- CRP – C-reactive protein
- RF – risk factors
- SNP – *single* nucleotide *polimorphism*
- VLDL – very low density lipoproteins
- WHO – World Health Organization

INTRODUCTION

GENERAL CARDIOVASCULAR RISC FACTORS

Cardiovascular disease (CVD) is the leading cause of the worldwide death rate according to the European Guidelines for the prevention of CVD, at the end of 2000, CVD accounted cause lethality to 1.9 million people in the EU, being responsible for 43% of all deaths from any cause of men and 55% of women. The clinical and population research carried out in recent decades demonstrated different risk factors (RF) caused by genetic, psychosocial and environmental conditions that increase the risk of atherosclerotic cardiovascular disease (coronary or peripheral). Changing these RF can decrease the mortality rate and in particular blood pressure control, stopping smoking and reducing the cholesterol levels. In the last years it was noted an alarming rise of metabolic diseases of the population of the world, especially of Diabetes and obesity. Therefore, cardiovascular diseases cause about 18 million deaths per year. According to the statistics conducted by the World Health Organisation (WHO) in 2007 it was recorded over 1 million people overweight, 300 million obese, and 20-30% of the world population present diagnostic criteria of metabolic syndrome, considered nowadays one of the leading causes of the cardiovascular morbidity and mortality in the developed countries as well as in the developing countries. A meta-analysis of extensive population studies showed that the presence of metabolic syndrome causes a 27-37% increase in the risk of total mortality and a 65-

93% risk of cardiovascular disease [3, 27]. Decisions regarding the cardiovascular risk management of the primary and secondary prevention is based on the knowledge of cardiovascular risk factors (CVRF) and on the establishing early cardiovascular risk (ECVR), and defined by the risk of fatal cardiovascular events in a defined period of time.

Several CVRF classifications are known. The risk factors represent variables that attached to a high risk of the disease. A certain variable is cataloged as a risk factor by comparing of the risk in the exposed person and of the unexposed person to the potential risk factor. The term of a risk factor was for the first time proposed by T. W. Kannel Dowber in 1961 in the first report of Framingham study [4, 18]. It was used for the allocation of CVD risk associated with the presence of some conditions (hypertension, hypercholesterolemia, smoking) [5, 29]. In the specialized literature different classifications of the cardiovascular risk factors are used. One of the most frequently used is classification of the traditional or conventional CVD risk factors (those that were mentioned above: hypertension, hypercholesterolemia, smoking, diabetes) as well as new factors or non-traditional risks (abdominal obesity, microalbuminuria, anemia, metabolic syndrome biomarkers). Between these two categories there is no clear delimitation. The association of two or more risk factors have a a multiplicative effect and it is not merely additive. CVD risk is represented by the actions and the consequences of all risk factors which act simultaneously or sequentially on the body, causing atherogenesis/atherosclerosis shown subclinically or clinically as a coronary heart disease, cerebrovascular disease, peripheral arterial disease and aortic aneurysm [6, 9, 20]. The subclinical atherosclerosis can be quantified by non-invasive methods (ankle-brachial index,

carotid intima-media thickening, calcification score determination of blood pressure, arterial stiffness). In general atherosclerotic CVD is the product of numerous causal risk factors. Most risk factors seemingly modest, but in combination can lead to a substantially higher risk than one major risk factor by itself. Because of this, the systems of estimation of overall risk have been developed to help clinicians to evaluate the effects of combinations of risk factors in the planning of therapeutic strategies. The term "global risk assessment" is probably improper because no system of risk estimation includes all known risk factors. There are many risk assessment systems. The best known and probably the most widely used on global scale is the Framingham risk score [7, 12, 27], but there are other validated methods recommended by the international guidelines for calculating cardiovascular risk: chart SCORE[1] (recommended especially for European people) and UKPDS score (especially recommended for diabetics). A remarkable improvement in the analysis of risk factors was achieved by the INTERHEART study [8, 11] which evaluated the importance of multiple cardiovascular risk factors and the power of their combination with the risk of the acute myocardial infarction. The examined factors were proved to be significant in the terms of the following prediction: ratio apoB/apoA1, smoking, diabetes, hypertension, abdominal obesity, psychosocial factors, physical inactivity, alcohol consumption and low consumption of fruit and vegetables. But the most important conclusion of the study was that the simultaneous presence of these risk factors explains 90% of major cardiac clinical events.

[1] SCORE – **S**ystematic **Co**ronary **R**isc **E**valuation: High & Low Cardiovascular Risc Charts (Evaluarea sistematică a riscului coronarian).

In the last three decades, more than half of the reduction of CVD mortality has been attributed to the change in population weight risk factors: first, by reducing the cholesterol amount and high blood pressure (hypertension) as well as smoking reducing. But this is overshadowed by an increase of other risk factors, especially obesity and type 2 diabetes mellitus (DM). Similarly, the aging of the population increases risks of the cardiovascular events.

A few interventions has effectively changed the lifestyle of individuals. For example, the awareness of the healthy lifestyle increased the factor that prevents CVD and has helped to reduce smoking and cholesterol levels. New lifestyle influence on the risk factors also should be applied either before or already in combination with the pharmacological therapy. However, the legislation meant to decrease the content of salt and fatty foods as well as smoking is cost-effective for the CVD prevention. The decrease in cholesterol levels by administration of statins and the hypertension control improving will be cost-effective if people with an increased RCV are included. Important notes: a broad category of patients receiving the fat-lowering drug treatment or low blood pressure (BP) fails to achieve therapeutic goals due to non appropriate treatment, with clinical and economic consequences.

CHAPTER I

GENERAL CARDIOVASCULAR RISK FACTORS

1. ASSESSMENT OF TOTAL CARDIOVASCULAR RISK

Considering that atherosclerosis is the product of many risk factors, all the current medical guidelines for CVD prevention are clinically recommended to assess total CVR. Depending on the individual's total CVR, the prevention of CVD, which is initiated states that the higher the risk the more intense the preventive action should be. Before making a decision, if a person is apparently healthy, we should to estimate the total risk depending on several factors, identified in Table 1, which is derived from the SCORE diagram. This indicates that a person with a cholesterol level of 10 mmol/L may presents a risk to 10 times lower than an individual with cholesterol of 5 mmol/L, provided that the first person is a woman and the second – a smoker hypertensive man.

A recent meta-analysis involves a reduction by dosing of antihypertensive medications CVR, but still maintains the idea that the absolute reduction is possible to individuals with a high baseline risk. This idea was confirmed by the meta-analyzes, which also showed a better residual result to persons with a high basal risk during the treatment, which have been previously supported by an intervention.

The clinicians often require certain limitations of the decision to resort to an intervention, and it seemed to be problematic as long as the risk is continuous and there is no limit rise, with which passing a drug is indicated automatically or if you do not get to the limit, therewill be no changes in the lifestyle. The risk categories listed in this chapter, are a successful tool in the relationship between patients and the doctor. The clinicians recognize, however, that many people in the community die with a lower risk. Therefore, the strategy for high-risk individuals should be added in public health measures in order to promote a healthy lifestyle and reduce the CVR factors.

For clinicians it is essential to assess the ability of CVR quickly and accurately. This requirement led to the development of the risk diagram used in 1994 and 1998. This diagram guides the risk to develop by the concept proposed by Anderson using the following criteria: age, sex, smoking status, blood cholesterol levels and systolic blood pressure in order to estimate the risk of a coronary artery for a period of 10 years. There were many problems with this chart, which were highlighted in 2007, the Fourth Task Force of the European Society of Cardiology (Fourth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice). This led to the elaboration of the SCORE chart which estimates the risk of fatal CVD over a period of 10 years. The SCORE Diagram was developed in order to estimate the highest and lowest risk of the European population and it is applicable to the Caucasian people.

Table 1. The major risk factors

Modifiable risk factors (which can not be influenced): • age; • gender; • heredity
Non-modifiable risk factors (which can be influenced): • hypertension; • hypercholesterolemia • Diabetes; • smoking; • obesity; • sedentary • Other risk factors: fibrinogen, C-reactive protein
Protecting factors: • HDL cholesterol; • physical activity • estrogen; • moderate alcohol intaking

There are major risk factors, which combination with the risk of cardiovascular disease highly significant, and the contributors (CVR that increase in a manner less significant). The major risk factors are defined by the World Health Organization (WHO) by three principles:

- A high prevalence in the population,

- An independent significant impact on the risk of coronary heart disease or stroke,

- the treatment or control of them that could reduce the risk.

CVRF can be considered: **modifiabl**e – factors which could be managed by a diet or treatment, eg: smoking, obesity, dyslipidemia, diabetes, hypertension, or **non-modifiable** – factors which can not be managed, such as age, sex, stature/height, heredity. The concept of **classic risk factors** is also used (those factors that are demonstrated by the studies of a number of population related with CVR) **and the new risk factors** (for which there are more recent studies which may be involved in different points of the linker the physio pathogenic, for example lipoprotein (A), homocysteine and the proinflammatory or prothrombotic factors). There are also cardiovascular risk factors that can't increase the risk of atherosclerotic condition, but

they can lead to other heart conditions (eg. alcohol can lead to dilated cardiomyopathy).

Table 2. The risk factor objectives and goals for the major cardiovascular risk factors

Objectives and goals	
Smoking	Not tobacco exposure in any form.
Physical activity	At least 150 minutes per week of moderate aerobic (30 min/5 days per week) or 75 min each week of intense aerobic (15 min/5 days a week), or a combination, thereof.
Diet	Limitation of saturated fats with an emphasis on whole grains, vegetables, fruits and fish
Bodyweight	BMI – 20-25 kg/m2. Chest circumference <94 cm (men); <80 cm (female)
Blood pressure	< 140/90 mm Hg
Lipids **LDL, HDL-C Triglicerids**	Very high risk: <1.8 mmol/l (< 70 mg/dL), or reduced to 50% at the limit between 1.8 and 3.5 mmol/L High risk: <2.6mmol/L (<100 mg/dL), or reduced to 50% at the limit between 2.6 and the 5.2 mmol/L (100 and 200 mg/dL). Moderate risk: <3.0 mmol/L (<115 mg/dL). The objective values >1.0 mmol/L (> 40 mg/dL) in men and >1.2 mmol/L (>45 mg/dL) indicating a low risk in women. The objective values <1.7 mmol/L (<150 mg/dL) indicates a low risk and the high levels indicating the need to demonstrate other risk factors.
Diabetes mellitus	HbA1c <7% (< 53 mmol/mol)

2. THE CLASSICAL CARDIOVASCULAR RISK FACTORS

2.1. NON-MODIFIBLE RISK FACTORS

AGE

Over 83% of population affected by any coronary heart disease is younger than 65 years. For both sexes, the risk of CVD increases with age. The age limit for the occurrence of CVD risk is over 45 years for men and 55 years for women. With increasing age, decreased CVR, the advantage regarding women's premenopausal, is wasted.

One of the explanations is that the the majority of CVFR have a higher prevalence with age (hypertension, dyslipidemia, obesity, diabetes). At the older ages, women who suffer a heart attack have a lower survival rate than men. The age of the risk of a person with multiple cardiovascular risk factors is the age of a person of the same gender with the same level of risk, but with the ideal risk factors (E.g., smoking, total cholesterol – 4 mmol/L and the BP – 120 mmHg). The age of the risk is an intuitive and easy to understand method of illustrating the probable reduction in life expectancy of a young person with an absolute low risk and the relative risk of cardiovascular disease is exposed to high if preventive measures are not taken. Table 2, showing various combinations of risk factors is included in Annex web in order to provide a more accurate estimation of the age of the risks. The age of the risk is also calculated automatically as part of the latest update of the chart Score.

The age of the risk has been shown to be independent from the used cardiovascular symptoms, which avoid the dilemma of whether we use the risk estimation system based on

total CV mortality or cardiovascular cases. The age of the risk for any population may be used, no matter of the reference and the risk of the secular changes in mortality rate, and thus, it avoids the need for rectification. Currently, the age of the risk is recommended to helps the risk communication, particularly among young people.

Predicting the risk of CVD in 10 years versus the lifelong

Conventional schemes of cardiovascular risk prediction estimate cases of CVR for a period of 10 years. CVR prediction of models during the lifetime identifies individuals at high risk models both in the short term and long term. Such models expose the risk provided in the context and the risks related to combining diseases during the remaining lifetime of an individual.

CVD risk predicting during a period of 10 years currently allows the identification of risk which should benefit from a short-term drug treatment. The problem of the short term risk is that it is mostly determined by age and, consequently, fewer younger people, especially women, have access to treatment. Therefore it has been argued that they in their lifetime risk estimation could improve information about the risk, particularly among young people and women.

There is lack of evidence for the lifetime risks in the treatment decisions. Enough information about the lifetime risk assessment is also and classifications have a significant risk. Assurance in the estimates of lifetime cardiovascular risk for some groups with increased risk of mortality due to combined necardiovasculare causes of disease could be difficult to interpret. The most important fact is that there is a lack of evidence of the benefits of lifelong preventive therapy (ie blood pressure

or lipid-lowering drugs) in young people with short period of action, but it is with greater risks for their lives.

For these reasons, we recommend that risk stratification for the treatment decisions should be based on the duration of action of the risk factor. However, age predisposing and the relative risk could be useful tools in communicating the risk for people with a high level of the factor risk but who have absolute low risk to cardiovascular events in 10 years like some young people. Another approach is also used, if the absolute risk is low and relative risk is high or the age risk indicates the need for advice for the activ life style and awareness that drug therapy may require a person's age consideration. Either – the age risk of a person or risk factors during life – are closer than the absolute relative risk, there is no evidence that provides good basis for decisions of medication.

A family history

The presence in family history CVD endpoints preterm labor, represents a rough indicator, but a simple risk for developing of CVD, reflecting both the genetic traits and a common environment of family members. Death presence in the family history of cardiovascular genesis is associated with an increased risk of cardiovascular disease and an early appearence during their lives. Several studies that have assessed simultaneously the impact of family history and the genetic scores have reported that the family history is associated with a significant incidence of CVD in relation to genetic scores. There are small studies regarding family history which improved the ability to predict the occurrence of CVD beside the conventional risk factors for the disease. There could be one explanation it is that family history may have different connotations and that the conven-

tional risk factors may explain only partially impact of family history. Family history of the premature cardiovascular disease is presented by a simple, cheap database, but which can be also a part of cardiovascular assessment of the risk in all cases.

A family history could be a modifier of risks when assessing the SCORE and it is used to manage its optimal when we are close to a decision threshold: a positive family history encouraging the use of more intense interventions of more intense while a negative family history would be reported as a less intensive treatment.

The genetic markers

The genetic screening and advising are effective under certain conditions, such as family hypercholesterolemia. This subchapter will focus on the genetic screening of the general population with high CVR.

A series of recent studies have identified the genes of the genome of the "candidates" group associated with CVD. Because the effect of each genetic polymorphism is small, most research has utilized it to summarize the genetic component scores. In the specialized literature there is a disagreement concerning the determination of genes and polymorphisms uninucleotidice (SNP) suitable to be included in a genetic risk score and which method should be used for the calculation this score.

The genetic Score combination with incidence of CVD has been studied prospectively and adjusted in order to verify the main CVR factors. Most of the studies revealed a significant combination with relative risks varied between 1.02 and 1.49 that was for each increase in a single unit of the score. The genetic Score ability to predict the cardiovascular events beside the traditional factors CVR (defined by NRI) has been reflected in about

half of the studies. NRI is a statistical measure of quantifying the utility of adding new variables to the equation of risk prediction. The biggest advances in NRI have been observed in the participants with intermediate risk, while participants with high risk prooved to be not a significant improvement or even absence of it. One study has estimated that the additional coronary disease, which may occur in each of 318-th person with intermediate risk, who have been screened, could be prevented by measuring a specific genetic score of CAD, plus establishing the risk factors wich is a very important factor since the frequency of polymorphisms could be different, and results may vary in the population. Recently a genetic risk score based on the 27 genetic variants, allowed to identify subjects with increased risk of coronary heart disease, which mostly will benefit from statin therapy, even after adjusting the family history. However, it is possible that some combinations reported to be modified, and studies require positive results for replication in order to be confirmed.

Nowadays there are also available multiple commercial assays allowing a light assessment almost complete of the genome of an individual and in this sense strong pressure is applied to use this information for the purpose of predicting the genetic risk and transforming genetic testing to an extent of the routine. Considering the lack of an agreement about what should be included and how genetic markers for genetic risk scores should be calculated and uncertainties related to the prediction of cardiovascular risk prediction use of genetic markers for of CVD is not recommended.

Gender

The incidence of ischemic heart disease (IHD) is statistically significant lower in women than in men before the age of

50 years. After the menopause, women CVR increases progressively going similar to the men in the eighth decade of life. In the middle aged population, the risk of IHD is 2-5 times higher in men than in women.

A substudy of the INTERHEART three showed that women make an average of the first acute myocardial infarction (AMI) by 9 years later than men. The associated risk factors to the risk of AMI similarly between women and men are dyslipidemia, smoking, obesity, diet and psychosocial factors. However, there were differences between the sexes: the risk associated with hypertension, diabetes, physical inactivity and smoking history as higher in women. The younger age of occurrence of acute myocardial infarc- in men is explained by the higher levels for plasma lipid and smoking before 60 years for men, especially because smoking is more common in males in most countries. In the past the, estrogens were considered protective factors for atherosclerosis in women, but randomized studies concerning hormone replacement therapy have led to reconsideration of the relationship between the estrogen and the risk of AMI.

The heredity

CVRF is considered family history of the premature BCV, defined as the CVD (eg AMI) in the first degree male relatives <55 years and women <65 years.

2.2. MODIFIBLE RISK FACTORS

Obesity

Obesity is one of a major CVRF with increasing prevalence in developed countries, particularly because of environmental

factors and social particularities of a diet and sedentary. For the definition of obesity multiple measurements are used (Table 8), which can be used additionally or separately. The status of overweight and obesity is correlated with the existence of other CVRF: hypertension, dyslipidemia, diabetes, proinflammatory and prothrombotic processes.

The BMI limitation of the parameter is the fact that neither reflects the fat distribution (visceral versus the subcutaneous) nor differentiates among muscle and fat. There have been, therefore, proposed other parameters such as the repor of the abdominal circumference at the hip circumference in waist circumference (waist to hip ratio). The abdominal circumference (AC) is correlated with the amount of fat intra-abdominal or visceral disease, characterized by high lipolytic activity with overexposure of the liver by the portal circulation from increased levels of fatty acids and secretion of substances with vascular effects directly (leptin, resistin, TNF-alpha, PAI-1).

The ratio of waist circumference at the hip circumference is a parameter derived from abdominal fat in order to report overall body size. In the INTERHEART study, this ratio was correlated significantly and progressively with the risk of AMI.

Table 3. Degree assess indices the of obesity

Body mass index (BMI) (kg/m^2)	**The ratio of weight (in kilograms) and height squared (in meters) (G/h^2)**	**The BMI = 25 to 29.9 kg/m^2 – overweight The BMI = 30 kg/m^2 – obesity The BMI> 40 kg/m^2 – morbid obesity**
Abdominal circumference (Cm)	The circumference measured at cord or halfway between the costal margin and iliac crests	NCEP/ATPIII: >102 cm in men and >88 cm in women IDF: >94 cm for men and >80 cm in women

The ratio at the waist circumference of the hip circumference	The ratio of the two circumferences that reflects the type of obesity	> 0.95 (B) and >0.81 (F) – associate CVR moderately high

IDF – International Diabetes Federation; The BMI – body mass index; NCEP/ATPIII – National Cholesterol Education Program/Adult Treatment Panel III; CVR – cardiovascular risk.

During the last years attention is drawn to the presence of a new cardiovascular risk factor – obesity with normal weight. It is defined by normal body mass index (BMI <25 kg/m2) and excess body fat. The cutoff value above which the body adiposity is increased in these patients has not been established yet, but the largest study published till now defines excess fat based on sex-specific proportions (over 23.1% in men, and more than 33.3%, in women, the adipose tissue of lean body mass).

Which Index of obesity is the best sign that announces a cardiovascular risk?

The body mass index (BMI) [weight (kg)/height (m^2)] can be measured easily and is widely used to define categories of body weight [11]. The amount of body fat distribution is imporant. The adipose tissue stored in the abdomen (abdominal fat) has a higher risk than fat localized under the skin.

There are various types of body fat measurements. Most of the data are available for the BMI, waist, hip circumference report and waist circumference. The optimal level for measuring in waist circumference is the half the distance from the lower edge of upper anterior iliac crest ribs in the vertical position. WHO sills for the waist circumference are the most widely

accepted in Europe. Based on these thresholds, two levels of action are highly recommended:

(I) (I) waist circumference ≥ 94 cm in men and ≥ 80 cm in women is the threshold to which any additional weight should not be added.

(II) waist circumference ≥ 102 cm in men and ≥ 88 cm in women is the threshold at which they should be recommended to lose weight.

These thresholds were calculated based on Caucasian population, and it is obvious that different cut-offs for the anthropometric measurements are required in different races and ethnicities. A meta-analysis conclusion was that both the BMI and waist circumference are strongly associated with continuous to CVD and diabetes mellitus (DM) type 2 [22]. Therefore, BMI is sufficient, in general, in routine practice.

Does „healthy metabolic obesity" exist?

The phenotype of „healthy metabolic obesity" (WHO) which is defined by the presence of obesity in the absence of metabolic risk factors, earned an increased interest. Some studies claim that a specific subgroup of obese people is resistant to metabolic complications such as high blood pressure and insulin resistance. However, the individuals present a higher risk of mortality from all causes compared to the healthy weight of individuals in the metabolic point of view [13, 14]. Long term results of the study support the idea that (Whitehall WHO) it is rather a transitional stage during which it runs in the direction of glucose metabolic abnormalities, and it is a certain „state" [15].

The paradox of obesity established heart disease

At a certain level population, obesity is associated with cardiovascular risks. However, among people with determined CVD there is a contradicting evidence. Systematic evaluations of patients with CVD or undergoing percutaneous coronary intervention suggested „obesity paradox" whereby obesity occurs protectively [18, 16]. That is also applied to HF patients. However, such evidence should not be misinterpreted for recommendation of a BMI greater goal for those with determined CVD, since in this case the reverse causality could be operating base. The cardiopulmonary fitness may influence the relationship between adiposity and obesity paradox in clinical prognosis. Those individuals with incorrect way of life and normal body weight have a higher risk of mortality than the right people, no matter their BMI. Overweight and obese individuals have similar mortality risk compared with individuals with normal weight [17]. In addition, EPIC study results suggest that the sedentary lifestyle influence on mortality seems to be higher than that of high BMI [18].

Treatment goals and methods

CVD risk has a continuously positive connection with BMI and other measures of the body fat. Because all causes of mortality appears to increase due to levels of the BMI <20, we do not recommend such low levels of the BMI as a treatment goals [19].

Although the diet, exercise and changes in behavior are the pillars of the therapy for the overweight and obesity which are often unsuccessful during long-term treatment. The medical therapy with orlistat and/or the bariatric surgery are additional options. A recent meta-analysis indicate that patients undergoing bariatric surgery have a risk of stroke, MI, cardio-

vascular events and reduced mortality compared with non-chirurgicale controls.

Sedentary lifestyle

Sedentary lifestyle is associated with an increased 1.5-2 times CVR for active people. In the INTERHEART study, exercise was defined as the moderate for walking, cycling, gardening, and important for running, football, in both cases taking into account the performance of physical exercise for at least 4 hours a week. The research showed that exercise was a protective factor for the occurrence of AMI of 0.86 (95% confidence interval 0.76 to 0.97).

The mechanisms by which physical activity play a role of a cardiovascular protector are multiple: maintaining an appropriate body weight, HDL cholesterol, increase lowering triglycerides, increasing insulin sensitivity, lowering blood pressure, improving oxygen uptake by the myocardium and widening coronary arteries.

Smoking

Smoking is a major risk factor for the atherosclerotic disease (coronary, carotid, peripheral), including passive smoking which is proven to increase CVR [10]. Stratification risk should be made on the basis of total use of cigarettes (expressed, for example, as a number of packages per year; this index is calculated as the product of the number of packs smoked per day by the number of years of smoking). Cardiovascular risk is bigger when smoking is begun before the age of 15 years old.

Cigarette smoking mecanisms increasing the CVR are: increased total cholesterol and decrease HDL-cholesterol, platelet activation and leukocyte, increased fibrinogen circulating

endothelial dysfunction with the promotion of the crack of vulnerable plaques, increased heart rate and blood pressure, arterial vasoconstriction (including coronary spasm) and the effects of worsening of myocardial ischemia due to carbon monoxide.

Smoking stopping is an effective method of reducing the CVR. In the primary prevention it has been shown that smoking stopping reduces the risk of AMI or stroke and secondary prevention a meta-analysis on the benefits of smoking stopping showed a decrease in mortality in patients with CAD, set with 36 ‰ (RR 0 64 (confidence interval (CI) 0.58 to 0.71 95%) for those who do not smoke.

Alcohol

CVR link with alcohol consumption is more complex. It is described in J correlation among alcohol and cardiovascular effect of volume consumed, with maximum intensive customers CVR and CVR lowest for the moderate drinkers compared to abstainers.

The major risk factors: smoking, hypertension (above 140/90 mmHg), HDL cholesterol (<40 mg/dL), family history of premature coronary heart disease and age (B>45, F>55 years). Coronary artery disease equivalents are peripheral arterial disease, including abdominal aortic aneurysms, carotid disease (transient ischemic injury, stroke, carotid stenosis> 50% asymptomatic), other atherosclerotic cardiovascular disease origins are renal artery stenosis and diabetes.

The optional targets refer to patients at very high risk of death or myocardial infarction, ie patients with an established cardiovascular disease that associates with one or more of the following: multiple factors the major risk, risk factors incom-

pletely controlled, risk factors of syndrome metabolic and patients with acute coronary syndromes.

Thus, it is known that excessive alcohol consumption (> 90 g/day for at least 5 years) is one risk factor for the development of dilated cardiomyopathy (CVD) [23], representing the cause of more than a quarter of cases of CMD, increases the hypertensive risc and, at the same time, the risk of developing the bleeding stroke or subarachnoid hemorrhage.

Excessive alcohol consumption could generate the appearance of arrhythmias, especially supraventricular (atrial fibrillation in the so-called "holiday heart syndrome,").

Not only the absolute values of blood pressure (BP) are CVRF but also pulse pressure (the difference between systolic and diastolic BP), which growth reflects the presence of hypertension predominantly systolic, represents an independent risk factor for the CV mortality (particularly coronary and AVC), especially after the age of 55.

As a result, reduced TA measures of lifestyle modification and pharmacological treatment have a very significant impact on the cardiovascular mortality reduction in primary prevention. Among the lifestyle measures continue to be essential low-salt diet, weight loss and moderate alcohol consumption of ethanol. To all these it should be added, however, pharmacological measures to achieve normal BP values.

Dyslipidemia

Dyslipidemia includes a number of disorders of lipid metabolism with potential for induction and maintenance of the phenomenon of atherosclerotic condition: the abnormal classical elements (increased total cholesterol, LDL cholesterol and decrease HDL-cholesterol) have been recently de-

scribed as the imbalance lipid (apolipoproteins changes, increasing of the number of small dense LDL particles, lipoprotein A, triglyceride-rich lipoproteins and fragments thereof). According to these variables, the classical lipid of risk factors are described too.

Table 4. The classical factors and new components of the lipid balance

Clasical factors	**New factors**
• **Total Cholesterol** • **LDL-cholesterol** • **HDL cholesterol**	• The apolipoprotein B, apolipoprotein AI • Triglycerides, triglyceride-rich lipoproteins fragments • Small dense LDL, oxidized LDL, oxidized LDL autoantibodies • Lipoprotein (A)

Epidemiological studies (Framingham Study, Multiple Risk Factor Intervention Trial – MRFIT, Atherosderosis Risk in Communities – ARIC etc.) showed a direct relationship between serum total cholesterol as well as cardiovascular morbidity and mortality [4]. Cardiovascular risk increases by 2-3% for each percentage increase in total cholesterol. In the INTERHEART study, dyslipidemia is defined by the ratio apoB/apoAI and contributs 49% of the population attributable to the risk. Special populations where there is no increase in CVR isolated hypercholesterolemia (young women smoking), but there is a combination with other CVFR (smoking, hypertension and diabetes) increase the cumulative CVR. Also, clinical studies (LRC-CPPT – The Lipid Research Clinics Coronary Primary Prevention Trial) which used lipid-lowering therapies have shown that the reduction in cholesterol is associated with reduced cardiovascular morbidity and mortality in patients with or without cardiovascular disease identified.

Epidemiological and clinical studies have shown that for the reduction of 30 mg/dL of LDL-cholesterol in plasma there is a decrease of 30% CVR. As a result, the reduction of serum LDL cholesterol is the primary target of therapy to individuals with dyslipidemia, causing marked reduction in risks for coronary death, nonfatal myocardial infarction and revascularization procedure sand stroke.

Guidelines National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) established in patients with cardiovascular disease targets concentrations of LDL cholesterol <100 mg/dL or <70 mg/dL (depending on the accumulation of risk factors).

Unlike LDL cholesterol, HDL cholesterol level is increased by the cardiovascular protective factor. This inverses the relationship between HDL levels and CVR is explained by the HDL rate in reverse cholesterol transport and is mobilized from the periphery to be catabolized in the liver, but also involving other antiatherogen mechanisms: antioxidant function, relieving the inflammatory cascades, protecting procoagulant activity.

A value of serum HDL cholesterol below 40 mg/dl is an important predictive factor for the CVD. The low levels of HDL with metabolic syndrome are elements of hypertriglyceridemia and their combination with other CVFR (abdominal obesity, hypertension, diabetes mellitus) are frequent and leading to an increase in the CVR. The crucial role of dyslipidemia, in particular hypercholesterolemia, developing CVD is documented beyond doubt for the genetic and pathological studies, interventional and observational.

In plasma lipids such as cholesterol and triglycerides circulating in the form of lipoproteins in combination with different proteins (apoproteins). The main carrier of the plasma

cholesterol (LDL-C) is atherogenic. The role of triglyceride-rich lipoproteins are currently under active investigation: Chylomicrons and very low density lipoproteins (VLDL) seemingly are not atherogenic, but in high concentrations these lipoproteins can cause pancreatitis. The remaining lipoproteins (total cholesterol – LDL-C HDL-C +] have recently been identified in Mendelian randomized studies, as pro-atherogenic lipoproteins.

2.3. NEW RISK FACTORS

The total cholesterol and low density lipoprotein

LDL-C is, normally, the majority of cholesterol carriers. At the high concentrations of cholesterol in plasma there is a strong positive combination between the risk of CVD and total cholesterol, as well as combination with LDL-C. This combination is valid for both men and women and for those without CVD and CVD wich is already established.

Evidence lowering plasma LDL-C reduces the risk of CVD and is unequivocal; results of the epidemiological studies and experiments with and without statins, using angiographic and clinical objectives, confirm that reducing LDL-C is a priority for the prevention of CVD. Meta-analysis of several statin trials showed a reduction in CVD by lowering LDL-C dependent-dose. Lowering LDL-C by 1.0 mmol/L is associated with reduced mortality by 20-25% CVD and nonfatal MI.

Apolipoprotein B

The levels of apolipoprotein B (apoB – the main atherogenic apoprotein of lipoproteins) was measured in the same studies with LDL-C. It seems that apoB is a risk marker similar

to the LDL-C. Also, laboratory errors in the determination of apo are fewer as compared with those observed in the determination of LDL-C, in particular in patients with hypertriglyceridaemia [> 3.4 mmol/L (> 300 mg/dL)], but there are no evidence that apoB is a better predictor of CVD than LDL-C.

Triglycerides

Hypertriglyceridemia is an independent significant risk factor associated with hypercholesterolemia but it is a much smaller factor. Risk associated with a much stronger condition than moderate hypertriglyceridemia with very severe condition [> 10 mmol/L (> ~ 900 mg/dL)], is a risk factor for the pancreatitis. No randomized trials were conducted that would provide sufficient evidence regarding targets on levels of triglycerides. Meta-analyzes suggest that the target triglyceride could reduce CVD, in particular subgroups with high triglyceride levels and low HDL-C. Currently, postprandial triglycerides> 1.7 mmol/L continues to be considered a marker of increased risk, but levels ≤ 1.7 mmol/L is not indicative of therapeutic targets.

High density lipoproteins

Low HDL-C is independently associated with increased risk of of CVD. Low HDL-C could even compete with hypercholesterolemia (due to elevated LDL-C), as a risk factor for the development of coronary heart disease. The combination of moderately elevated levels for triglycerides and low HDL-C is very common in patients with type 2 diabetes, abdominal obesity and insulin resistance in patients who are physically inactive. The lipid pattern is also characterized by the presence of small LDL particles, dense and atherogenic. HDL-C <1.0 mmol/L (<40 mg/dL) in men and <1.2 mmol/L (<45 mg/dL) in women can be considered a marker

for increased risk. Mendelian randomization recent studies question the role HDL-C in CVD. Physical activity and other life style factors remain to be an important means to achieve high levels for HDL-C, to the detriment of the drug therapy.

Lipoprotein A

Lipoprotein A – Lp (A)– it is a low-density lipoprotein to which is attached an additional protein called apolipoprotein A high concentrations for Lp (A)are associated with an increased risk of coronary heart disease and myocardial ischaemia and randomized studies Mendelian CVD causal role in support of the Lp (A). There is no randomized trial to confirm that reducing Lp (A)may decrease risk of CVD. Nowadays there is no justification for the general population screening for the Lp (A), but it may be considered in patients at moderate risk to strengthen risk assessment or patients with a family history of early CVD.

Apolipoprotein A1 (apoA1) is one of the major apoproteins, high density lipoprotein. It is beyond doubt that the ratio apoB: apoA1 is one of the strongest CVR markers. However, there is insufficient evidence to support this variable as a therapeutic target. Apolipotroteine level measurement is not accessible to all physicians in Europe because it is more expensive than currently used lipid variables and adds only a moderate surplus of information, based on lipid parameters applied at the moment, and it is therefore not recommended.

Lipoprotein variables

LDL-C

LDL-C could be measured directly, but in most of the studies in several laboratories LDL-C is calculated using the Friedewald's formula

- in mmol/L: LDL-C = Total cholesterol – HDL-C (0.45 x triglycerides)
- in mg/dL: LDL-C = Total cholesterol – HDL-C (0.2 x triglycerides)

The result is valid only when the concentration of triglycerides is <4.5 mmol/L (<~ 400 mg/dL). Similar problems may be encountered when LDL-C level is low [<1.3 mmol/L (<50 mg/dL)]. Correct methods may be less susceptible to plasma triglyceride levels. Recent data have shown that the direct methods can be influenced when triglyceride levels are high. Also, the values obtained by using different direct methods are not necessarily identical, especially for low and high LDL-C.

Non-HDL-C (the exact evidence-based food nonrepaus)

Non-HDL-C contains cholesterol, low density and intermediate density lipoprotein and VLDL, thus collecting all information concerning the pro-atherogenic lipoproteins. Non-HDL-C predict the CVD risk better than LDL-C. The limits of LDL-C can be transferred to the limits of non-HDL-C by adding 0.8 mmol/L (30 mg/dL). Calculated by simple lowering of total cholesterol[2], HDL-C, non-HDL-C, triglycerides do not require the concentration of <4.5 mmol/L. Therefore, it is really a method of calculating LDL-C improved for the patients with a elevated serum triglycerides and also has an additional advantage, because there is no need for patients to abstain from food before collecting of blood for analysis. It turned out the role of non-HDL-C as a therapeutic target, since non-HDL-C captures information on all atherogenic lipoproteins containing ApoB. We suggest that this is a reasonable thera-

[2] Non-HDL-C = colesterolul total – HDL-C

peutic alternative, while acknowledging that it was not a goal in therapeutic trials. Recently it has been shown that the remaining cholesterol [Total cholesterol – (HDL-C + LDL-C)] is a causative factor in atherosclerotic condition Mendelian randomized studies. This parameter is not suggested as a predictor and a therapeutic target.

Table 5. The targets for the LDL-C and non-HDL-C according to NCEP (ATP III)

Risk Category	The target for LDL-C (mg/dl)	The target for non-HDL-C mg/dl	
High	Coronary heart disease or equivalents (10 year risk – 20%)	< 100 Optional < 70	< 130 Optional <100
Moderately high	More than 2 risk factors, risk to 10 years – 10-20%	< 130 Optional < 100	< 160 Optional KBO
Moderate	More than 2 risk factors, with 10-year risk <10%	< 130	< 160
Low	0-1 risk factors	< 160	< 190

Exclusion of secondary dyslipidemia and familial dyslipidaemia

The presence of secondary dyslipidemia in other diseases must be excluded before starting treatment, because treatment of the disease will favor hyperlipidemia in the absence of antilipid therapy. This is especially characteristic in hypothyroidism. Secondary dyslipidemias can also be caused by alcohol abuse, diabetes, Coushing syndrome, liver and kidney disease, treatment with certain drugs (eg. Steroids). Patients who may have genetic dyslipidemias, such as familial hypercholesterolemia, can be identified due to extreme lipid abnormalities and/or because of family his-

tory. If possible, these patients should be sent to experts for evaluation. Treatment recommendations in this guide may not apply to this specific type of patients, which is an approach in more detail in guide about dyslipidemias of European Society of Atherosclerosis. An LDL-C level >5.1 mmol/L (>200 mg/dL) in patients who are under the specific therapy requires careful consideration of a possible familial hypercholesterolemia. However, in the presence of early CVD or family history, a possible familial hypercholesterolaemia could be considered to lower LDL-C levels.

Diabetes

Insulin resistance, hyperinsulinemia and hyperglycemia are pathophysiological and associated with atherosclerotic cardiovascular disease. Even outside the defining blood glucose for diabetes, there is a relationship between glycemia and RCV. For non-diabetic values, in classifying patients' values are used both fasting values and oral glucose tolerance test (OGTT) (with measurement values at two hours after administration of 75 g glucose) (Figure 1) [20].

People with diabetes are, on average, subjected to a double risk of CVD. A simple questionnaire on DM can guide us which

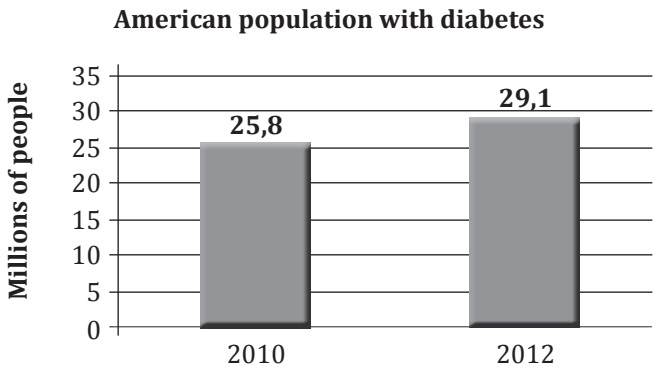

Fig. 1. The incidence of diabetes patients in the USA

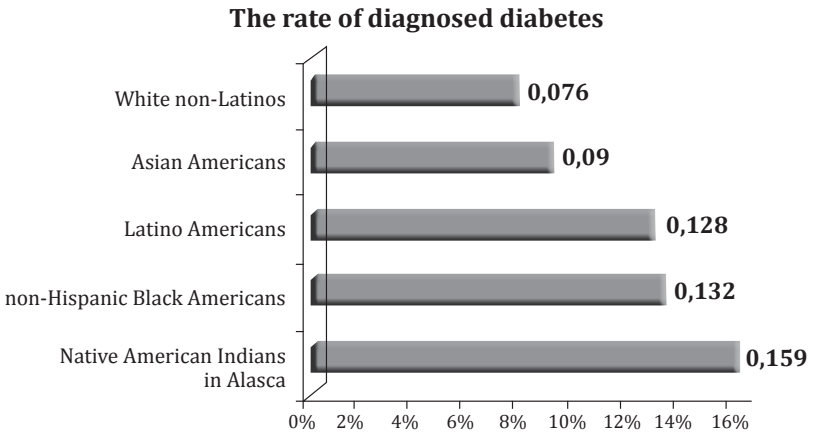

Fig. 2. The rate of diagnosed diabetes patients in the US dependency race

patients without CVD need to be tested for diabetes. Keeping as close to the recommended values of BP, lipid levels, blood glucose, HbA1c is important to prevent CVD. A clear reduction in CVD mortality in patients with diabetes occurred after better management of risk factors, although the increased prevalence of diabetes continues to create pressure on all health care systems. Targets, in particular glycemic control and lipid control in some cases, should be applied with less stringent to elderly parients with diabetes, people with longer duration of diabetes, people with evidence of CVD and for children.

There is some evidence for a very high relative risk in younger individuals with T2DM (age 40 years) and additional guidance regarding the necessary care. Except for glucose management, prevention of CVD has the same general principles as in people without diabetes. Achieving a low BP and LDL-cholesterol and low total cholesterol concentrations are particularly important objectives. Many of the goals of treatment are strict-

er for patients with DM. Characteristic of patients with T2DM is that they have many risk factors for CVD, and each treatment is in accordance with the existing instructions.

Lifestyle changes

ESA (European Society of Cardiologists) and the European Association for the Study of Diabetes said that lifestyle management is the first step for prevention and correction of DM. Most patients with diabetes are obese, so weight control is a central component. More types of diets can be adopted, where the predominance of fruits, vegetables, whole grains and sources of protein with low fat is more important than the exact proportions of total energy provided by major macronutrients. The amount of salt should be restricted. Specific dietary recommendations include limited consumption of saturated and trans fats, and alcohol consumption monitoring carbohydrates and increased consumption of dietary fiber in the diet. A Mediterranean-type diet is acceptable if the sources of monounsaturated fats are derived from oil. A combination of aerobic and resistance exercise is effective.

Table 6. Classification of glycemic control guidelines according to IDF/WHO

Classification	Glicemie à jeun (mg/dl)	2:00 glucose OGTT (mg/dl)
Normal	< 109	< 140
Glicemy à jeun	110-125	< 140
Impaired glucose tolerance	< 126	140-199
Diabetes	> 126	> 200

In the INTERHEART study, the presence of diabetes mellitus (DM) contributed 10% to the population equivalent. Thus,

in patients with type 1 diabetes, increased 2-3 times CVR occurs only in people who developed diabetic nephropathy, whereas in type 2 diabetes, CVR is not conditioned by the appearance of other complications. In addition, diabetic patients more frequently associated with other CVRF: Obesity, hypertension, dyslipidemia, increased plasma fibrinogen.

Controlling these risk factors and glycemic values must be aggressive in these patients (LDL-cholesterol value – 100 mg/dL, and the optimal BP <130/80 mmHg). Optimal control of diabetes leads to decreased rate of cardiovascular complications in preventing progression of diabetes and glycemic control. How to promote and maintain the TA is less known, however, the strengthening of healthcare providers in finding sustainable ways to raise BP is essential. Smoking increases the risk of diabetes, CVD and premature death and should be strongly discouraged. Lifestyle changes can prevent the development of diabetes in people at high risk, which in turn lowers microvascular and macrovascular risk probability.

Cardiovascular risk

At diagnosis or people with a short duration of illness, DZ doesn't prezent a risk factor of CVD. In general, the risk of CVD risk approach equivalence after a decade or people with proteinuria and low eGFR (estimated glomerular filtration rate). Recent data suggests that patients who develop diabetes at a younger age have a high level of complications. People with pre-existing diabetes and CVD have higher vascular risk than people with CVD without diabetes and a substantially lower life expectancy.

Statins are recommended for all new cases of diagnosis of T2DM, after a certain age (40 years currently recommended).

This recommendation reflects life period with the highest vascular risk at mentioned patients. However, some patients with DM at 40-50 years may have a decreased risk of CVD in 10 years, due to BP and lipid levels at normal levels, being non-smoking, and in such cases an important role is the way of thinking of the doctor. Equally, in some 40 years' patients with type 2 diabetes with evidence of target organ injury or significant risk factors may be given statins.

Glucose control

UKPDS – prospective study of diabetes conducted in the UK – has established the importance of decreasing intensive glucose levels in reducing CVD risk in new patients diagnosed with diabetes, but not receiving modern therapy to reduce BP and lipid levels, but the best evidence supporting metformin, which makes it become the first-line drug therapy. Three recent studies have been conducted in order to see whether cardiovascular events can be reduced further through more intensive treatment of glucose levels and a reduction in HbA1c levels. The results were surprising, with sudden increases of CVD deaths in action to control cardiovascular risk in diabetes (ACCORD) and tended to increase in CVD death (VADT). The results prompted concerns about intensive lowering glucose levels and the opportunity to follow strict records of it, especially in older people with diabetes and people with existing CVD. Subsequently, a meta-analysis of intensive control of glucose, including data from the UKPDS prospective clinical Piogitazone Study about macrovascular events (PROactive), ACCORD, Action in Diabetes and Vascular Disease, Evaluation Control Preterax and Diamicron MR (ADVANCE) and VADT, showed significant reductions of nonfatal MI and CVD events,

but no effect on stroke or total mortality. Additional analyzes of these studies suggested that the benefits of CVD decreased HbA1c by an average of 0.9% over 5 years, and it was much less than normal cholesterol and BP reductions observed by administering statins and antihypertensive agent. Four recent studies with new therapy of diabetes DPP-4 and GLP-1 in patients with DM and CVD high existing risk demonstrated safety of use, but not superiority regard to the risk of CVD. There was however an increase in the rate of hospitalization of patients with heart failure (HF) with saxagliptin when evaluating the vascular results occurred in patients with diabetes – Thrombosis study in Myocardial Infarction (TIMI savor). Very recently, the empagliflozin inhibitor showed a substantial reduction in deaths from CVD (38%), all-cause mortality (38%), and the hospitalization of HF (35%) compared to standard treatment, suggesting that the SLGT2 inhibitor use should appear earlier in the management of patients with diabetes and CVD. The model of the study by non-fatal MI and stroke, which were not reduced by active treatment, and rapid separation of the mortality curves suggests that the beneficial mechanism referred more to the cardiorenal hemodynamic effects than atherothrombotic actions or effects reducing the level of glucose. It requires more research to understand the study results.

High blood pressure

The high level of blood pressure is a leading risk factor for the worldwide disease rate, accounting for 9.4 million deaths and about 7.0% of disability adjusted globally in 2010. Compared to 1990, the impact of increased levels of TA increased by 2.1 million deaths. Overall, the prevalence of hypertension is 30-45% in adults aged ≥ 18 years with a steep increase with aging.

The high level of blood pressure is a risk factor for coronary artery pathology, pathology of the peripheral arteries, chronic kidney disease and atrial fibrillation. The risk of death either coronary artery disease or stroke increased progressively and linearly from a lowest level – 115 mmHg – the systolic and upward 75 mmHg diastolic, although the absolute risk curves flatten the lower bands blood pressure.

Office blood pressure is recommended for screening and diagnosis of hypertension which should be based on at least two measurements to visit and at least 2 visits. If the blood pressure is slightly elevated, measurements must be made over a period of months to get an acceptable definition of normal individual blood pressure and decision for drug treatment. If blood pressure is significantly increased or accompanied by target organ damage, cardiovascular factors or other established cardiovascular disease or kidney disease, repeated measurement of blood pressure is required in a shorter time in order to make decisions for treatment.

Measuring office blood pressure

Auscultatory or oscillometric semiautomatic sphygmomanometers must be valid and regularly checked. Blood pressure measuring is preferred on the upper arm and the dimensions must be adapted to arm circumference. If possible, several automatic recording measurements of blood pressure is made in the office, the patient is placed in an isolated room and this method could be considered as a better means of reproducing office blood pressure, closer than data provided at ambulatory blood pressure measurements throughout the day. Measuring blood pressure outside the medical office is usually assessed by ambulatory monitoring of blood pressure or blood

pressure measurements at home, performed by itself and is usually lower than blood pressure office, and the difference increases with office blood pressure increasing.

The following principles and general comments should be considered:

- The procedure must be adequately explained to a patient with oral and written instructions;

- Interpretation of the results must take into account the fact that the reproduction of blood pressure measurements outside medical practice is good for 24 hours, day and night average blood pressure, but less for shorter periods;

- Measurement of blood pressure in ambulatory and home blood pressure monitoring provide information on the somewhat different blood pressure levels. These two methods should therefore be regarded as complementary rather than competitive;

- Devices must be validated and calibrated regularly, at least once every 6 months;

- Both ambulatory and home blood pressure measured values are closely related to prognosis.

Blood pressure at night seems to be a stronger predictor than daytime blood pressure. Blood pressure from outside medical office may be useful not only in untreated patients but also those treated in order to monitor treatment effects and enhance the quality of the drug treatment.

The diagnostic assessment in hypertensive patients

Laboratory tests should include assessment of hemoglobin, fasting plasma glucose and serum tests for total cholesterol, HDL-C, triglycerides, potassium, uric acid, creatinine (kidney function setting) and thyrotropin (menopause in women). Uro-

gram should include albumin: creatinine ratio test dipstick, sediment and proteinuria dipstick test is positive if quantitative. Echocardiography and funduscopy may also be considered. Routine measurement of biomarkers additional and/or vascular imaging methods are not recommended.

Risk stratification in hypertension

The decision to start pharmacological treatment depends not only on the blood pressure and cardiovascular risk, fully described in Section 2. However, even subclinical organ damage in hypertension predict cardiovascular death independently of SCORE, and the combination can improve risk prediction, particularly in subjects with moderate risk (SCORE – 1-4%). Echocardiography is more effective than ECG diagnosis of left ventricular hypertrophy as well as prediction of cardiovascular risk and help the more precise stratification of overall risk and prescribe proper treatment. Albumin: creatine ratio >30 mg/g in the urine is an indicator of subclinical hypertensive patients.

Lifestyle changes

Improving lifestyles, body weight control and regular physical activity may be sufficient for patients with a higher-normal degree of hypertension and should be always recommended in patients receiving antihypertensive treatment, as along as the way might reduce the dose of these drugs to control blood pressure levels. Specific change in the lifestyle of hypertensive patients is the salt intake restriction. At the individual level, the effective salt reduction is not easy. At least, this advice should be given to the patient to avoid adding salt or consumption of highly salted products. The result of the decrease in blood pressure levels is a potassium levels increase,

which was seen in the DASH diet (rich in fruits, vegetables and dairy products with low fat content and a small amount of cholesterol and saturated fat), patients with hypertension in general should be advised to eat more fruits and vegetables and reduce the intake of saturated fat and cholesterol.

Antihypertensive drugs

The large number of randomized methods used to lower blood pressure, both active treatment or placebo, using different compounds, confirm that: the greatest benefits in the treatment of decreasing blood pressure are due to the lower level by themselves and are largely independent of medicines used; thiazide diuretics and related diuretics thiazides (chlorthalidone and indapamide), ß-blockers, calcium antagonists, inhibitors of angiotensin-converting enzyme and blockers of the angiotensin receptor may decrease adequate blood pressure levels and reduce the risk of deaths of cardiovascular genesis and morbidity. However, these drugs are all suitable for the start and control of blood pressure levels either alone or in combination. Some aspects should be taken into consideration for each group of antihypertensive drugs.

Position of ß-blockers as the first choice drugs for decrease in blood pressure levels has been made in discussions. A meta-analysis of 147 reports of randomized trials showed only a slight inferiority of ß-blockers in preventing stroke (17% reduction instead of 29% reduction with other agents), but a similar effect in preventing coronary heart disease and heart failure was of greater efficiency in patients with a recent heart attack. In any case, since the ß-blocking agents induce an increase in weight, they have an adverse effect on lipid metabolism increase (compared with other drugs), and with the incidence of

diabetes, they are not preferred in hypertensive patients with multiple metabolic risk factors and conditions that increase the risk of onset of diabetes (such as obesity, high fasting glucose) or the incidence of diabetes, they are not preferred in hypertensive patients with multiple risk factors and metabolic conditions that increase the risk of onset of diabetes (such as obesity, high fasting glucose). However, this does not apply to vasodilating ß-blockers, such as carvedilol and nebivolol, which have less or no dysmetabolic action and inducing a reduced incidence of diabetes compared with ordinary ß-blockers.

Thiazide diuretics are considered as diabetogenic and dyslipidemic effects, especially when used in high doses. Thiazides have often been administered together with ß-blockers in studies that have shown a high risk of producing diabetes.

Angiotensin converting enzyme inhibitors and angiotensin receptor blockers are particularly effective in reducing left ventricular hypertrophy, microalbuminuria and proteinuria reduction, preservation of renal function and prevents end stage renal disease. Evidence of the benefits of other classes of agents are more limited. α1-adrenoblocants agents acting at central level (α2-adrenergic agonists, and receptor agonists imidazolinium), medication Antialdosterone and renin inhibitor, aliskiren have less effect in lowering blood pressure in hypertension, but no data documenting their ability to improve cardiovascular capacity. All these agents have been frequently used as a supplementary drug in studies documenting cardiovascular protection and can thus be used for combination therapy in addition to the recommended combinations.

Preferred drugs are effective 24 hours. Simplification of treatment improves adherence to therapy, and effective control for 24 hour blood pressure control is important in terms of

prognosis, in addition to the blood pressure control in the doctor's office. Long acting drugs also minimize variations in blood pressure, which can provide protection against the risk of progression of organ damage and cardiovascular events. No class of drugs lowering overall blood pressure is feasible and there is no evidence that different choices should be made based on age or sex (except the use of angiotensin converting enzyme inhibitors of angiotensin and angiotensin receptor blocker in women of childbearing age because of possible teratogenic effects). Some agents should be considered as the preferred choice in specific circumstances as they were used in studies involving patients with these conditions or due to a higher effectiveness in certain types of organ damage.

Compound treatment

Pressure control for most patients is necessary in order to administer the combined therapy. Adding a drug from another class may be considered a recommended treatment strategy, unless the initial drug must be withdrawn because of side effects or lack of any effect of blood pressure lowering. Excessive reduction of blood pressure after combining drugs from two different classes is about five times larger than doubling the dose of a single drug and the side effects reduction associated with other drugs. The combination of two drugs may also offer advantages to start treatment, especially in patients with a very high risk which was earlier established. Pressure control may be desirable. Test samples are performed to obtain the result mainly from the combination of a diuretic with an ACE inhibitor, an angiotensin II receptor blocker or a calcium antagonist. Despite the evidence of reduction in earnings, a ß-blocker/diuretic combination favors the development of diabetes and

this combination should be avoided, unless it is necessary for other reasons. The combination of an inhibitor of the enzyme converting angiotensin II and angiotensin II receptor blocking agent is not recommended. The specific benefits of such a combination in patients with nephropathy and proteinuria (due to a higher antiproteic effect) are to expect confirmation in event-based testing and if such a combination is used, then patients should be closely monitored. For 15-20% of patients with hypertension, while the combination of the three drugs is required pressure control is performed so that a combination of three anti-hypertensive lower fixed doses in a single tablet can be enhanced, because reducing the number of tablets per day improves adhesion, which is low in patients with hypertension. The most rational combinations appear to be a blocker of the renin-angiotensin system, a calcium antagonist and a diuretic effective dose.

There are few randomized trials comparing different treatment goals. Hence, any recommendation on targets derived largely from studies obtained by randomized controlled trials which compared largely different treatment regimens and reported levels of achieved blood pressure.

Table 7. Grugs indicated in case of hypertension in special situations

Conditions	Drug
Asymptomatic organic disorders	
LVH	ACE-I, calcium antagonists, ARB
Asymptomatic atherosclerosis	Calcium antagonists, ACE-I
Microalbuminuria	ACE-I, ARB
Renal dysfunction	ACE-I, ARB
Cardiovascular events	
Brain attack	Any drug that lowers BP

Old myocardial infarction	ß-blockers, ACE-I, ARB
Angina pectoris	ß-blockers, calcium antagonists
Heart failure	Diuretics, ß-blockers, ACE-I, ARB, mineralocorticoid receptor antagonists
Aortic aneurysm	ß-blockers
Fibrillation prevention	I believe ARB, ACE-I, ß-blockers or antagonists mineralocorticozi
Atrial rate control	ß-blockers, calcium antagonists nonhidroperidinici
ESRD/proteinuria	ACE-I, ARB
Peripheral arterial disease	ACE-I, Calcium antagonists
Other special situations	
The elderly	Diuretics, calcium antagonists
Diabetes	ACE-I, ARB
Pregnancy	Methyldopa, ß-blockers, calcium antagonists
Dark skinned people	Diuretics, calcium antagonists

There is sufficient evidence to recommend that systolic blood pressure should be lowered to 140 mmHg and diastolic blood pressure to 90 mmHg in all cases where hypertensive patients were children. Evidence is lacking in the elderly hypertensive patients, the benefit of lowering systolic blood pressure to 140 mmHg has not been tested in randomized trials. A target of 90 mmHg in diastolic blood pressure is always recommended, except in patients with diabetes, in this case the recommended value is 85 mmHg. However, it must be found that diastolic blood pressure between 80 and 85 mm Hg are generally well tolerated and safe. Analyses obtained from studies conducted widely, although suffering from the limitation imposed by the comparison groups, non-randomized, suggest that at least in the case of high-risk hypertensive patients we find that there is no advantage in lowering systolic blood pressure to 130 mmHg, except, perhaps

if the is a risk of stroke. J-curve phenomenon reaching to 130 mmHg systolic blood pressure can not be ruled out, mainly in patients with advanced atherosclerotic disease and/or fragility. Publication of primary results of systolic blood pressure intervention trials (SPRINT), comparing treatment benefit in systolic blood pressure to a target of 120 mmHg with the treatment of a target of 140 mmHg, contested the above recommendations aimed at high-risk patients without Diabetes. Frail elderly people were poorly represented in this process. Targeting a systolic blood pressure of 120 mmHg versus 140 mmHg (average 121 mmHg and 136 mmHg, respectively, in the first year), resulted in lower rates of fatal cardiovascular events while death was caused by other reasons. However, high rates of adverse effects (hypotension, syncope, electrolyte disturbances and acute renal failure) have been observed in the intensive treatment. The clinical trial has opened a strategy close to usual care with frequent visits which can help you adjust antihypertensive treatment if serious side effects appeared, and this minimizes the risk of events. SPRINT is generally found problematic to patients with diabetes and the elderly. Basing on the current data it can still be prudent to recommend lowering systolic/diastolic values in the range of 130-139/80-85 mmHg, and possibly close to lower values in this range in all hypertensive patients.

Psychosocial factors

Psychosocial factors, as they defined in the INTERHEART study, include professional or personal stress, financial stress, stressful life events, depression, perceived ability to life situations control, lack of social support. Study results showed that psychosocial factors may contribute a significant proportion to the risk of AMI values in this range in all hypertensive patients.

Clinical depression has been shown to be associated with an increased risk of CVD in both sexes, and in patients with established CVD and depression increased risk of recurrent cardiovascular events. Another proven CVRF is the poor socioeconomic status correlated with incidence and prevalence of CVD and implicitly with CVD mortality.

Low socioeconomic status, level of education as defined below, low income, having an unprestigious job or living in a poor residential area, confer an increased risk of coronary heart disease; relative risk (RR) of coronary heart disease mortality being 1.3-2.0. Compared with Framingham risk score, adding social deprivation CVR assess made it possible to reduce substantially the unassigned risk.

People isolated or disconnected from those around them are at an increased risk of developing coronary heart disease, which becomes the cause of their death. Similarly, lack of social support increases the risk of coronary heart disease and its prognosis worsens.

Acute mental stressors can serve as triggers of acute coronary syndrome. These stressors include exposure to natural disasters and personal stressors (eg emotional destruction or other serious life events), which show strong negative emotions acute (eg outbursts of anger or pain). The death of the major incidence of myocardial infarction increases 21 times within the first 24 hours, with a steady decline in the coming days. Chronic stress at work (eg working hours, overtime extensive psychological overloads, unfairness and tension in the workplace) predicts the appearance of premature coronary heart disease in men with a relative risk of 1.2-1.5 . In addition, family-term stressful conditions increase the risk of coronary heart disease (RR – 2.7 to 4.0). Clinical depression and depressive symptoms predict the

occurrence of coronary heart disease (RR – 1.6, respectively 1.9) and may worsen prognosis of (RR – 1.6, respectively 2.4). Vital exhaustion, most likely, is the somatic symptoms of depression, which contributes significantly to the occurrence of coronary heart disease (population attributable risk is 21.1% of women and 27.7% of men). Panic attacks also increase the risk of coronary heart disease incidence (RR – 4.2). Anxiety is an independent risk factor for coronary heart disease, the incidence of RR – 1.3, and the cardiac death due to myocardial infarction (OR 1.2), and other cardiac events (OR 1.7). Meta-analyzes have reported a risk 1.5 times higher of CVD incidence, a 1.2 times higher risk of coronary heart disease and 1.7 times bigger for stroke in patients with schizophrenia and a risk of 1 3 times higher for heart attack even after adjusting for depression in patients with post-traumatic stress disorder accumulated.

Hostility is a trait characterized by expressing distrust, anger and tendency to engage in aggressive situations and maladaptive social relations. A meta-analysis confirmed that the anger and hostility are associated with a small but significant risk of cardiovascular events in both healthy population and population with cardiovascular disease (RR – 1.2). Type D personality ("hard") implies a sustainable tendency to experience a broad spectrum of negative emotions (negative affectivity) and to inhibit self-expression in relations with others (social inhibition). Type D personality has been demonstrated to predict a vague prognosis in patients with coronary heart disease (RR – 2.2). Most commonly, psychosocial risk factors are dispersed in individual and group. For example, both women and men with a low socioeconomic status and/or a chronic stress are more likely to be depressed, hostile and socially isolated. INTERHEART study showed that a group of psychosocial

risk (ie social isolation, stress at work or in family life and depression) are associated with an increased risk of myocardial infarction (RR – 3.5 for women and 2 3 men). The population attributable risk was constituted 40% of women and 25% of men.The mechanisms linking psychosocial factors to those with cardiovascular disease include: unhealthy lifestyle (smoking frequently unhealthy foods, reduced physical activity) and low responsiveness to the recommendations on lifestyle changes or cardiovascular medication. In addition, depression and/or chronic stress are associated with alterations in autonomic function in the hypothalamic-pituitary and other markers, endocrine homeostasis and inflammatory processes that affect endothelial function and myocardial perfusion. The increased risk in patients with depression may also be a result of the adverse effects of tricyclic antidepressants.

Evaluation of psychosocial factors in patients and in people with cardiovascular risk factors should be taken into consideration, to be later used as a modifier of risk in predicting cardiovascular risk, especially in people with SCORE risk near the threshold limit. In addition, psychosocial help to identify possible barriers to lifestyle changes and adherence to medication are needed. Standardized methods are available to assess psychosocial factors in multiple languages and countries. Alternatively, a preliminary assessment of psychosocial factors can be done by collecting anamnesis, as shown in Table 7.

Cardiovascular risk factors described recently

In general, the biomarkers can be divided into inflammatory [for example, high sensitive C-reactive protein (CRP), fibrinogen], thrombotic agents (e.g., homocysteine, phospholipase A2 associated lipoprotein) and associated markers glu-

cose-lipid (e.g., apolipoproteins) and organospecific markers (for example kidney, heart). However, in order to estimate the global cardiovascular risk, these differences (classifications) are not generally relevant. Also, in terms of a risk stratification (ie, prediction of future cardiovascular events), whether a biomarker is associated causally with CVD may be a marker of preclinical disease is equally irrelevant. Among the largest biomarkers study and discussion is highly sensitive C-reactive protein. This biomarker has shown consistently in large prospective studies features of a risk factor for metabolic factors that integrates multiple low-grade inflammation and the relative risk approach that of classical cardiovascular risk factors. However, its contribution to the existing methods for cardiovascular risk assess is probably low.

Meta-analyzes and systematic reviews suggest that the vast majority of hemodynamic and urinary biomarkers have no or a limited capacity to improve risk classification. However, the extent to which they were tested for their ability to contribute to risk stratification varies considerably, with strong evidence of reported interference. Organospecifics can still be useful biomarkers to guide therapy in certain circumstances (eg albuminuria in hypertension or diabetes can predict renal dysfunction and may provide Renoprotective intervention). If, despite these recommendations, biomarkers are used as modifiers of risk, it is important to note that a similar unfavorable biomarker may be associated with a higher risk, while a favorable profile is associated with a calculated low risk. The extent to which biomarkers influence the calculated risk is generally unknown, but in literature it is almost universally lower than the relative risk (adjusted) reported by these biomarkers. Therefore, in these patients, especially those with moderate risks,

profile, only small adjustments are justified risk, and patients who clearly have a high or low risk should not be reclassified basing on biomarkers.

Homocysteine

The first association of increased concentrations of homocysteine (Hcys) atherosclerosis and serum was based on autopsy studies in patients with homozygous deficiency of necessary enzymes in the metabolism of homocysteine (for example cystathione-betasintetaza, methylenetetrahydrofolate reductase). In patients with severe atherosclerosis these shortcomings develop since childhood, and many of them show a first MAI until the age of 20 years. Hcys has a toxic impact on the endothelium, and it's prothrombotic increases collagen synthesis and decreases availability of nitric oxide. In the lab, hyperhomocysteinemia is defined by a higher level of Hcys 12-16 umol/1. A level between 15 and 100 umol/1 is considered moderately increased and over 100 umol/1 is severely increased. The main cause of hiperhomocisteinemiei remains genetics. The main mutation found in MTHFR C677T mutations in the population has gene type, ie A1298C. Plasma levels Hcys in patients with genetic defects may be increased in the metabolism of folate deficiency or folic acid metabolism altered with hypothyroidism, renal insufficiency, psoriasis, etc. These patients have an increased atherosclerosis risk in coronary arteries, peripheral and cerebral. Also homocysteine level is an independent predictor of mortality in patients with angiographically documented coronary artery disease. Serum can be restored to normal by treatment with folic acid, vitamins B1, B6.

Lipoprotein A

Lipoprotein A – Lp (A)– which is a particle containing an ester of cholesterol and apolipoprotein B 100 of LDL-cholesterol differs by the presence of glycoprotein Apo, plasminogen analogue. In vitro and in vivo have been shown the promotion of thrombogenesis and atherogenesis, representing independently a moderate CVRF. A meta-analysis including 31 prospective studies reported a relative risk of 1.5 (95% CI, 1.3-1.6) in patients with elevated Lp (A)in the upper third to the bottom third of the distribution of Lp (A)(corresponding to average values in these categories 50 versus 5 mg/dL). More recently, a meta-analysis including 126 634 individuals, found an independent association between Lp (A)and risk of IHD, but with a modest increase in risk – relative risk of 1.13 (95% CI, 1,09-1.18) to 3.5-fold increases in the value of Lp (A). The relative risk of ischemic stroke was 1.10 (95% CI, 1.02 to 1.18). The coexistence of high levels of LDL with one low HDL or HTA CVR further increase in patients with elevated Lp (A).

Proinflammatory factors

Each atherosclerotic lesion feature represents a certain stage of an inflammatory process pressure, which entitles the Russell Ross in 1999 to write the first lines of his article: "Atherosclerosis is an inflammatory disease." This complex process that occurs at the level of vascular atherosclerotic plaque can turn into vulnerable plaque and the answer to the traditional risk factors favoring a first time endothelial dysfunction.

The clinical evidence related to this case include increased circulating levels of inflammatory markers in atherosclerotic vascular disease, especially in conditions of instability (eg fibrinogen, C-reactive protein, serum amyloid A41, inter-

leukin – 642, interleukin – 1843 TNF- cc, pregnancy associated plasma protein – PAPP-A44, leukocyte adhesion molecules ICAM-1, VCAM, selectins 45 etc.). This theory is supported by epidemiological studies that have demonstrated the prognostic implications of increased circulating inflammatory markers in correlation with physiological studies described above. Among all of the possible inflammatory markers, the PCR was studied in detail [26]. Produced in the liver in response to interleukin-6, CRP is an acute phase reactant, which was originally considered rather as a witness of a "passive" vascular inflammation. Studies in recent years have provided evidence to support the idea that CRP plays, in fact, an active role in atherogenesis.

In addition to coronary events, highly sensitive CRP (English. Hs-CRP) is a predictor of impaired cerebrovascular and peripheral vascular disease and sudden death [23]. The association between metabolic syndrome and increased PCR and the additive effect of these elements risk marker was proven in predicting coronary risk and the development of diabetes.

In 2003, was published a scientific statement by the American Heart Association and the Center for Diseases Control and Prevention, in which it was emphasized that as inflammatory markers and current evidence supports the introduction into clinical practice only CRP, ie type testing hs-CRP expressed in mg/l. Risk categories were relatively proven and hs-CRP levels are: low <1 mg/dl, average – 1-3 mg/dl, high> 3 mg/dl.

Thus, the primary prevention is dosing in patients with CVR indicated at 10 years between 10 and 20%. Dosing is not required in patients with CVR >20% or demonstrated in patients with atherosclerotic disease where intensive treatment should be done anyway, regardless of hs-CRP; the risk <10% is unlikely to be a risk, appreciated by hs-CRP.

The secondary prevention in patients with stable coronary disease or acute coronary syndromes, hs-CRP may be useful as an independent marker for assessing recurrent events (cardiovascular death, MI, restenosis after PCI); there is still evidence that therapeutic interventions with proven efficacy in the secondary prevention should be modified depending on the level of hs-CRP.

Prothrombotic factors

Thrombosis plays a central role in the pathogenesis of acute coronary syndromes, processes involving both platelets and clotting factors. A hemostatic important factor associated with the risk of IHD is fibrinogen.

Thus, the high level of fibrinogen was significantly associated with independent lipid profile of the CVR. Other haemostatic factors are correlated with increased CVR activated factor VII, plasminogen activator inhibitor-1 (PAI-1), tissue plasminogen activator (tPA), von Willebrand factor (which is a marker of endothelial dysfunction).

Relatively common in the population of genetic defects that lead to a procoagulant potential are known as thrombophilia (e.g., Factor V Leiden mutation, the mutation Factor II – prothrombin G20210A, deficits of protein C, S or antithrombin III).

Preclinical Measurement of vascular lesions

• Routine screening and imaging methods for predicting of the cardiovascular events are generally not recommended in clinical practice.

• imaging methods can be considered as risk modifiers cardiovascular risk assessment, for example in people with car-

diovascular risk factors calculation based on conventional risk assessment limits the major decision threshold.

Although the majority of BCV can be explained by traditional risk factors in all cases there is a substantial variation in the degree of atherosclerosis. Thus, interest in using noninvasive imaging techniques to improve cardiovascular risk assessment continued. In people with calculated cardiovascular risks based on the major risk factors, conventional, about threshold decision, some imaging techniques can be considered as risk modifiers for improving risk prediction and decision making.

Coronary artery calcification

Coronary artery calcification was analyzed by means of electron beam CT scan or several incidences. Calcifications indicate a subclinical stage of a late coronary atherosclerosis. Atherosclerotic coronary arteries do not always necessarily indicate the presence of calcifications. The plaque formation correlate with the degree of calcification of the coronary. Coronary artery calcification is not an indicator of instability of an atherosclerotic plaque.

In patients with acute coronary syndrome, coronary artery calcification extent is more pronounced than in those without coronary disease. Quantify calcification of the coronary arteries is quite consistently noted in all studies. Most studies use Agatston score. Value of the score can be increased further if the age and gender are considered percentile. A score that shows the coronary artery calcification Agatston units ≥ 300 or ≥ 75th percentile for the age, sex and ethnicity is considered an indicator of increased cardiovascular risk.

The calcification of the coronary arteries demonstrated a very high negative predictive value, since Agatston score of

0 has a negative predictive value of almost 100% causes of a significant coronary artery narrowing. However, studies have questioned the negative predictive value of coronary artery calcification as a significant stenosis in the absence of calcification if it is possible. Many prospective studies have demonstrated the association with coronary artery calcification of coronary heart disease, Agatston score represents an independent predictor of coronary heart disease. So it is important that coronary artery calcification can improve cardiovascular risk prediction, in addition to conventional risk factors.

The degree of calcification of the coronary artery can be considered in individuals with SCORE calculated risks around 5% or 10%. Although recent studies have Demonstator presence of coronary artery calcifications in low-risk populations, predictive added value of cardiovascular events remains to be demonstrated. There are concerns regarding costs and radiation exposure. For coronary artery calcification score, radiation exposure techniques selected properly is 1 mSv.

Carotid ultrasonography

Population studies have shown the link between the severity of atherosclerosis in one arterial territory and involvement in the process of other arteries. Therefore, early detection of arterial disease in apparently healthy individuals has been concentrated on the study of peripheral arteries, particularly the carotid arteries. Carotid ultrasound assessment of risk using the measurement is based on the thickness of the media vascular tunica (GTVM) and the presence and characteristics of atherosclerotic plaques. Media vascular tunica thickness indicates not only the presence of early atherosclerosis, and hypertrophy/hyperplasia of smooth muscle.

There is a gradual increase in cardiovascular risk with increasing thickness of media vascular tunica, and a value of 0.9 mm is considered abnormal. The risk of stroke associated with media vascular tunica thickness is nonlinear, increasing the risk of occurrence of stroke is much faster in the presence of a smaller media vascular tunica thickness compared with a greater value presence, thereof. Media tunica thickness vascular risk increase associated with cardiovascular events is also nonlinear. Media tunica thickness of carotid vascular level is an independent predictor of CVD and seems to be more predictive in women than in men. Lack of standardization in terms of defining and measuring the thickness of the media tunica vascular, intra-subject variability of high and low reproducibility are of great importance. A recent meta-analysis failed to demonstrate the added value of media vascular tunica thickness compared with the Framingham risk score in predicting future CVD, even in the intermediate risk group. Thus, the investigation of ultrasound for determining the thickness of the carotid media vascular tunica with the aim of improving the risk assessment is not recommended.

The plate is usually defined as the presence of focal thickening of the wall, which is at least 50% higher than in the vicinity of the vessel wall, or a region with a length of ≥ 1.5 mm IMT, which protrudes into the lumen. Plates can be characterized by the number, size and irregularity. The plates are linked to both coronary events, as well as the cerebrovascular and the plates ecolucente (as opposed to the calcified) increases the number of ischemic cerebrovascular accidents. Many studies performed to estimate the higher stresses CVD measures indicating plaque area and thickness, but not just vascular media tunica thickness.

Therefore, even if no formal analyzes were performed revaluation carotid artery plaque assessment using ultrasound may be considered in some cases as a modifier of risk prediction of cardiovascular risk.

Arterial stiffness

Arterial stiffness is measured typically using pulse wave velocity or the aorta (PWV) or arterial augmentation index. An increase in arterial stiffness is usually associated with arterial wall injury, which is found in patients with hypertension. Although the relationship between aortic stiffness and CVD is continuous, pulse wave velocity in the aorta threshold of 12 m/s conservative estimate suggests a significant alteration of aortic function in a hypertensive middle-aged range. A meta-analysis showed that arterial stiffness predicts future risk of CVD and contributes to the classification. However, the validity of this conclusion is matched the evidence of substantial prejudice to the publication. The Working Group concluded that arterial stiffness may serve as a useful biomarker to improve prediction of cardiovascular risk in patients who are at risk threshold decision, but its systematic use to improve risk assessment in the general population is not recommended.

Ankle-brachial index

Ankle-brachial index test is made easy and reproducible, and it is used for detection of asymptomatic atherosclerotic disease. An ankle-brachial index <0.9% indicates a certainty of more than 50% stenosis between the aorta and peripheral arteries of the leg. Due to acceptable sensitivity (79%) and specificity (90%), ankle-brachial index <0.9% is considered a reliable marker of peripheral artery disease. Both the an-

kle-brachial index value, and the medical history confirmation play an important role in peripheral artery disease, as 50-89% of patients with ankle-brachial index <0.9% did not have typical claudication, while 12-27 % of patients over 55 years old are asymptomatic. Ankle-brachial index is inversely proportional cardiovascular risk, but there is controversy regarding its potential to reclassify patients into different risk categories.

Echocardiography

In diagnosing left ventricular hypertrophy, echocardiography is more sensitive than electrocardiography and accurately quantifies mass and left ventricular geometric shapes. Cardiac abnormalities detected by echocardiography have additional predictive power. Given the lack of convincing evidence that echocardiography helps to improve cardiovascular risk and revaluation due to logistical challenges in change, this imaging tool is not recommended to improve cardiovascular risk prediction.

CHAPTER II

SCORES OF CARDIOVASCULAR RISK

CVRF estimate of the combined effect on cardiovascular morbidity and mortality risk scores involves the use of the major risk factors to be included basing on their prognostic weight. Thus, more such cardiovascular risk scores were published which were based on large population studies (eg. The Framingham score), adapted to specific geographic regions (eg. The score SCORE). These scores used age, gender, smoking status, total cholesterol and blood pressure for predicting coronary risk over a period of 10 years.

Framingham score

Framingham score is calculated basing on the equations that take into account gender, age, total cholesterol, HDL cholesterol, smoking status, and systolic BP by assigning a number of points depending on the presence and magnitude of each factor. A simpler form for use in practice is derived from this score as coronary risk maps (Coronary Risk Charts). To assess the risk of CV morbidity and mortality, the score set arbitrary limits of <10% for low risk, intermediate risk 10-20% and> 20% increased risk, which involves pharmacological intervention (Annex 1).

Score SCORE

SCORE prognostic score (Annex 2) has the advantage that it is derived from European cohort studies that included more

than 200 000 individuals; it can be calculated using a computer provided by the European Society of Cardiology in www.heart-score.org. Unlike the Framingham score, score SCORE:

• relate to CV mortality and not the total CV events;

• considers territories with noncoronarian atherosclerosis deaths (AVC);

• adapted to median ages at which the risk steeply changes with age;

• in European countries there are separate scores for high risk or low risk, they have complete data about mortality.

Score is implemented for patients without a known vascular disease, aged up to 65 years. Patients with an atherosclerotic vascular disease have a high risk of a cardiovascular disease and should be treated intensivly as basic.

It proposes improving the predictive ability by taking the SCORE map and markers of subclinical organ (such as plaques in the carotid artery, pulse wave velocity, increased LV mass index).

Cardiovascular risk (CVR) for a period of 10 years

There are many systems for the evaluation of CVR in apparently healthy individuals (Table 2). In practice, the estimation is performed by CVR multiple systems simultaneously (Framingham, SCORE, ASSIGN, Q-Risk, Proc CUORE). In practice most systems of risk assessment are performed simultaneously. When the population being tested is comparable to the population of deriving evaluation systems risk factors. Since 2003, the European guidelines for CVD prevention in clinical practice has recommended using the SCORE system because it is based on the data from the European cohort. SCORE risk functions have been validated in other countries. Table 8 lists

the advantages of the SCORE chart. SCORE system estimates the risk of atherosclerotic first event for a period of 10 years.

Codes diseases, therefore, can be called atherosclerotic are included in the International Classification of Diseases (International Classification of All Diseases). They are: coronary artery disease, stroke and abdominal aortic aneurysm. Traditionally, many systems only estimated abdominal aortic aneurysm, however more recently a number of systemic estimates were redirected to assess all risk of CVD. If we compare the mortality of cardiovascular disease mortality in total, there is an imbalance, because later prevails and the first is not widely spread. The rate of non-fatal events is dependent on the found definitions and methods.

Table 8. Advantages and limitations in using the SCORE risk charts

Benefits
• Intuitive, easy to use.
• Establish a common language for healthcare professionals.
• Allows a more objective assessment of risk.
• Consider the multifactorial nature of CVD.
• Allows flexibility in management; if the ideal level for a risk factor is not achieved, the overall risk could be further decreased by reducing other risk factors.
• Deals with the problem of the absolute low youth risk with multiple risk factors: the relative risk diagram helps to illustrate how a young person with an absolute low risk may be at a relatively high risk, calculating the "age risk "of an individual could also be used in this situation.
Restrictions
• Risc assessments of fatal cardiovascular causes, but not total (fatal + non-lethal), highlighted in the text.
• Adapted for different European populations, but not different ethnic groups within these populations. Limited to the major risk determinants.

People with low moderate risk (calculated diagram SCORE <5%) should receive advice for lifestyle to maintain the status of risk from low to moderate.

People with high risk (calculated by SCORE chart: ≥ 5% and <10%) include intensive lifestyle modification and may be candidates for a drug therapy.

People with very high risk (calculated by SCORE chart: ≥ 10%) often need medication. In people over 60, these thresholds should be interpreted more lenient because their age-specific risk is normally around these levels even when other factors of CVR levels are "normal". In particular, it should be avoided uncritical initiating drug treatments for all elderly with greater risks than 10% threshold.

Using graphs risk should be qualified by knowledge of the following aspects:

• Charts help to estimate risk, but must be interpreted in the light of medical knowledge and experience, and given the risk factors that may change calculations.

• The relative risks can be high in young people although absolute risks are low for the next 10 years because the cases occur, usually later in their life. Chart relative risk or estimation age risk can be helpful in identifying and advising those persons.

• The risk lower in women due to the fact that the risk is postponed by 10 years. The risk of women aged 60 years is similar to that of a man of 50 years. Finally, more women than men die from CVD.

• Workflows can be used to give some indication of the effects of reducing risk factors, given that there will be a time lag before reducing risk and that the results of randomized clinical trials generally obtain better estimates of benefits of interventions. The smoking stoppage generally reduces by half their risk.

It is noteworthy that Romania the lead for countries with high cardiovascular risk (Annex 2). Framingham score against a threshold of 20% risk of cardiovascular morbidity and mortality corresponds to a threshold of 5% of cardiovascular mortality in SCORE score.

Thus, patients at risk of cardiovascular death more than 5%, according to this score, are considered to be at high risk and require intensive monitoring and treatment and tailored risk factors present. People with low risk will receive advice on changing their lifestyle in order to maintain the risk level.

SCORE data indicates that the risk of total cardiovascular events in men is approximately 3 times bigger than the risk of CVD and therefore total risk of CVD in the SCORE chart 5% stands for fatal CVR + nonfatal 15%; women are multiplied by four and less than 3 in the elderly group, in which fatal event, appears first.

As it is noted in the Introduction, levels that require certain interventions are problematic to define. Obviously, decisions related to initiating any treatment should be based on patients preferences.

A particular problem relates to young people with a high level of risk factors, where an absolute low risk conceals a very high relative risk, requiring intensive lifestyle changes. There are several highlighted reports about risks for young people (see 2.5.1). These include diagrams using relative risk or "risk age" or "Risk over life." Their goal is to communicate that life style changes can substantially reduce the relative risk and decreasing factors that occur with age. Another issue concerns the elderly. At a certain age, mostly for males, estimated risk of death from cardiovascular causes is beyond the level of 5-10%, based on age and sex, even if other risk factors are low.

The role of HDL-C in predicting risk was systematically reviewed using the SCORE chart data. HDL-C has a moderate but useful redefining risk assessment. Evaluation of HDL-C is only important for the upper limits for intensive risk modification of 5%, where a lot of directions to normalize its level will be recommended if HDL-C level is lower.

SCORE diagram illustrating containing HDL-C is commonly used. SCORE electronic version was amended to introduce HDL-C data for a more accurate assessment.

The role of triglycerides as a predictor of CVD has been discussed for many years. Triglycerides resting reveals risk in the univariate analysis, but their effect is mitigated by other factors including HDL-C, the impact of additional risk factors body weight, family history and new risk markers are in relation to the diagonals on paper, and the least is more difficult to determine. It would be stressful because, although other risk factors have been identified, their contribution is very modest both in terms of CV risk estimation and reclassification of another class of individual risk.

SCORE diagonals risk include risks relative section with instructions. It can be seen that Annex 2 demonstrates the relative but not absolute values. Therefore, a person ranked in the top right box with multiple risk factors has a risk 12 times bigger than the person in the left bottom, with the risk factors in the normal range. This can be helpful in indications related to the way of life for a young person with an absolute low risk but relatively high.

SCORE grid is available in two versions, one for regions with low risk (Belgium, France, Greece, Italy, Luxembourg, Spain, Switzerland and Portugal) and other regions at risk, which fits our country, together with European countries which

were not mentioned in the previous listing. In the SCORE grid it should be noted that there are subjects without known CVD address, age up to 65 years. SCORE grid has several functions:

- Highlights the risk of fatal cardiovascular event within 10 years of the table without further calculations;
- Estimates by comparing the relative risk of a cell (in grid square) with any other, of the same age;
- Asseses the impact of a risk factor improvement (subject passes from one risk category to another by smoking stoppage, lowering total cholesterol, etc.);
- Highlights the effect of the action of a risk factor (increase in risk with increasing age, precocious risk as a general low).

CHAPTER III

WHAT IS CARDIOVASCULAR DISEASE PREVENTION

1. DEFINITION AND CORRELATIONS

Prevention of cardiovascular disease (CVD) is defined as a set of coordinated actions publicly and individually, aimed at eliminating or minimizing the impact of CVD and associated diseases of the population. CVD remains the leading cause of morbidity and mortality, even taking into account improved performance lately. Mortality from the coronary heart age-related disease has decreased since 1980, especially in high-income areas. Currently, the rate of cases of coronary heart disease has fallen by half compared to the 80s in many countries in Europe, thanks to preventive measures, such as success in smoking legislation. However, inequality between countries persist and risk factors, particularly obesity and diabetes mellitus (DM) have increased substantially.

If prevention should be applied following the instructions, it would markedly reduce the prevalence of CVD. Therefore, not only the prevalence of risk factors is something worrying, but it is limited implementation of preventive measures either. Prevention should be submitted to the general population as well as the individuals by promoting a healthy lifestyle, especially those who are in the risk categories moderate to high risk of CVD or have already been diagnosed with CVD, combating unhealthy life style (eg. non correspundent diet, inactivity, smoking) and by optimizing risk factors. Prevention is effective

when excluding harmful habits would enable prevention of at least 80% of cases of CVD and even 40% of cancer.

2. PHYSICAL ACTIVITY

Lack of physical activity is the major lifestyle problem since childhood. Few children currently practice sports, and most are sedentary adulthood. Also, fewer patients with cardiovascular disease participate in exercise programs, especially with the presence of heart failure [26]. It is estimated that at least 60% of the world population does not meet the recommended minimum of 30 minutes of moderate physical activity daily. The proportion of those who do no do physical exercise once a week is 25%. The risk of developing cardiovascular disease is at least 1.5 times bigger in inactive people, the major impact on young people, where there is currently a striking decrease in physical activity levels of 12 to 21 years is a stabilizing trend in middle age (30-64 years) and even improved in old age. The combination of excessive caloric intake and insufficient physical exercise is a contributing factor to the development of metabolic syndrome.

The latest report published by the AHA in December 2009 on CHD and stroke stated that almost a third (31.9%) of children aged between 2 and 9 years of age are overweight or obese. In a 2008 study on primary prevention it was shown that people who do physical exercise in their free time have a risk of 27% (in case of intense physical activity) and 12% (moderate activity) lower the incidence of coronary heart disease or mortality, compared to people with low levels of physical activity or who do not exercise at all [18].

In secondary prevention, reduction of total mortality as a result of just practicing exercise was estimated at 27% and cardiac mortality – 31%.

The effects of appropriate physical activity:

- ✓ weight maintainance or reduction in people with excess weight;
- ✓ lipid profile effect on the growth, primarily of triglyceride and decreased HDL-cholesterol;
- ✓ insulin sensitivity increase;
- ✓ blood pressure reduction;
- ✓ increase of compliance measures influencing other risk factors, thus reducing CVD incidence and mortality.

Any growth, low to moderate level exercise has positive effects (eg use the stairs instead of the elevator). Everyone can see how physical activity can be more attractive (walking, cycling, gardening).

The European prevention guide has shown that 30 minutes of moderately vigorous exercise on most days of the week will reduce risk and increase physical tone. In practice, this recommendation may be achieved by performing minimum 30 minutes of moderate-intensity physical activity at least 5 days a week or 20 minutes of vigorous activity three days a week or the combination of the two regimes. Aerobic activities (step brisk walking, running, dancing, swimming, games) must be added to muscle toning exercises at least 2 days a week (jumps, pushups, squats, lifting weights, elastic bands 8-12 repetitions per set) [5]. Additional benefits are obtained by moderate activity for 300 minutes (5 hours) per week, or 150 minutes of vigorous activity or a combination of both procedures.

Physical workout recommendations are based on information gained through stress testing, ECG or standard, or

preferably by measuring and assessing direct gas exchange oxygen consumption.One of the most important components of secondary prevention is the heart recovery. The term cardiac recovery refers to the coordinated, comprehensive, goal to optimize the physical, psychological and social status to slow patient's heart to stabilize and even regress atherosclerosis process, thus reducing morbidity and mortality.

3. NUTRITION

Table 9. Recommendations on nutrition

Recommendations	Class	Level	No
A healthy diet is recommended as a fundamental element of CVD prevention in all people.	I	B	3II

a. Recommendation class.

b. Level of evidence.

c. Reference to support the recommendations.

CVR can be influenced by eating habits through an effect on risk factors such as cholesterol, BP, weight and DM, or through other effects. Table 12 summarizes the characteristics of a healthy diet.

Most evidence on the relationship between nutrition and CVD is based on observational studies and randomized trials, assessing the impact of diet on limited parameters. It studied the impact of diet on three levels: specific nutrients, specific food/specific food groups and food patterns, the Mediterranean diet is the most studied.

The nutrients that are of interest with regard to CVD are fatty acids (mainly affecting levels of lipoproteins), minerals (mainly affecting BP), vitamins and fibers.

Fatty acids:

For CVD prevention, types of consumed fats are more important than total fat content.

Table 10. Characteristics of a Healthy Diet

• Saturated fatty acids must be <10% of total energy intake, substituting polyunsaturated fatty acids.
• trans unsaturated fatty acids: as little as possible, preferably without any input from processed foods and less than 1% of total energy intake of natural origin
• Less than 5 g of salt per day.
• 30-45 g of fiber per day, preferably from whole grain products.
• ≥ 200 grams of fruit per day (2-3 servings).
• ≥ 200 g of vegetables per day (2-3 servings).
• fish: 1-2 times per week, including one portion of oily fish.
• 30 grams unsalted nuts per day.
• Drinking alcohol should be limited to 2 drinks per day (20 g/day of alcohol) for men and one drink per day (10 g/day of alcohol) for women.
• Consumption of sugar, sweetened soft drinks and alcoholic beverages should be discouraged.

CVD risk is reduced by 2-3% when 1% of energy intake coming from saturated fat is replaced with polyunsaturated fatty acids. The same results has not been clearly demonstrated in replacing the carbohydrate and monounsaturated fatty acids (Mufasa). Saturated fatty acid intake should be reduced to at most 10% of energy by replacing it with polyunsaturated fatty acids. Mufasa have a favorable effect on HDL-C levels when they replace saturated fats or carbohydrates, but there is little evidence that Mufasa reduce RCV.cs of a Healthy Diet

Polyunsaturated fatty acids lower the levels of LDL-C and, to a lesser extent, HDL-C levels where they replace saturated fats. Polyunsaturated acids can be divided into two groups: omega-6 fatty acids from plant foods and omega-3 fatty acids

from fish oil and fat. In the subclass of omega-3 fatty acids, eicosapentaenoic acid and docosahexaenoic acid (EPA/DHA) are particularly important. They do not alter serum cholesterol levels and, as for cardioprotective therapies currently available, it is not clear whether they exert a favorable effect on all causes and CVD mortality in stroke [4, 25].

Trans acids are a subset of unsaturated fatty acids that have been proven to be particularly harmful because of the unfavorable impact on both the total cholesterol (up), as well as on the level of HDL-C (downward). These fatty acids are formed during the industrial processing (hardening) of fats and are shown, for example, in bakery margarines and products. A meta-analysis of prospective cohort studies demonstrated that a 2% increase in average energy consumption of trans fats increases the risk of CVD by 23% [16]. It is recommended that only 1% of total daily energy intake should be achieved in ingesting trans fatty acids, so the less, the better.

The impact of dietary cholesterol on serum cholesterol level is weak compared to the impact of the fatty acid composition of the diet. When the guidelines are followed to reduce saturated fat intake, this goal also leads to a reduction in the intake of dietary cholesterol. Therefore, some guidelines (including this one) about a healthy diet does not offer a specific guidance on dietary cholesterol intake, while others recommend intake limited to 300 mg/day.

Minerals:

A meta-analysis estimated that even a modest reduction in sodium (intake of 1 g/day) reduced SBP by 3.1 mmHg in hypertensive and normotensive patients by 1.6 mmHg [17]. Studies of dietary approaches to stop hypertension (DASH) showed

a response relationship between reduced sodium and reduced TA [28]. In most Western countries, salt intake is high (9-10 g/day), while the maximum recommended intake is 5 g/day. Admitted optimum level could be one of less than 3 g/day. Although the relationship between salt intake and BP remains controversial, all samples do justify salt reduction as an important way to prevent CVD and stroke. On average, 80% of salt intake comes from processed foods, while only 20% is added later. Reducing daily salt intake can be achieved by various food dietary choices (fewer processed foods, many basic foods) and by formulating foods (low salt content).

Potassium has favorable effects on TA. The main sources of potassium are fruits and vegetables. A statistically significant inverse association between potassium intake and risk of incident stroke [RR 0.76 (95% CI 0.66, 0.89)]. [19] In addition to reducing sodium intake, increased potassium intake helps reduce BP.

Vitamins:

Many control – cases and prospective observational studies have observed an inverse relation between levels of vitamin A and E and the risk of CVD. However, intervention trials have failed to confirm these observational studies. Also, the B vitamins (B6, B12 and folic acid) and vitamin C studies have not shown beneficial effects. The bottom third of the serum level of vitamin D, total cardiovascular mortality is 35% higher [RR 1.35 (95% CI 1.13, 1.61)] than in the upper third [20]. A 41% higher risk of cardiovascular mortality [RR 1.41 (95% CI 1.18, 1.68)] and a 57% higher risk of mortality from all causes [RR 1.57 (95% CI 1.36, 1.81)] has been reported in the smallest vs. highest percentage [21]. A much smaller effect was seen in RCT: there was an 11% risk reduction in all-cause mortality for

vitamin D3 supplementation [RR 0.89 (95% CI 0.80, 0,99)], but not for vitamin D2 supplementation[20]. Therefore, no conclusions can yet be drawn about the role played by additional intake of vitamin D [type of supplement (D2 or D3), dosage and duration] in cardiovascular prevention.

Fibers:

Recent meta-analyzes of prospective studies show that a higher intake of 7 g/day of total fiber is associated with a lower risk of CVD by 9% [RR 0.91 (95% CI 0.87, 0.94)] and higher daily intake of fiber (10 g/day) is associated with a risk of stroke by 16% lower [RR 0.84 (95% CI 0.75, 0.94)] and a lower risk of 6 % of type 2 diabetes [RR 0.94 (95% CI 0.91, 0.97)] [22, 23, 24]. There is still no evidence for a similar relation with the fiber in fruits and vegetables. Although the mechanism has not been fully elucidated, it is known that high fiber intake reduces postprandial glucose responses after meals rich in carbohydrates and lowers total cholesterol (Equivalent to 77 g) and vegetables (equivalent to 80 g) per day, while the all-cause mortality has not further decreased by the intake of more than five portions [25]. A meta-analysis reported a reduction in the risk of stroke by 11% [HR 0.89 (95% CI 0.83, 0.97)] for three to five daily portions of fruit and vegetables by 26% [0.74 RR (95% CI 0.69, 0.79)] for more than five portions, compared with less than three portions [26]. Another study on CVD metaanalitic reported a decrease of 4% CVD risk [RR 0.96 (95% CI 0.93, 0.99)] for each additional portion of fruit and vegetables per day [27].

Walnuts:

A meta-analysis of prospective studies showed that daily consumption of 30 g of walnuts reduces the risk of CVD by 30%

[HR 0.71 (95% CI 0.59, 0.85)] [328]. Walnuts provide a great deal of energy.

Fish:

The protective effect of fish consumption on CVD is attributed to the content of n-3 fatty acids. Risk estimates gathered from prospective cohort studies show that eating fish at least once a week results in a 16% reduction in CVD risk [RR 0.85 (95% CI 0.75, 0.95)], compared to the consumption in an amount of less than that [29]. A meta-analysis has shown that the consumption of fish two to four times a week reduces the risk of stroke by 6% [RR 0.94 (95% CI 0.90, 0.98)], compared to the consumption of more fish at least once a week [13]. The relation between the intake of fish and CVR is not linear, especially when the input is zero or very low, the risk is in this case increases. Therefore, the impact on public health in the general population has a high potential growth after moderate consumption of fish.

As fish oil, three randomized controlled prevention trials have been published. All three trials, post-MI or CHD patients who received an additional amount of 400-1000 g EPA/DHA daily did not observe a reduction in cardiovascular events in the intervention group. A recent meta-analysis of 20 studies, the most recurrent cardiovascular prevention events often using fish oil supplements, showed no benefit on CV outcomes [15].

Alcoholic beverages:

Drinking three glasses (or more) drinks a day is a factor that is associated with an increased risk of CVD. The results of epidemiological studies suggest a lower risk of CVD from moderate alcohol consumption . This association seems to be ex-

plained according to the special characteristics of abstinence, although the potential for confusion and causes reverse track can not be completely ruled [21]. Moreover, a recent andomized Mendelian, including analysis of 59 epidemiological studies has questioned any beneficial effect of moderate alcohol consumption, suggesting that the lowest risk for the results of CVD were found in abstinent and that ingesting any amount of alcohol is associated with elevation for HT and BMI [22].

Soft drinks and sugar:

Sugar sweetened soft drinks are the single biggest source of calories in the US and an important source of calories in Europe. In children and adolescents, drinks can be responsible for 10-15% of the calories consumed. Regular consumption of soft drinks was associated with overweight, metabolic syndrome and type 2 diabetes Substitution of soft drinks sweetened with sugar, artificially sweetened drinks, resulted in weight gain in children [23]. Beverages sweetened with sugar cause an increase in weight in adults. Regular consumption of beverages sweetened with sugar (two servings a day, compared to one serving per month) was associated with the risk of CVD 35% higher in women, even after other factors are calculated. They are unhealthy lifestyle and diets where artificially sweetened drinks were not associated with CVD. WHO guideline recommended daily energy intake of no more than 10% of sugar (mono and disaccharides), which includes added sugar and sugar present in fruits and fruit juices [24].

CLINICAL CASES

CLINICAL CASE REPORT NR. 1

Patient X, 60, second-degree disability, was hospitalized following complaints: headache, dizziness, fatigue, coughing mostly wet in the morning, with yellowish expectoration.

Existing diseases history:

Hypertensive for 15 years, maximum values 220/120 mmHg. The manage permanent preparations are nebivolol, indapamide, cardiomagnil, lisinopril, amlodipine. Suffering from diabetes for 8 years, from February 2014 insulin is administers

Medical history of life:

Living satisfactory. Smoking – a 36-year smoker, smokes 10 cigarettes per day. Alcohol – denies. Tuberculosis, hepatitis, sexually transmitted diseases – denies. Colicistectomie – 2012. Mother – hypertensive at the age of 44 years.

General Inspection:

General condition – medium built. Position – active. Consciousness – clear. Skin – pale, dry, rashes. Osteoarticular system – without peculiarities. Peripheral edema (gambiense) weak handed. BMI – 31.6. Waist circumference – 107 cm.

Respiratory system:

Free nasal breathing. Striker – clear sound lung. Auscultation – vesicular murmur tightened throughout both lung fields, crepitation in the lower lobe crackles bilaterally. FR-18.

Cardiovascular system:

The shock apex in space i/c V line medioclaviculară left.

Rhythmic heart sounds. Focus Zg.II Ao. TA – 180/110 mmHg, FCC – 75.

Digestive system:

Abdomen soft, on palpation painless. Liver and spleen are not palpated. Free bowel movement.

Urinary system:

Free painless urination. Giordan topotament sign – bilateral negative.

Presumptive diagnosis:

Hypertension gr. III very high additional risk.

Type II diabetes, subcompensated. Acute chronic bronchitis.

Corroborating:

1. Complete blood counts: show Iron Deficiency Anemia (Hb – 115 g/l, er – 3.2 x 10 ^ 12).

2. Biochemistry: glucose – 7 mmol/l, total cholesterol – 6.0 mmol/l, triglycerides – 1.9 mmol/l, LDL-cholesterol – 2.5 mmol/L, HDL-cholesterol – 0.9 mmol /it.

3. Summary examination of urine: proteinuria – 0.06.

4.Profilul glycemic: I – 5.9 mmol/l, II- 7.2 mmol/l, III – 6.9 mmol/l

5. ECG – sinus rhythm, frequency 76. AEC – horizontal. Extrasystolic ventricular raid. Signs of myocardial hypertrophy VS.

6. Exam Echocardiography – signs of hypertrophy, SIV – 16 (6-11) PPVS – 15 (6-11). Heart cavities are not dilatete: AS – 38 (20-40), AD – 38 (20-40), VS – 44 (35-56), VD – 23 (7-26). EF – 56%.

7. USG org. + internal kidneys – condition after cholecystectomy. Moderate changes, diffuse liver and pancreas parenchyma.

Clinical diagnosis:

Hypertensive heart, subcompensated. Hypertension gr. III very high additional risk. Extrasystolic ventricular raid. Type II diabetes, subcompensated. Acute chronic bronchitis. Fieriprivă anemia gr. I. Dislepidemie. Obesity gr. I (WHO).

QUESTIONS:

1. Determine modifiable risk factors and modifiable?

Modifiable risk factors: smoking, obesity, sedentary lifestyle, dyslipidaemia, diabetes, hypertension.

Non-modifiable risk factors: age, sex, heredity.

2. Estimate the risk of cardiovascular mortality for the next 10 years according to SCORE score?

The risk of total cardiovascular event in the next 10 years is> 15%.

3. Present on patient criteria defining metabolic syndrome?

Yes, they are present, namely:

Abdominal obesity – 107 cm

Fasting plasma glucose change

TA – 180/110 mmHg

Low HDL-cholesterol (0.9 mmol/l)

Triglycerides (1.9 mmol/l).

CLINICAL CASE REPORT NR. 2

Patients X., 55, from urban Moldova.

No complaints when we visited, addresses for prophylactic control.

Family history:

* Father – heart attack at 53, dyslipidemia, obesity grade
* Mother – hypertension

Personal history:

* HTA to 49
* 2009, overweight

Living and working:

* driver
* Irregular meals zone
* sedentary way of life
* nonsmoker
* not consume coffee or alcohol.

Disease history:

* It is considered ill about 10 years, TA max – 170/90 mmHg. Manages regular outpatient treatment (indapamide, bisoprolol, lisinopril, nifedipine), with a positive effect.

Objective:

* Overweight patient (G = 92kg, T = 175, BMI = 30 kg/m2, CA = 96 cm)
* TA = 140/80 mmHg; FCC = 70 b/min
* Laboratory investigations:
* Blood glucose = 5.4 mmol/l; HbA1c = 6.0%
* Cholesterol = 6, 1 mmol/l; HDL-C = 0.8 mmol/l; triglycerides = 2.04 mmol/l; Calculated LDL – 4.2 mmol/l
* Ionogram normal.

Question:

1. What are the cardiovascular risk factors in our patient?

2. What is the risk in the next 10 years for fatal CVD (Score score)?

3. What is assumed diagnosis?

4. What therapeutic recommendations will be given to this patient?

Answers:

1.Age: The risk increases with age. Men over 45 years have an increased cardiovascular risk.

2.Gender: Men have a higher risk of cardiovascular disease early in life than women.

3.Heredity: If family history there were cardiovascular and metabolic type dyslipidemia, cerebrovascular accident, myocardial infarction, angina pectoris or sudden death especially before the age of 55 years, then there is a considerable risk of being prone to cardiovascular disease.

4.Hypertension: High blood pressure increases the effort made by the heart, leading to increased risk of myocardial infarction, stroke or heart failure. This condition often progresses silently, with no signs or symptoms that alert patients about this disease. It is therefore important to measure blood pressure at regular intervals.

Dyslipidemias:

Obesity:

* 2. Calculation of CV risk by Score – 4%, indicating moderate risk of fatal CVD in 10 years.

* 3. What is assumed diagnosis?

- Grade II hypertension, high additional risk.
- Mixed Dyslipidemia
- Obesity gr. I WHO (BMI = 30 kg/m2)

4. What therapeutic recommendations will be given to this patient?

* A healthy lifestyle: healthy eating, fruit and vegetables, fish at least 2 times a week.

* Avoid alcohol consumption

* Weight loss

* Administration strictly to the treatment prescribed by your doctor.

* Physician regular control (BP, lipid profile).

CLINICAL CASE REPORT NR. 3

F.P. patient, 48 years old, female, urban.

Family history:

* Father – HTA, died 66 years ago MI
* mother – hypertension

Personal history:

* without significant APP;
* has been detected several occasions values of 150/95 mmHg BP approx.

Living and working:

* dental technician
* fat meal
* irregular physical activity
* smoking.

Disease history:

* patient of normal weight (G = 66 kg, H 164 cm, BMI = 24.5 kg/m2, CA = 78 cm)
* FCC = 72 b/min, TA = 155/95 mmHg (mean of 3 measurements), 145/95 mmHg standing.

Laboratory (available at the time of consultation)

* The CBC within normal limits
* Blood glucose 4.5 mmol/l
* Total cholesterol 4.36 mmol/L, HDL-C = 1.21 mmol/l, TG = 3.57 mmol/l, LDL-C = 2.90 mmol/l.

Questions:

1. What are the cardiovascular risk factors in our patient?
2. What are the recommendations for cardiovascular risk assessment?
3. What is the absolute and relative cardiovascular risk in our patient?

4. What do we do if we have an increased risk?

Answers:

1. Age: The risk increases with age. If you are a man over 45 or a woman over age 55 or menopause, you have an increased cardiovascular risk.

2.Heredity: The disease predisposition can be inherited which, together with environmental factors and common habits, favor the disease. Thus, if parents and/or siblings were hypertensive, diabetic or had a heart attack at a young age (under 55 years), there is "a chance" to suffer the same disease.

3. CVR hypertension is recognized as a factor of the coronary role in the development of the disease (CAD), cerebrovascular disease, heart failure (HF), chronic kidney disease (CRD), as well as peripheral artery disease (PAD). Hypertensives develop CVD 5 years earlier (95% CI 4.8-5.2) than normotensives. HTA association with other CVR factors, with the presence of target organ damage (AOT) and comorbidities, affect cardiovascular morbidity and mortality. A decrease of 10-15 mm Hg systolic and diastolic blood pressure of 5-8 mm Hg in a half-life can lead to morbidity and mortality by cardiovascular diseases. Given the importance of hypertension as a risk factor, determining its value, any adult is a simple procedure, but very important for primary prevention. The age of 18 is onset for screening, and frequent guidelines measurements. They are recommended every 2 years.

4. Dyslipidemia: Increased serum lipids can determine independently or in combination with other CVR factors, atherosclerosis. The lipid fractions have a different atherogenic role. It is recognized that the so-called "atherogenic triad" fraction increases level of small dense LDL-cholesterol and VLDL fraction (determined as serum triglycerides) and low HDL-choles-

terol. Reducing the levels of LDL cholesterol with statins and decreasing the incidence of CAD means, the revascularization, and ischemic attacks by about one-fifth, Annual 12.

4. In general, this case refers to recommendations of the lifestyle and need of medical support, including medication.

Lifestyle interventions include:

* weight loss in overweight or obese;

* reducing the intake of sodium chloride at <3.8 g/day (sodium intake of <1.5 g/day or 65 mmol/day);

* reducing alcohol consumption to no more than 10-30 g ethanol per day in men (1-3 standard measures of strong drink 1-3 glasses of wine or beer bottles 1-3) and a maximum of 10 to 20 g ethanol per day in women (1-2 such drinks/day);

* regular physical activity in sedentary individuals;

* generally hypertensive patients should be advised to consume more fruits and vegetables (4-5 servings per day).

CLINICAL CASE REPORT NR. 4

Patient aged 46 years, in urban areas.

Family history:

* Father – type 2 diabetes, dyslipidemia, obesity grade I,
* Mother – HTA.

Personal history:

* Without significant APP
* 2004 overweight (20 kg weight gained in the last 2 years).

Living and working:

* electritian
* Irregular meals zone
* frequently consumes fast food, carbonated drinks
* sedentary
* smokes 10 cigarettes/day
*does not consume coffee or alcohol.

Disease history:

* periodic examination at work: TA = 145/70 mmHg; FCC = 80/min, sinus rhythm; = fasting plasma glucose 5.8 mmol/l

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* Overweight patient (G = 81 kg, BMI = 27 kg/m2, CA = 96 cm)
* Moderate symptoms of hyperglycemia discrete dry mouth, polyuria
* Complain about general weakness and vertigo, aggravated in the last 6 months.
* Blood glucose = 12.5 mmol/l; HbA1c = 11.1%
* Cholesterol = 6, 24 mmol/l; HDL-C = 0.88 mmol/l; triglycerides 3.04 mmol/l; Calculated LDL-C – 3.36 mmol/l
* TA = 170/100 mmHg; AV = 80/min sinus rhythm

* Ionogram normal.

Questions:

1. What are the cardiovascular risk factors in the patient?

2. What is supposed diagnosis?

3. What are the therapeutic recommendations that you will give this patient?

Answers:

1. Age: The risk increases with age. If you are a man over 45 or a woman over age 55 or menopause, you have an increased cardiovascular risk.

2. Gender: Men have a higher risk of cardiovascular disease much earlier in life than women.

3. Heredity: The disease predisposition can be inheritated, which together with environmental factors and common habits, favors the disease. Thus, if parents and/or siblings were hypertensive, diabetic or had a heart attack at a young age (under 55 years), there is "a chance" to suffer the same disease.

4. Smoking: Regardless of the presence of other risk factors, a smoker has a risk two times bigger of having a heart attack than a non-smoking person. Cigarettes containing low nicotine ("light" – light) do not reduce the risk because carbon monoxide is harmfull in cigarettes. Moreover, this explains the increased risk for the passive smokers. Smoking quitting reduces the risk of dying from a heart attack or stroke and it was clearly proven scientifically.

High blood pressure

Dyslipidemias

What is supposed diagnosis?

- newly discovered type 2 diabetes, unbalanced
- severe combined dyslipidaemia
- hypertension stage II, additional risk very high.

• Obesity gr. WHO II (BMI = 27 kg/m2)

3. What are the therapeutic recommendations for this patient?

* Choose a healthy lifestyle: a diet low in fat and rich in dietary fiber!

* Take salt, caffeine, alcohol moderatly (as little as possible or occasionally).

* Start regular exercises (at least walking).

* Do not smoke.

* Evaluate your cardiovascular risk through regular monthly visits to the family doctor.

* Control your blood pressure and cholesterol.

* Control your blood glucose regularly.

* Strictly follow the treatment prescribed by your doctor and inform him about its effects, and reduce consumption of saturated fat and cholesterol.

CLINICAL CASE REPORT NR. 5

L. N. patient, 65 in urban areas.

Family history:

- father – HTA;
- mother – hypertension, type 2 diabetes, dyslipidemia, obesity grade II, died at 71 after an acute myocardial infarction.

Personal history:

- without significant APP;
- several occasions of TA values of about 190/110 mmHg have been detected.

Living and working conditions:

- an accountant
- diet rich in fat, irregular meals
- irregular physical activity
- smoker

Disease history:

- patient with grade II obesity (G = 96 kg, H 162 cm, BMI = 36.57 kg/m2, CA = 89 cm)
- FCC = 74 b/min, TA = 160/100 mmHg (mean of 3 measurements) 150/95 mmHg standing.

Laboratory (available at the time of consultation):

- The CBC without particularities Blood glucose = 7.6 mmol/l
- Total cholesterol =5.7 mmol/L, HDL-C = 0,9 mmol/l, TG = 3.73 mmol/l, LDL-C = 2.91 mmol/l.

Questions:

1. List the cardiovascular risk factors in the patient, grouping them into modifiable and non-modifiable.
2. What laboratory indices are required to estimate cardiovascular risk?
3. What advice could you give to this case?

Among the non modifiable factors we can mention:

• Age, as the risk increases with age. If you are a man over 45 or a woman over age 55 or menopause, you have an increased cardiovascular risk;

• Heredity: the disease predisposition cab be inherited which, together with environmental factors and common habits, favors the disease. Thus, if parents and/or siblings were hypertensive, diabetic or had a heart attack at a young age (under 55 years), there is „a chance" to suffer the same disease.

Modifiable factors:

• **hypertension** is recognized as an important factor in the development of CVR role of coronary artery disease (CAD), cerebrovascular disease, heart failure (HF), chronic kidney disease (CKD), and peripheral arterial disease (PAD). Hypertensives develop CVD 5 years earlier (95% CI 4.8-5.2) than normotensions. HTA is associated with other factors CVR, wich is with the presence of target organ damage (AOT) and comorbidities, affects cardiovascular morbidity and mortality. A decrease of 10-15 mm Hg systolic and diastolic blood pressure of 5-8 mm Hg in a half-life can lead to morbidity and mortality of cardiovascular diseases. Given the importance of hypertension as a risk factor, determining its values in any adult is a simple procedure, but very important for primary prevention. The age of onset for screening, and frequency measurement guidelines is 18 years old. It is recommended every 2 years;

• **dyslipidemia:** Increased serum lipids can determine independently or in combination with other CVR factors, atherosclerosis. The lipid fractions have a different atherogenic role. The so-called "atherogenic triad" faction is recognized to increase the level of small dense LDL-cholesterol and VLDL fraction (determined as serum triglycerides) and low HDL-cholesterol. Reducing the levels of LDL cholesterol with statins de-

crease the incidence of CAD, and it means the revascularization, and decreasing ischemic attacks by about one-fifth Annual 12;

• **obesity** is estimated depending on the BMI; presence of **diabetes** is also a major negative element that requires special measures. A diabetic patient starts from the beginning with a high cardiovascular risk, regardless of the presence of other risk factors. In CVR assessing the most informative is the lipid profile.

• **cholesterol** is a fat that is normally found in the blood and in all cells. A high cholesterol level is bad because it is accumulated in arteries, with negative consequences outlined above. Total cholesterol is made up of several fractions. The most important are HDL cholesterol (called "good" cholesterol) and LDL ("bad" cholesterol). Triglycerides are other components, "fatty" blood. Their growth is equally devastating, especially to women and diabetics.

In order to reduce CVR it is needed:

• a diet low in animal fats (meat, dairy, eggs), which is imposed even if you do a treatment with cholesterol-lowering drugs. Consumption of vegetables and fruit. With the help of the diet you can reduce cholesterol by 5% and thus, decrease the cardiovascular risk by 2% for each percentage of low cholesterol

• If the therapy normalizes fat or various side effects occur, or reduce the treatment should be stopped without any medical indication;

• If you are diabetic, diabetes control can help reduce lipids (particularly triglycerides). However, medication is often necessary to reduce the fat and the level to be achieved is lower than normal;

• daily physical activity: a good way to „burn" fat;

• elimination of other risk factors: obesity, alcohol (in quantities greater than moderate).

CLINICAL CASE REPORT NR. 6

The patient X, 68 years old. Admitted to the cardiology department with the following complaints: breathlessness on moderate exercise, constrictive nature pain pericordiale irradiation in the left shoulder blade, moderate physical exertion, headache, general weakness.

Disease history:

The patient was treated out. 2010 – transient ischemic stroke, was admitted to the neurology ward for 10 days. Condition has worsened in 3 days, the symptoms mentioned above. Was urgently hospitalized for diagnosis and treatment.

Life history:

CPI suffer, hypertension over 10 years. The patient was treated out. 2010 – transient ischemic stroke, was admitted to the neurology ward for 10 days. Condition has worsened in 3 days, the symptoms mentioned above. Was urgently hospitalized for diagnosis and treatment.

In ward admission (objective):

Overweight, hiperstenic, BMI = 32. Skin of pale xanthelasma viewing.In the lungs – rough breathing, crackles absent. Rhythmic heart sounds mitigated. Volume increased, abdomen soft, painless. Urinary free seat in a day.TA – 140/90 mmHg, Ps = 74/min.

Laboratory investigations:

AGS, ionogramma within the norm.

Biochemical analysis of blood: urea – 6 mmol/L,

creatinine – 83 mkmol/l, total cholesterol = 7.3 mmol/l, triglycerides – 2.03 mmol/l, glucose – 7.2 mmol/l. Abdominal ultrasound: diffuse changes in the liver and pancreas parenchyma, moderate hepatomegaly.

Questions:

1. What factors indicate the presence of the risk of the atherosclerosis development in the given patient?

• Complaints presents clinical pectoral angina, mostly caused by atherosclerosis of coronary vessels.

• Among concomitant diseases – diabetes, which the pathogenesis of the disease leads to the development of dyslipidemia.

• The patient man, smoker, which increases the risk of dyslipidemia and the risk of cardiovascular pathology.

• From the history – transient ischemic stroke

• Sedentary Lifestyle

• Obesity

2. At what level should be maintained LDL and total cholesterol in the given patient?

To establish the target level of cholesterol is necessary to establish SCORE index for the concerned patient. SCORE index equals to 20% – a very high risk.Increased cardiovascular risk total target values are: total cholesterol <4.5 mmol/l; LDL-cholesterol <2.5 mmol/l.

TESTS FOR INITIAL EVALUATION

1. C. S. Mentioned risk factor in cardiovascular disease is hereditary:

A. Physical inactivity

B. Dyslipidemia

C. Familial Hypercholesterolemia

D. Smoking

E. Diet high in saturated fat

2. C. S. Note the definition of cardiovascular risk factors:

A. Present in healthy individuals that are statistically associated with the likelihood of subsequent coronary heart disease

B. Characteristics that predispose acute myocardial infarction

C. Features that predispose development of diabetes

D. Involving lifestyle modification

E. Features necessary to establish a diagnostic cardiology

3. C. S. Indicate which cardiovascular risk factor predicts poor outcome with the occurrence of cardiovascular events:

A. Eating fast food

B. Alcohol Abuse

C. The abuse of foods high in saturated fat

D. Smoking

E. Inactivity

4. C. S. Note cardiovascular risk factor influencing the occurrence of psychological etiology of ischemic heart disease:

A. Type extroverted behavior
B. Type behavioral intravertit
C. Type A behavior
D. Type perceptive behavior
E. Type affective behavior

5. C. S. Specify which of the following cardiac diseases remain the leading cause of premature death:

A. Hypertensive Heart Disease
B. The disease Takotsubo
C. Atrial fibrillation
D. Coronary artery disease
E. Aneurysms of the aorta descending

6. C.M. Note that of these risk factors has a weaker prognostic value in cardiovascular diseases:

A. Age
B. Dyslipidemia
C. Hypertension
D. Hypercholesterolemia
E. Reduced carbohydrate tolerance

7. C. M. Specify which aims performing secondary prevention in cardiovascular diseases:

A. Improving disease progression
B. Preventing complications
C. Prevention of Atherosclerosis
D. Slowing the progression of atherosclerosis in asymptomatic individuals

E. Reducing progression of atherosclerosis in people with symptoms of heart disease

8. C.M. Specify which aims to carry out primary prevention of cardiovascular diseases:

A. Improving disease progression

B. Preventing complications

C. Prevention of Atherosclerosis

D. Slowing the progression of atherosclerosis in asymptomatic individuals

E. Reducing progression of atherosclerosis in people with symptoms of heart disease

9. C.M. Mentioned types of cardiovascular disease prevention:

A. Primary prevention

B. Secondary prevention

C. Prevention ICC

D. Prophylaxis of angina pectoris

E. Prevention of hypertension

10. C.M. Note the beneficial effects of exercise in cardiovascular diseases:

A. The normalization of body mass

B. The normalization of blood pressure

C. Increased fibrinogen

D. Reducing cholesterol

E. Reducing fibrinogen

11. C.M. List what risk factors influence cardiovascular disease:

A. Modifiable Risk Factors
B. Risk Factors modifiable
C. Less modifiable risk factors
D. Risk Factors endogenous
E. Exogenous risk factors

12. C.M. List the biological cardiovascular risk factors:

A. Reduced carbohydrate tolerante
B. Heredity
C. Sedentary
D. Hypercholesterolemia
E. Hypertension

13. C.M. Specify the risk factors predict the occurrence of cardiovascular events with unfavorable:

A. Diabetes
B. Hypertension
C. Metabolic syndrome.
D. Diffuse toxic goiter
E. Phaeochromocytoma

14. C.M. Indicate which risk factors are associated with severe coronary artery disease:

A. Older age
B. Dyslipidemia
C. Signs and symptoms of cardiovascular insufficiency
D. Smoking
E. Sedentary

15. C.M. List of modifiable cardiovascular risk factors:

A. Diet rich in cholesterol

B. Smoking

C. Age

D. Sedentary

E. Hypertension

16. C.M. Specify what three components must include a comprehensive action for the prevention of cardiovascular risk factors by the World Health Organization (WHO):

A. Primary prevention

B. Population Strategy

C. Strategy for high-risk population

D. Secondary prevention

E. Strategy decreased risk population

17. C.M. People with cardiovascular risk are those with:

A. Multiple risk factors, which give a risk score ≥ 5%.

B. Crossing increased level of a single risk factor, ex. ≥ 180/110 mmHg or BP ≥ 160/110 mmHg persistent; these values must be treated regardless of the presence of other risk factors.

C. Total cholesterol ≥ 8 mmol/L (320mg/dL), LDL-C ≥ 6 mmol/L (240 mg/dL).

D. Diabetes (relative risk is 5 women and 3 men).

E. Multiple risk factors, which give a risk score ≥ 20%.

18. C.M. List Score grid functions:

A. Highlights the risk of fatal cardiovascular event within 10 years of the table without further calculations.

B. Estimate by comparing the relative risk of a cell (in grid square) with any other in the same age category.

C. Evaluate the impact of a risk factor improvement (subject passes from one risk category to another by stopping smoking, lowering cholesterol toatl etc.).

D. Estimates absolute risk by comparing a cell (in grid square) with any other in the same age category.

E. Highlights of the action effect of a risk factor (increase in risk with increasing age, precocious risk is generally low).

TESTS FOR THE FINAL EVALUATION

SIMPLE COMPLEMENT

1. C. S. Highlight which of the following CVRF have been demonstrated by population studies:

A. Modifiable factors
B. New factors
C. Modifiable factors
D. Classic factors
E. Contributors factors

2. C. S. Indicate what age is considered the limit for the occurrence of CVD risk:

A. Women> 55 years, men> 45 years
B. Women> 45 years, men> 55 years
C. Women> 47 years, men> 40 years
D. Women> 50 years, men> 45 years
E. Women> 55 years, men> 46 years

3. C. S. Indicate which of the following is considered modifiable CVRF:

A. Age
B. Race
C. Smoking
D. Height
E. Sex

4. C. S. Please indicate which of the following factors are considered psychosocial risk factor:

A. Occupational stress

B. Sport

C. Alcohol

D. Inactivity

E. Fatigue

5. C. S. Indicate which of the following BMI indicates morbid obesity:

A. >30 kg/m^2

B. from 25 to 29.5 kg/m^2

C. >40 kg/m^2

D. from 19 to 24.9 kg/m^2

E. <18 kg/m^2

6. C. S. Specify which phrase about homocysteine is true:

A. Homocysteine has protective effects on the endothelium.

B. Patients with hyperhomocysteinemia have decreased atherosclerotic risk.

C. Homocysteine has antithrombotic effect.

D. Homocysteine reduces the availability of nitric oxide.

E. Homocysteine concentration may be reduced by vitamin B12.

7. C. S. Specify which of the mentioned risk factors take part from modifiable risk factors in cardiovascular diseases:

A. Age

B. Family history of coronary heart disease

C. Dyslipidemia

D. Hypertension
E. Sedentariness

8. C. S. Note which mentioned risk factors take part from endogenous risk factors for cardiovascular disease:
A. Age
B. Family history of coronary heart disease
C. Dyslipidemia
D. Smoking
E. Sedentariness

9. C. S. Specify which of the listed below risk factors for cardiovascular disease are considered unchangeable:
A. Age
B. Dyslipidemia
C. Hypertension
D. Sedentariness
E. Diet rich in saturated fat and cholesterol

10. C. S. Indicate which risk factor in cardiovascular disease is hereditary:
A. Sedentariness
B. Dyslipidemia
C. Familial Hypercholesterolemia
D. Smoking
E. Diet high in saturated fat

11. C. S. Note the definition of cardiovascular risk factors:
A. Characteristics present in healthy individuals that are statistically associated with the likelihood of subsequent coronary heart disease.

B. Characteristics that predispose acute myocardial infarction.

C. Features that predispose development of diabetes.

D. Involving lifestyle modification

E. Features necessary to establish a diagnostic cardiology.

12. C. S. Indicate which predicts cardiovascular risk with an unfavorable appearance of cardiovascular events:

A. Eating fast food

B. Alcohol Abuse

C. The abuse of foods high in saturated fat

D. Smoking

E. Inactivity

13. C. S. Show exogenous cardiovascular risk factor:

A. Physical inactivity

B. Smoking

C. Age

D. Family history of coronary heart disease

E. Food rich in cholesterol

14. C. S. Note cardiovascular risk factor influencing the occurrence of psychological etiology of ischemic heart disease:

A. Type extroverted behavior

B. Type behavioral intravertit

C. Type A behavior

D. Type perceptive behavior

E. Type affective behavior

15. C. S. Specify which is modifiable cardiovascular risk factor:

A. Heredity

B. Sex
C. Hypertension
D. Height/stature
E. Age

16. C. S. Specify which cardiovascular risk factor is unchangeable:
A. Heredity
B. Dyslipidemia
C. Hypertension
D. Obesity
E. Smoking

17. C. S. Specify which limit obesity is to measure waist circumference:
A. >85 cm for men and> 75 cm in women
B. >90 cm for men and> 85 cm in women
C. >102 cm in men and> 88 cm in women
D. >88 cm for men and> 102 cm in women
E. >106 cm in men and> 95 cm in women

18. C. S. Indicate that cardiovascular risk factors described recently:
A. Heredity
B. Sex
C. Hypertension
D. Homocysteine
E. Age

19. C. S. Indicate which of the following is true:
A. For women over 65 years is a cardiovascular risk factor.

B. Smoking is a risk factor unchangeable.
C. Of men: women in cardiovascular risk is 1:1.
D. Hypercholesterolemia is not a risk factor.
E. For women over 55 years is a cardiovascular risk factor.

20. C. S. Indicate which of the following cardiovascular risk factors is unchangeable:
A. Sex
B. Smoking
C. Obesity
D. Inactivity
E. Excessive consumption of fat

21. C. S. Complete statement: Homocysteine is a risk factor ...:
A. Modifiable.
B. Exogenously.
C. Again.
D. Unchangeable.
E. There is a cardiovascular risk factor.

22. C. S. Specify which type of cholesterol lowering is a cardiovascular risk factor:
A. LDL-cholesterol
B. HDL cholesterol
C. Triglycerides
D. VLDL-cholesterol
E. Chylomicrons

23. C. S. Mention of LDL-cholesterol value corresponding to a patient who is in the group of moderate cardiovascular risk:
A. LDL-cholesterol <2 mmol/l

B. LDL-cholesterol <3 mmol/l
C. LDL-cholesterol> 3 mmol/l
D. LDL-cholesterol> 4 mmol/l
E. LDL-cholesterol> 5 mmol/l

24. C. S. Specify which of the following heart disease remains the leading cause of premature death:
A. Hypertensive Heart Disease
B. The disease Takotsubo
C. Atrial fibrillation
D. Coronary artery disease
E. Aneurysms of the aorta descending

25. C. S. Please indicate the correct value of waist circumference according to the latest estimates:
A. Abdominal Circumference <85 males and> 80 women
B. Waist circumference in men and 85 in women = 80
C. Waist circumference <94 in men and <80 in women
D. Waist circumference> 95 males and> 90 women
E. Waist circumference = 100 men and 90 women

27. C. S. Set the correct score evaluation score an individual who is in the group of moderate cardiovascular risk:
A. A score greater than or equal to 1% and 5% at 5 years
B. A score greater than or equal to 1% and 5% in 10 years
C. A score of less than 1% and 5% to 10 years
D. A score greater than or equal to 3% and 5% in 10 years
E. A score greater than 5% in 10 years

MULTIPLE COMPLEMENT

1. C.M. List mechanisms antiatherogen:

A. The function of antioxidant

B. Improving the inflammatory cascades

C. Protection procoagulant activity

D. Each 1% reduction in HbA1c yield decreased by 14% cardiovascular risk.

E. Worsening inflammatory cascade

2. M.C. Specify what mechanisms smoking increases cardiovascular risk:

A. Increased total cholesterol and decrease HDL-cholesterol

B. Increase in HDL cholesterol and lower LDL cholesterol

C. Increased fibrinogen circular.

D. Increases FCC and TA.

E. The arterial vasoconstrictor.

3. M.C. Which of the following are listed risks of drinking alcohol?

A. Risk Hypertensive

B. The risk of hemorrhagic stroke

C. Risk of subarachnoid hemorrhage

D. Risk of arrhythmias

E. Risk hypotensive

4. M.C. Appointed anti-atherogenic mechanisms of HDL cholesterol:

A. Antioxidant Function

B. Improving the inflammatory cascade

C. Action procoagulant
D. Protection against procoagulant activity
E. oxidizing function

5. M.C. Which of the following refers appointed ways to influence lifestyle:
A. Reducing the number of cigarettes smoked
B. Making monthly EKG
C. Encouraging physical activity
D. Promoting healthy eating
E. Administration of hypertensive

6. M.C. List the factors that explain the incidence of AMI more often and earlier in men:
A. Smoking
B. The high level of lipids
C. There are only factors V and X.
D. The most important in the pathogenesis of CVD is fibrinogen.
E. They achieved through tromboticelor effect and clotting factors.

9. M.C Please indicate which of the following statements relate to score SCORE:
A. It relates to cardiovascular mortality.
B. Reporting fatal cardiovascular events.
C. It is adjusted median ages.
D. It is intended for individuals with known CVD.
E. Highlights of the action effect as a risk factor.

10. M.C. That the factors listed below are associated with normal weight obesity:

A. Status proinflammatory

B. increased oxidative stress

C. Increased cardiovascular mortality in women

D. Increased cardiovascular mortality in men

E. Cardiometabolic abnormalities, such as metabolic syndrome and its components

11. M.C. List the mechanisms by which physical activity plays a protective cardiovasculart:

A. Maintaining proper body weight

B. Decreased HDL cholesterol

C. Increase in HDL cholesterol

D. Increased blood pressure

E. Improving the uptake of oxygen by myocardium

12. M.C. Select which of the following is considered removing nicotine therapy:

A. Patches

B. Inhalers

C. Nasal sprays

D. Digoxin

E. Metronidazole

13. M.C. Specify primary cardiovascular risk factors:

A. Hypercholesterolemia

B. Hypertension

C. Smoking

D. Age

E. Dyslipidemia

14. M.C. Note categories of cardiovascular risk factors:
A. Modifiable
B. Unchanged
C. Biological
D. Primary
E. Secondary

15. M.C. Indicate which of cardiovascular risk factors are modifiable:
A. Smoking
B. Dyslipidemia
C. Heredity
D. Obesity
E. Hypertension

16. M.C. List the mechanisms by which smoking increases cardiovascular risk:
A. Increased total cholesterol and decrease HDL-cholesterol
B. The decrease in circulating fibrinogen
C. Platelet activation and leukocyte
D. The arterial vasoconstrictor
E. Slow heart rate and blood pressure

17. M.C. List cardiovascular risk factors described recently:
A. Homocysteine
B. Lipoprotein (A)
C. Age
D. Heredity
E. Proinflammatory factors

18. M.C. List the mechanisms by which physical activity plays a cardiovascular protector:

A. Decreased HDL cholesterol
B. Decrease triglyceride
C. Decreased insulin sensitivity
D. Reducing blood pressure
E. Improving the uptake of oxygen by myocardium

19. M.C. List the new components of the lipid balance sheet:

A. Apolipoprotein B
B. Total Cholesterol
C. Triglycerides
D. Small dense LDL
E. oxidized LDL

20. M.C. Lipid balance factors listed classics:

A. Triglycerides
B. Total Cholesterol
C. Oxidized LDL
D. HDL-cholesterol
E. LDL-cholesterol

21. M.C. Specify total cardiovascular risk management components:

A. Empathetic communication with patient
B. Patient involvement in identifying risk factors
C. Involving Members healthcare
D. Promoting a healthy lifestyle
E. Drug Administration placebo

22. M.C. Indicate that cardiovascular risk factors are considered modifiable:

A. Age

B. Smoking

C. Obesity

D. Sex

E. Hypertension

23. M.C. List the general recommendations to be adapted to local cultural habits:

A. It has consumed a variety of foods high in fat.

B. It is necessary to adjust the caloric intake to prevent overweight.

C. It should encourage the consumption of fruit, vegetables, cereals and bread, fish (particularly fatty fish), lean meat, low fat dairy products.

D. Replacing saturated fats with foods mentioned above monounsaturated and polyunsaturated fats and vegetable and marine, to reduce total fat to <30% of energy, of which more than 1/3 is saturated fat.

E. Reducing salt intake if blood pressure is raised by avoiding adding salt to meals and cooking and choosing fresh or frozen unsalted foods.

24. M.C. HBP listed consequences that increase cardiovascular risk:

A. Risk of stroke 7 times

B. Risk of heart failure 3 times

C. 4-fold risk of coronary artery disease

D. Risk of overall cardiovascular mortality 2 times

E. Risk of lower limb arterial and aorta 2 times

25. M.C. List of cardiovascular risk factors in hypertensive patients:

A. The existence of metabolic syndrome

B. Sedentary: exercise less than 30 minutes 3 times a week

C. Excessive alcohol consumption: less than 300 ml of wine per day in men and 200 ml per day in women

D. HDL-cholesterol> 0.40 g/l (1 mmol/l)

E. LDL-cholesterol> 1.60 g/l (4.1 mmol/l)

26. M.C. List cardiovascular risk factors:

A. Age male 50 years

B. Age at woman over 60

C. Cholesterol LDL-C> 1 mmol/l

D. LDL-cholesterol> 4.1 mmol/l

E. LDL-cholesterol <1.60 g

A N N E X

ANNEX 1.
FRAMINGHAM CORONARY HEART DISEASE RISK SCORE

step 1

Age		
Years	LDL Pts	Chol Pts
30-34	-1	[-1]
35-39	0	[0]
40-44	1	[1]
45-49	2	[2]
50-54	3	[3]
55-59	4	[4]
60-64	5	[5]
65-69	6	[6]
70-74	7	[7]

step 2

LDL-C		
(mg/dl)	(mmol/l)	LDL Pts
<100	<2,59	- 3
100-129	2,60-3.36	0
130-159	3,37-4,14	0
160-190	4,15-4,92	0
≥190	≥ 4,92	2

Colesterol		
(mg/dl)	(mmol/l)	Chol Pts
<160	<4,14	- 3
160-199	4,15-5.17	0
200-239	5,18-6,21	0
240-279	6,22-7,24	0
≥280	≥ 7,25	2

step 3

HDL-C			
(mg/dl)	(mmol/l)	LDL Pts	Chol Pts
<35	<0,90	2	[2]
35-44	0,91-1.16	1	[1]
45-49	1,17-1,29	0	[0]
50-59	1,30-1,55	0	[0]
≥60	≥ 1,56	-1	[-1]

step 4

Blood Pressure					
Systolic (mmHg)	<80	80-84	85-89	90-99	≥100
<120	0.(0) pts				
120-129		0,(0) pts			
130-139			1.(1) pts		
140-159				2.(2)pts	
≥160					3.(3) pts

Note: When systolic and diastolic pressures provide different estimates for point scores, use the higher number

step 5

Diabetes		
	LDL-Pts	Chol Pts
No	0	[0]
Yes	2	[2]

Nivelul 6

Smoker		
	LDL-Pts	Chol Pts
No	0	[0]
Yes	2	[2]

Sum from steps (1-6)
step 7

Adding up the points	
Age	_____
LDL-C or Chol	_____
HDL-C	_____
Blood Pressure	_____
Diabetes	_____
Smoker	_____
Point total	_____

Key	
Culor	Relative Risk
green	very low
white	low
yellow	moderate
rose	higt
red	very higt

(Determine CHD risk from point total)
step 8

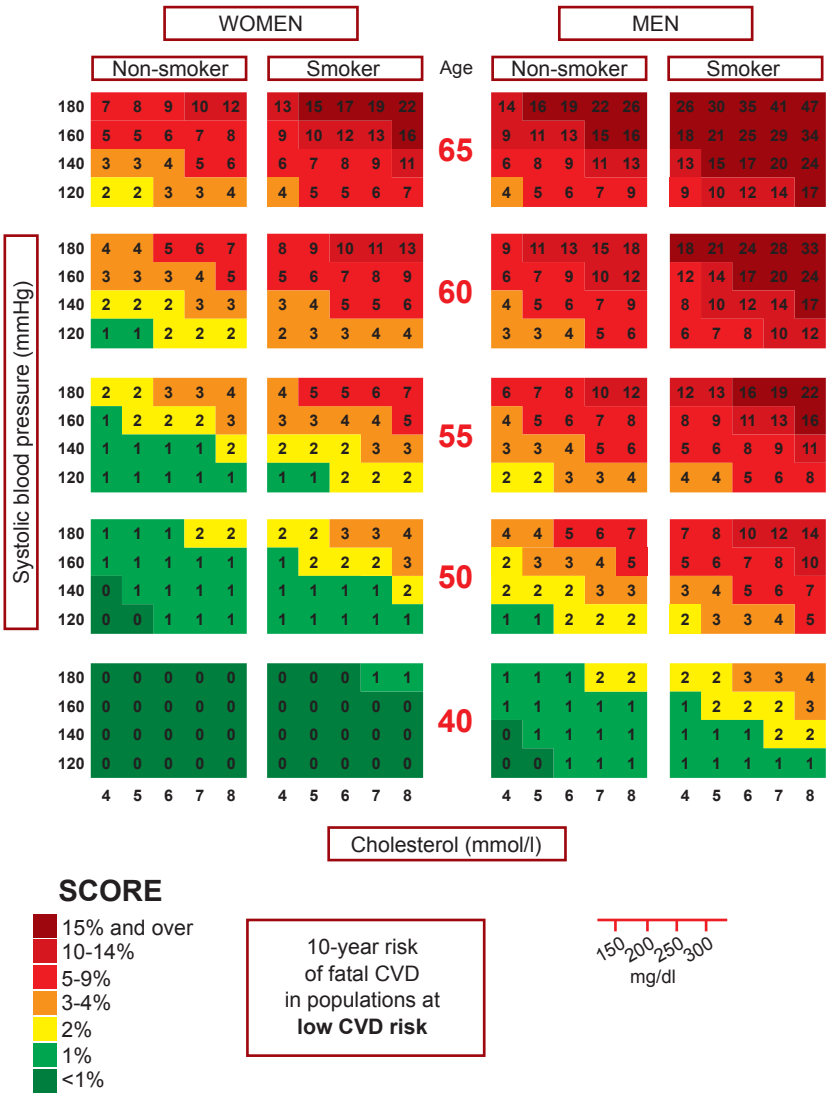
CHD Risk			
LDL Pts total	10 Yr CHD risk	Chol Pts Total	10 Yr CHD risk
<-3	1%		
-2	2%		
-1	2%	[-1]	[2%]
0	3%	[0]	[3%]
1	4%	[1]	[3%]
2	4%	[2]	[4%]
3	6%	[3]	[5%]
4	7%	[4]	[7%]
5	9%	[5]	[8%]
6	11%	[6]	[10%]
7	14%	[7]	[13%]
8	18%	[8]	[16%]
9	22%	[9]	[20%]
10	27%	[10]	[25%]
11	33%	[11]	[31%]
12	40%	[12]	[37%]
13	47%	[13]	[45%]
≥14	≥56	[14]	[≥53%]

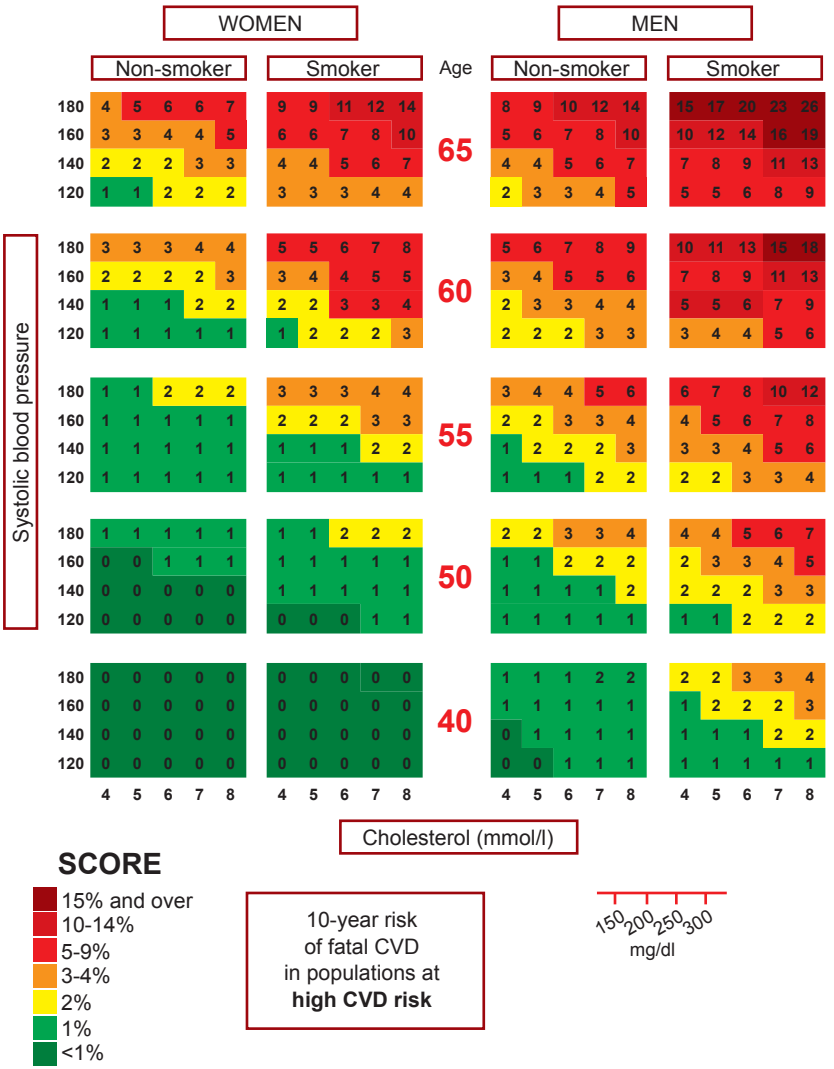
- Hard CHD events exclude angina pectoris
- Low risk was calculated for a person the same age, optimal blood pressure, LDL-C 100-129 mg/dl or colesterol 160-199 mg/dl, HDL-C 45 mg/dl for men or 55 mg/dl for women, non-smoker, no diabets
- Risk estimates were derived from the experience of the Framingham Heart Study, a predominantly Caucasian population in Massachusets, USA

Compare to average person your age
step 9

Comparative Risk			
Age (years)	Average 10 Yr CHD Risk	Average 10 Yr Hard CHD Risk	Low 10Yr CHD Risk
30-34	3%	1%	2%
35-39	5%	4%	3%
40-44	7%	4%	4%
45-49	11%	8%	4%
50-54	14%	10%	6%
55-59	16%	13%	7%
60-64	21%	20%	9%
65-69	25%	22%	11%
70-74	30%	25%	14%

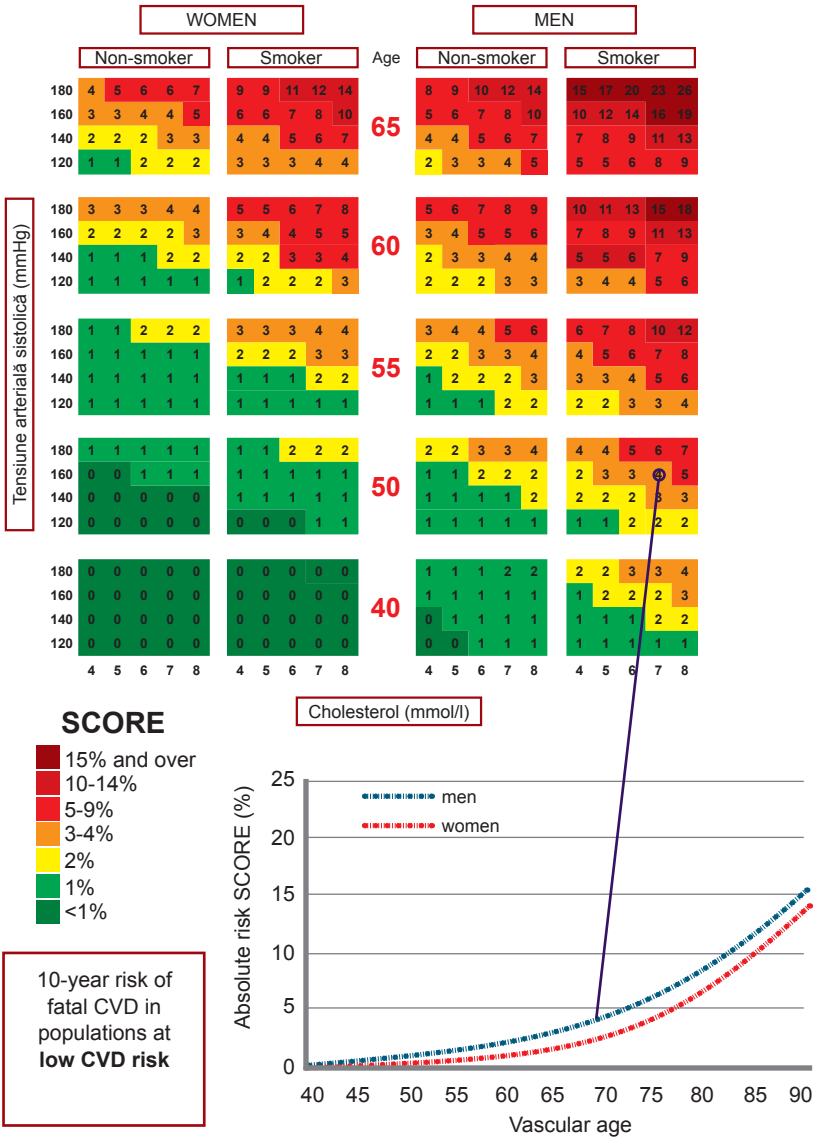
ANNEX 2.
SCORE GRID FOR HIGH-RISK POPULATIONS AND THE ENVIRONMENT





SCORE chart: Risk of cardiovascular events 10 years the population increased cardiovascular risk: Albania, Algeria, Armenia, Austria, Belarus, Bulgaria, Croația, Cehia, Danemarca, Egipt, Estonia, Finlanda, Georgia, Islanda, Irlanda, Israel, Letonia, Liban, Libia, Lituania, Macedonia, Marea Britanie, Maroc, Moldova, Norvegia, Olanda, România, San Marino, Serbia şi Muntenegru, Slovacia, Slovenia, Tunisia, Turcia, Ucraina, Ungaria.

ANNEX 3.
SCORE GRID AFTER CALCULATING CARDIOVASCULAR RISK



ANNEX 4.
RISK ESTIMATION METHODS 5X5

Probability	CONSEQUENCE				
	1 insignificant	2 small	3 moderate	4 great	5 catastrophic
A. very likely	medium	higt	higt	extremely	extremely
B. probable	medium	medium	higt	higt	extremely
C. moderate	low	medium	higt	higt	higt
D. unlikely	low	low	medium	medium	higt
E. rare	low	low	medium	medium	higt

ANNEX 5.
RISK ASSESSMENT MATRIX

Severity / Probability	RISK ASSESSMENT MATRIX			
	Catastrophic (1)	Critical (2)	Marginal (3)	Negligible (4)
Frequent (A)	higt	higt	serios	medium
Probabile (B)	higt	higt	serios	medium
Occasional (C)	higt	serios	medium	low
Remote (D)	serios	medium	medium	low
Improbabil (E)	medium	medium	medium	low
Eliminated (F)	eliminated			

ANNEX 6.
ASSESSMENT OF CARDIOVASCULAR RISK IN THE PRESENCE OF SUBCLINICAL ORGAN DAMAGE

	HVS-	HVS+	MAU-	MAU+
Score <5%				
Score ≥5-10%				
Score ≥10-20%				
Score ≥20%				

low risk to 10 years
the average 10-a years
high risk to 10 years
very high risk to 10 years

HVS-left ventricular hypertrophy; MAU: microalbuminurile

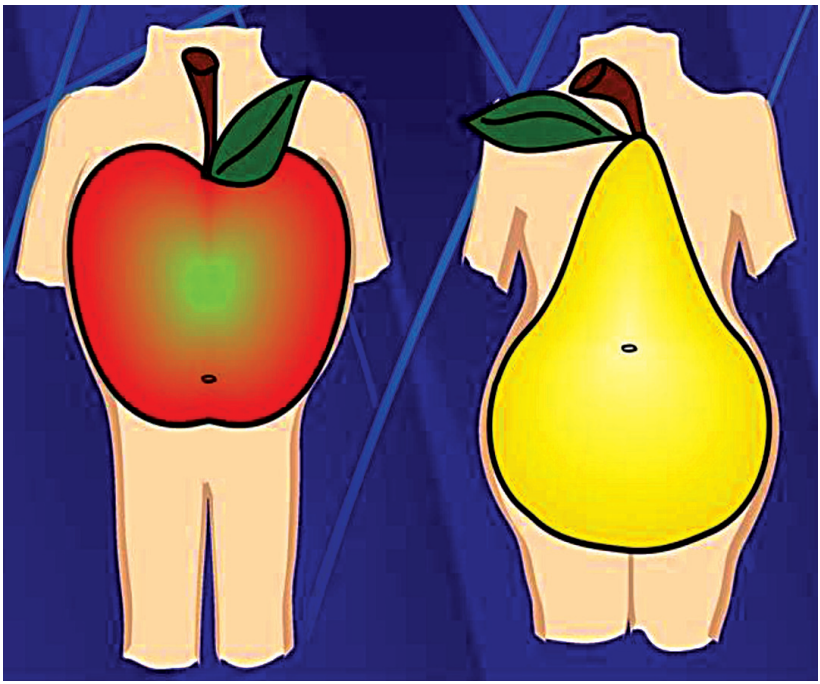
ANNEX 7.
CALCULATING RISK OF DEATH OR MI AFTER UNSTABLE ANGINA/SCA CONFIRMED BY TROPONONEI GROWTH AND TREADMILL TEST BEFORE DISCHARGE

		Risc of Cardiac Death or MI at 5 Months		
Exercise ECG		Troponin T		
Categoria de risc după ECG	Rezultat	>0.2 mg/l	0.2-0.06 mg/l	< 0.06 mg/l
High Risk	Low maximal workload (Less than Bruce II, <3 min), AND ST depression ≥0.1 mV in ≥ 3 leads	34%	19%	22%
Intermediate Risk	EITHER a low maximal workload arhieved. OR ST depression ≥0.1 mV in ≥ 3 leads	16%	9%	7%
Low Risk	Low maximal workload exceeded, AND without ST depression ≥0.1 mV in ≥ 3 leads	5%	7%	1%
?	Unable to perform exercise ECG	27%	16%	3%

Note: The confidence intervals for the quoted risk of cardiac death or myocardial infarction will be wide and may overlap for many of these categories. Furthermore, the results of Troponins and Exercise ECG tests are continuous rather than categorical variables, and should be interpreted accordingly. Thus these categories should be interpreted as indicating the general degree of cardiac risk, rather than a precise figure.

References:
Lindahl B., Andren B., Ohlsson J., Venge P., Welentin L. and the FRISC Study Group. Risk stratification in unstable coronary artery disease. Addtive value of troponin T determination and predischarge exercise. Eur. Heart J 1997; 18: 762-70.
Guidelnes for the management of patiens with acute coronary syndromes without persistent ECG ST segment elevation. Heart 2000; 85:133-142

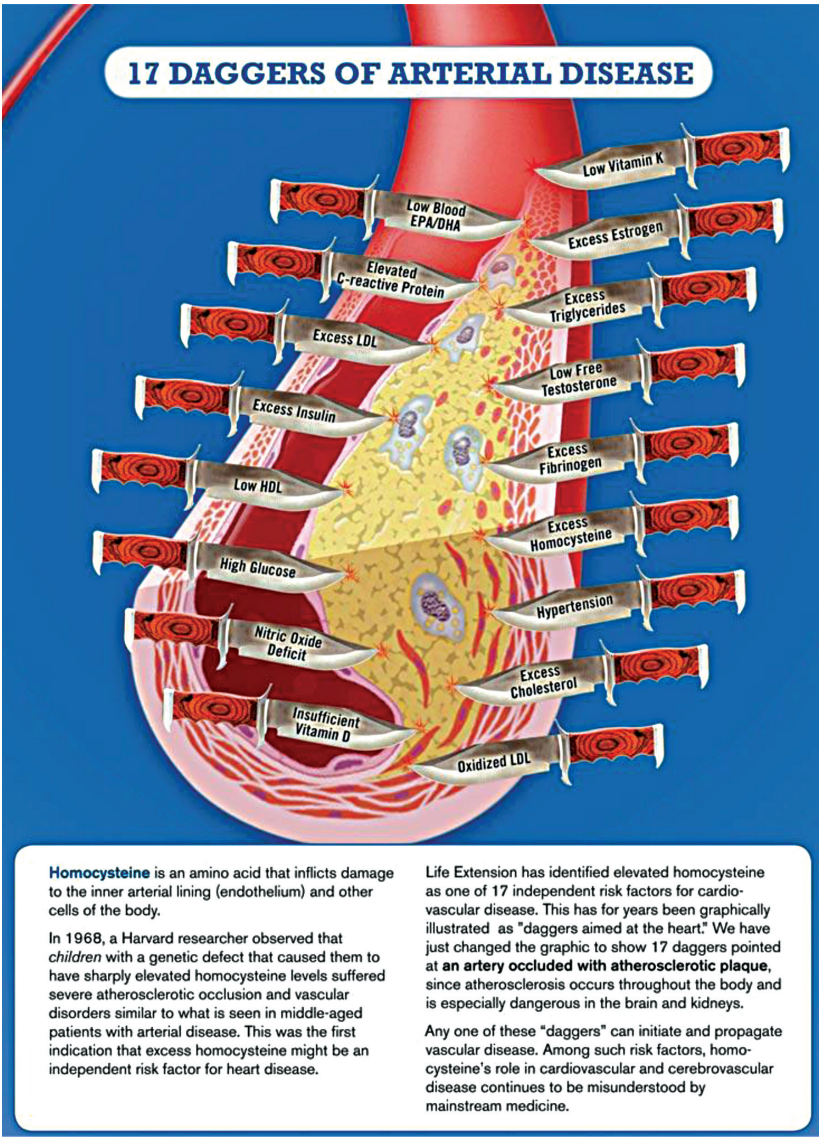
ANNEX 8.
CONSTITUTIONAL TYPES IN MEN AND WOMEN



ANNEX 9.
TABLE TO CALCULATE BODY MASS INDEX

kg/cm	154	156	158	160	162	164	166	168	170	172	174	176	178	180	182	184	186	188	190	192	194	196	198	200
48	20	20	19	19	18	18	17	17	17	16	16	16	15	15	15	14	14	14	13	13	13	13	12	12
50	21	21	20	20	19	19	18	18	17	17	17	16	16	15	15	15	15	14	14	14	13	13	13	13
52	21	21	21	20	20	19	19	18	18	18	17	17	16	16	16	15	15	15	14	14	14	14	13	13
54	23	22	22	21	21	20	20	19	19	18	18	17	17	17	16	16	16	15	15	15	14	14	14	14
56	24	23	22	22	21	21	20	20	19	19	19	18	18	17	17	17	16	16	16	15	15	15	14	14
58	25	24	23	23	22	22	21	21	20	20	19	19	18	18	18	17	17	16	16	16	15	15	15	15
60	26	25	24	23	23	22	22	21	21	20	20	19	19	19	18	18	17	17	17	16	16	16	15	15
62	26	26	25	24	24	23	23	22	22	21	21	20	20	19	19	18	18	18	17	17	17	16	16	16
64	27	26	26	25	24	24	23	23	22	22	21	21	20	20	19	19	19	18	18	17	17	17	16	16
66	28	27	26	26	25	25	24	23	23	22	22	21	21	20	20	29	19	19	18	18	18	17	17	17
68	29	28	27	27	26	25	25	24	24	23	23	22	22	21	21	20	20	19	19	18	18	18	17	17
70	30	29	28	27	27	26	25	25	24	24	23	23	22	22	21	21	20	20	19	19	19	18	18	18
72	30	30	29	28	27	27	26	26	25	24	24	23	23	22	22	21	21	20	20	20	19	19	18	18
74	31	30	30	29	28	28	27	26	26	25	24	24	23	23	22	22	21	21	21	20	20	19	19	19
76	32	31	30	30	29	28	28	27	26	26	25	25	24	24	23	22	22	22	21	21	20	20	19	19
78	33	32	31	31	30	29	28	28	27	26	26	25	25	24	24	23	23	22	22	21	21	20	20	20
80	34	33	32	31	31	30	29	28	28	27	26	26	25	25	24	24	23	23	22	22	21	21	20	20
82	35	34	33	32	31	31	30	29	28	28	27	27	26	25	25	24	24	23	23	22	22	21	21	21
84	35	35	34	33	32	31	31	30	29	28	28	27	27	26	25	25	24	24	23	23	22	22	21	21
86	36	35	34	34	33	32	31	31	30	29	28	28	27	27	26	25	25	24	24	23	23	22	22	22
88	37	36	35	34	34	33	32	31	30	30	29	28	28	27	27	26	25	25	24	24	23	23	22	22
90	38	37	36	35	34	34	33	32	31	30	30	29	28	28	27	27	26	26	25	24	24	23	23	23
92	39	38	37	36	35	34	33	33	32	31	30	30	29	28	28	27	27	26	26	25	24	24	24	23
94	40	39	38	37	36	35	34	33	33	32	31	30	30	29	28	28	27	27	26	26	25	25	24	24
96	41	39	39	38	37	36	35	34	33	32	32	31	30	30	29	28	28	27	27	26	26	25	25	24
98	42	41	39	38	37	36	36	35	34	33	32	32	31	30	30	29	28	28	27	27	26	26	25	25
100	42	41	40	39	38	37	36	35	35	34	33	32	32	31	30	30	29	28	28	27	27	26	26	25
102	43	42	41	40	39	38	37	36	35	35	34	33	32	32	31	30	30	29	28	28	27	27	26	26
104	44	43	42	41	40	39	38	37	36	35	34	34	33	32	31	31	30	29	29	28	28	27	27	26
106	45	44	42	41	40	39	39	38	37	36	35	34	34	33	32	31	31	30	29	29	28	28	27	27
108	46	44	43	42	41	40	39	38	37	37	36	35	34	33	33	32	31	31	30	29	29	28	28	27
110	46	45	44	43	42	41	40	39	38	37	36	36	35	34	33	33	32	31	31	30	29	29	29	29
112	47	46	45	44	43	42	41	40	39	38	37	36	35	35	34	33	32	32	31	30	30	29	29	28
114	48	47	46	45	43	42	41	40	39	39	38	37	36	35	34	34	33	32	32	31	30	30	29	29
116	49	48	47	45	44	43	43	41	40	39	38	37	37	36	35	34	34	33	32	32	31	30	30	29
118	50	49	47	46	45	44	43	42	41	40	39	38	37	36	36	35	34	33	33	32	31	31	30	30
120	51	49	48	47	46	45	44	43	42	41	40	39	38	37	36	35	35	34	33	32	32	31	31	30

ANNEX 10.
DAGGERS CARDIOVASCULAR DISEASES



ANSWERS TO TESTS FOR INITIAL EVALUATION

1. C
2. A
3. D
4. C
5. D
6. D, E
7. A, B, E
8. C, D
9. A, B
10. A, B, D, E
11. A, B, D, E
12. A, D
13. A, B, C
14. A, C
15. B, D
16. B, C, D
17. A, B, C, D
18. A, B, C, E

ANSWERS TO TESTS FOR THE FINAL EVALUATION

COMPLEMENT SIMPLE

1. C
2. A
3. C
4. A
5. C
6. D
7. E
8. C
9. A
10. C
11. A
12. D
13. E
14. C
15. C
16. A
17. C
18. D
19. A
20. A
21. C
22. B
23. B
24. D
25. C
26. B

COMPLEMENT MULTIPLE

1. A, B, C
2. A, C, D, E
3. A, B, C, D
4. A, B, D
5. A, C, D
6. A, B
7. A, B, C
8. A, D, E
9. A, C, E
10. A, B, C, E
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14. A, B, C
15. A, B, D, E
16. A, C, D
17. A, B, E
18. B, D, E
19. A, C, D, E
20. B, D, E
21. A, B, C, D
22. B, C, E
23. B, C, D, E
24. A, D, E
25. A, B, C, E
26. A, B, D

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