

# PARTICULARITIES REGARDING THE COMPREHENSIVE REHABILITATION OF THE REVASCULARIZED DIABETIC PATIENTS

## Part II

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**Abstract:** *Comprehensive rehabilitation is a concept developed in order to limit the physiopathologic and psychosocial consequences of the cardiac events and aims at limiting the risk of infarct and sudden death, at improving the cardiac symptomatology, at delaying or determining the reversion of the atherosclerotic process and at reintegrating the cardiac patients within their family and professional activity with a proper functional status.*

**Keywords:** *rehabilitation, diabetic patients*

**Rezumat:** *reabilitarea comprehensivă este un concept dezvoltat pentru a limita consecințele fiziopatologice și psihosociale ale evenimentelor cardiace și are ca obiective limitarea riscului de reinfarctizare și moarte subită, de ameliorare a simptomatologiei cardiace, de întârziere sau de determinare a reversiei procesului aterosclerotic și de a duce la reintegrarea pacientului cu boală cardiovasculară în familie și activitate profesională cu un status funcțional adecvat*

**Cuvinte cheie:** *reabilitare, pacienți diabetici*

## 2. SMOKING

Smoking – as a risk factor – There is very clear evidence of the side effects of smoking regarding health. (1) In the old smokers, smoking is responsible for 50% of the avoidable deaths and half of them are due to cardiovascular disorders. Smoking has a noxious effect on the cardiovascular system, irrespective of age. In MONICA project, more than a half of the non-fatal infarctions in the patients of 35-39 years old could have been attributed to smoking. These effects are proportioned with the daily smoking quantity and with the length of smoking. (2,3) If in the past, smoking was found mainly in men, today, smoking custom can also be detected in women. Moreover, recent data show that mortality due to cardiovascular diseases is higher in the female smokers than in the male smokers, (4,5) irrespective of the adjustment of the other risk factors. These were explained based on the different metabolismization of nicotine and by the differences in behaviour.

The impact of smoking in the progression of atherosclerosis is the highest in the diabetic patients and in the hypertensive ones. Passive smoking proved that it might raise the cardiovascular risk and it was possible that

its effect on the cardiovascular system be even higher than expected. It is well known that the cardiovascular risk in the patients with diagnosed coronary disease decreases right after quitting smoking, so that 2-3 years afterwards, the level is similar to that of the subjects who have never smoked, but with similar coronary affection, while the asymptomatic patients need more than 10 years in order to reach the same level. (3) In a cohort study on the patients with infarction who quitted smoking, it was observed that this measure had the most important effect on mortality.

Smoking assessment is made according to the WHO algorithm, with those 5 As:

A: 1 ASK: Do you smoke?

- no – the message that smoking increases the cardiovascular risk is strengthened.

- - yes

A: 2 ADVICE: Explain and advice clearly and firmly that:

- Smoking increases the risk of producing heart attack or/and ischemic stroke;

- Quitting smoking is one of the most important things for health and heart and people may quit smoking right now;

A: 3 ASSES: “Can you quit smoking now?”

- yes: assist in the preparation plan:

A: 4 ASSIST:

- set up the date;
- inform the family and the friends;
- ask whether they support the idea;
- throw away the cigarettes/tobacco;
- throw away the objects that suggest smoking;
- set up the next visit;

- no: get information about the danger on health and give it to the patient

A: 5 ARRANGE: On the next visit:

- congratulate your friend and strengthen the idea;
- if he/she relapsed, implement a stronger surveillance and ask for the support of the family. Quitting smoking will be encouraged in all smokers, irrespective of age. The strategies for quitting smoking involve behavioural, pharmacological and community interventions.

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Myocardial infraction, coronary surgery and angioplasty are sufficient events in order to impose quitting smoking in 20-60% of the patients who have experienced them. (6,7)

The hospitalization period of time after the myocardial infraction or after a coronary surgery is usually sufficient for the occurrence of withdrawal disorders regarding nicotine: irritability, emotivity, concentration disorders, nausea, headaches, so that these may be solved. Nicotine withdrawal may be made by reducing the number of smoked cigarettes, by replacing them with low nicotine contents or by nicotine substitution therapy (patch). The smokers who use the nicotine substitution methods register a double probability of refraining from smoking one year after, as against those who do not use this therapy. (8,9) Behavioural therapy, with or without substitution therapy, may increase the rate of long term abstinence. This type of therapy may be made by the physician, nurse or the by trained medical staff. (10) The support of the family, friends or of the work colleagues may play a crucial part in the attitude of refraining from smoking. (11)

The pharmacologic therapy has today two substances that proved their efficiency.

- BUPROPION – the need for smoking occurs in 27% of those who receive bupropion versus 56% of those who receive placebo, at the end of the seventh week. Out of the cardiovascular contraindications, severe hypertension is to be mentioned. The combination with nicotine substitution therapy is not recommended, due to the fact that it may increase the arterial tension. The recommended dosage is of 150 mg initially and it may be increased up to 300 mg; regarding the patients under insulin treatment, the dose will not exceed 150 mg.
- VARENICLIN is a substance approved by FDA (Food and Drug Administration) in May 2006 and by the European Union in September 2006. It is an  $\alpha 4\beta 2$  nicotinic receptor partial agonist, cytisine derived. Vareniclin is conditioned in tablets of 0,5 and 1 mg; the therapy starts with doses of 0,5 mg/day and it may reach up to 1 mg twice a day for 12 weeks, period of time that may be extended up to 24 weeks, if smoking has not been resumed. (12)

### 3. NUTRITION, OVERWEIGHT AND OBESITY

The part of nutrition in the etiology and prevention of atherosclerosis and of the cardiovascular diseases was largely studied. In the entire world, it is proved that there is a close relation between the fat food, level of cholesterol and the occurrence of the cardiovascular diseases. The relation is known to be a causal relation. All individuals are advised to consume food associated to a low risk of cardiovascular disease.

Food consumption patterns. Based on the available data, we may draw the conclusion that the alteration of one single nutrient may not alter the cardiovascular risk. Research was focused on the cardioprotective effect of the micro or macronutrients; (13)

**Table no. 1. Total risk management regarding the cardiovascular disease – body weight**

- (1) The body weight increase is associated to the total risk of the cardiovascular morbidity and mortality, especially due to the increase of the blood pressure and of the total cholesterol, to the reduction of the HDL-cholesterol and the increase of the probability for developing diabetes mellitus.
- (2) Body weight reduction is indicated in the obese patients (BMI (body mass index)  $\geq 30 \text{ kg/m}^2$ ) and will be taken into consideration regarding all overweight people (BMI  $\geq 25$  and  $30 \text{ kg/m}^2$ ).
- (3) Men with waist circumference of 94-102 cm and women with 80-88 cm are advised to put on weight. Men with waist circumference of  $>102$  cm and women  $> 88$  cm are advised to loose weight.
- (4) Caloric restriction and the regular physical exercises are the key for the weight control.

According to the European guidelines on cardiovascular disease prevention in clinical practice, 2007.

In Nurses' Health Study and the Health Professionals' Follow-up Study, a balanced diet, based on fruits and vegetables was inversely associated to the incidence of the coronary disease. In opposition, large quantities of red meat, butter, fats, eggs were associated to the increase of this risk. (14)

### Obesity and overweight – risk and management

In the societies that developed a high living standard, cardiovascular mortality decreased initially. This phenomenon was followed by a decrease of plasmatic cholesterol and of the arterial blood pressure by the improvement of the therapy, what brought about the reduction of the cardiovascular mortality. As against this, body weight and diabetes register an ascendant trend. Obesity has become epidemic, registering more than 1 billion of overweight people and more than 300 million obese people. The excess of adipose tissue is associated to the increase of the production of free fatty acids, hyperinsulinemia, insulin-resistance and dyslipidemia. (15,16)

There are discussions regarding the best index related to obesity and cardiovascular risk factors – BMI, WHR- Waist-Hip Circumference Ratio or WC - Waist Circumference. Recent studies proved that the regional distribution of the adipose tissue may be a better predictor than the total body weight. The central (visceral) excess of fats is strongly associated to the cardiovascular and metabolic risk. (17) All these indexes are cheap and universal.

The body mass index is extensively used upon the indication of the National Institute of Health and World Health Organization, defining overweight as BMI =  $25 - 29 \text{ kg/m}^2$ , and obesity with a BMI  $\geq 30 \text{ kg/m}^2$ . The increase of BMI is closely related to the cardiovascular risk.

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Waist circumference was studied as an additional factor for the risk assessment by associating it to the BMI and it was noticed that, regarding the same BMI, waist circumference may be an additional predictor of risk factors and of mortality increase in men and women. It defines two levels of action: 1-  $WC \geq 94$  in men and  $\geq 80$  in women indicate the limit starting from which the loss of weight is indicated. For now, these values are valid for the white race. (18)

Regarding the longitudinal studies in men and women, the increase of the WHR was associated to the increase of the cardiovascular mortality. In men, diabetes evolution was associated to WHR, even after the BMI adjustment. In INTERHEART study, it was observed that, both the increase of the WC and the WHR are associated to the myocardial infraction, even after the adjustment of the other risk factors and of the BMI. (19)

Physical training and the impact on the body weight, lipid metabolism and risk – sedentary lifestyle and obesity are critical all over the world. The promotion of physical training programmes and the ingestion of low caloric food represent the first measures in the rehabilitation strategies.

Recent studies proved that the physical exercise has an effect on the metabolism of the abdominal fats before the decrease of the body weight. This may stimulate the high risk persons, such as the revascularized diabetics, to start attending the physical training programmes. (20,21)

Nutritional treatment of the cardiovascular disease.

All patients with cardiovascular disease and with high risk of ischemic stroke, as in the case of diabetics, will be advised in relation with food, so that to reduce the cardiovascular risk. Indications will be made individually, insisting on diet, and by taking into account the other risk factors, such as: dyslipidemia, hypertension and obesity. Regarding the family, the contribution of the person who cooks and buys the food is essential.

General recommendations:

- Each food group will provide the necessary of nutrients, minerals and vitamins.
- Fish, fruits and vegetables intake, as well as integrated cereals, less salt and unfat milk will be encouraged to be consumed.
- Energetic intake will be adjusted with a view to maintain the ideal weight.
- The consumption of fish oil and omega 3-fatty acids may be associated in order to reduce the risk for fatal cardiovascular events.
- The consumption of fruits and vegetables and salt intake restriction are associated to a low arterial tension.

Specific recommendations:

- LDL-cholesterol may be reduced by:
  - The decrease of the intake of trans and saturated free fatty acids and by the reduction of the cholesterol taken from food; the trans and saturated

fats will be replaced with those polyunsaturated or of vegetal origin.

- The saturated lipids may be found in a large variety of foods, including meat and milk products, butter, cheese, cookies, biscuits, coconut or palm oil and a large number of cooked products.
- The trans fatty acids can be found in animal products: milk products and cow fat contain almost 3-6% of the fatty acids (% of the fatty acids), in pastry products: biscuits, cakes, fries, soup powders, margarine (containing between 1-30%). The patients are invited to read the food labels mentioning the composition.
- The soluble fibres and the phytosterols may help in the reduction of the plasmatic LDL-cholesterol.
- HDL-cholesterol may be increased by:
  - The increase of the level of the physical exercise in the inactive persons, weight decrease in the obese people and by controlling the glycaemia in the diabetic patients.
  - The consumption of refined sugars is related to the decreased of the HDL-cholesterol in certain susceptible individuals. These sugars will be replaced with complex sugars.
  - Olive oil may help in the increase of the HDL-cholesterol; an increase of the unsaturated lipids will be firmly recommended in the patients with metabolic syndrome.
  - Alcohol moderate consumption may increase the HDL-cholesterol; without being a positive indication, alcohol will not be forbidden in the patients with low HDL-cholesterol.
- Triglycerides may be decreased by:
  - The increase of the physical exercise in the sedentary patients, weight decrease in the obese people and by controlling the glycaemia in the diabetic patients.
  - Refined sugars and alcohol intake will be controlled, as it is associated to the plasmatic increase of triglycerides, in the susceptible patients.
  - Omega 3-acids intake will be encouraged, as it may contribute to the decrease of the triglycerides concentration.

Arterial tension may be decreased by:

- Weight decrease in the overweight or obese patients, the control of salt and alcohol intake and by the increase of potassium intake.
- The reduction of salt by consuming fresh food, and by avoiding salting excessively the food when cooking. The patients are invited to read the food labels in order to note the salt quantity.
- It is preferred to consume fruits and vegetables as a source of potassium, before the substitution treatment.

### Overweight and obesity management

The voluntary decrease of weight in the obese people may improve or prevent many of the obesity-related cardiovascular risk factors. It is important for the

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health professionals to understand the clinical effect of the weight loss, in order to be able to put into practice the most proper management strategies. (21)

### **Diet and behavioural intervention:**

There was a number of diets and behavioural interventions proposed in obesity. Overweight control depends on the balance between the energy intake and consumption. The diets differ in their total energetic intake, in glucides, proteins and lipids composition, energetic density and glycemic index. (22) The diets containing a small quantity of lipids are considered to be the standards for the reduction of weight, also having a benefic effect on the decrease of the LDL-cholesterol. The total of fats intake should not exceed 25-35% of energy. Glucide-poor diet may significantly decrease weight on short term, with benefic effects on triglycerides and HDL plasmatic cholesterol, but on long term, they are not sufficiently investigated. Alcohol is a major source of calories and its reduction plays an important part in weight decrease.

The behavioural intervention should lead to the change of lifestyle on long term. The behavioural change is facilitated by the use of clear objectives, self-monitoring and problems solving techniques. (23) The drug treatment of overweight has a modest effect and multiple side effects.

Orlistat inhibits the intestinal lypasis and prevents hydrolysis and absorption. The effect is modest, and gastrointestinal disorders may occur.

Sibutramine accentuates the sensation of saturation after a meal, while its metabolites inhibit noradrenalin and serotonin. The contraindications and the side effects are appreciable.

Rimonabant is an inhibitor of the endocannabinoid receptor that seems to induce a significant decrease in weight in combination with diet. It may improve glucose tolerance, beneficially influencing the lipid metabolism and it is associated with the modest reduction of the blood pressure.

### **4. BLOOD PRESSURE**

The decision to treat blood pressure depends on the systolic and diastolic blood pressure and on the total risk of assessment through SCORE charts. All patients that initially belong to the second and third degrees need pharmacologic therapy, due to the fact that the decrease of the blood pressure brought about the decrease of the cardiovascular mortality and morbidity. (24,25,26,27) Regarding the degrees 1-3, conciliation is recommended, in order that the patients should be able to change their lifestyle. Regarding the patients with a high risk for installed cardiovascular and renal diseases, with the affection of the target organs or with diabetes, the assessment for changing the lifestyle will be made earlier. The pharmacologic treatment will be promptly initiated in all hypertensive patients, irrespective of the degree, according to the indications mentioned in the table below. In all cases, all the risk factors will be taken into consideration and adjusted; in those where a cardiovascular or renal disease or diabetes is installed, a significant increase of the risk will be considered, while the target value will be of 130/80 mm Hg; for all the others, the risk will be checked on the SCORE graphic; all those with affected target organs will be considered as "increased risk" patients.

**Table no. 2. Management of the total cardiovascular risk – arterial hypertension**

SCORE RISK	CVD	Normal<130/85	Normally high 130-139/85-89	Degree 1	Degree 2	Degree 3
LOW < 1%		Changing lifestyle	Changing lifestyle	Changing lifestyle	+ pharmacologic therapy if persisting	pharmacologic therapy
MODE 1-4%		Changing lifestyle	Changing lifestyle	± pharmacologic therapy	+ pharmacologic therapy if persisting	pharmacologic therapy
INCREASED 5-9%		Changing lifestyle	± pharmacologic therapy	± pharmacologic therapy	pharmacologic therapy	pharmacologic therapy
MUCH INCREASED ≥10%		Changing lifestyle	± pharmacologic therapy	± pharmacologic therapy	pharmacologic therapy	pharmacologic therapy

According to the European guidelines on cardiovascular disease prevention in clinical practice, 2007.

The beta-blockers have detrimental effects on the lipid metabolism and increase the incidence of diabetes (in comparison with other drugs); they are not preferred in the metabolic syndrome, in obesity or in the conditions in which they increase the risk for diabetes. (28,29) The same is also valid in the case of tiazidic diabetes, especially in large doses. (30) As, they are usually administered together, their differentiated effect is assessed with difficulty.

### **Desirable blood pressure**

The therapeutic objective in arterial hypertension is the reduction of the total cardiovascular risk of morbidity and mortality on long term. This requires, besides the decrease of the blood pressure, the treatment of all reversible risk factors (smoking, dyslipidemia, diabetes) and the management of the associated classic conditions. The target for the blood pressure remains the value under 140, but irrespective of the means used, the control of values in

clinical trials does not exceed 60-70%. In all patients, blood pressure reduction will be made gradually, this being more carefully supervised in the old people, atherosclerotic and diabetic patients. Regarding these patients, orthostatic hypotension will be avoided by monitoring the symptomatology, the function of the vital organs and the wellbeing.

VALUE and INVEST trials proved that the hypertensive patients with controlled values under 140/90 register a reduced incidence of the cerebral stroke, myocardial infarction and a reduction of the cardiovascular mortality and morbidity. (31,32)

Regarding diabetics, a more intense treatment is recommended, as well as a small tension target (130/80mmHg). There is solid evidence in relation to the benefic effect (reduction of the micro and macrovascular complications) of the blood pressure reduction in the type 2 diabetics, as shown in the HOT and UKPDS studies (33,34) or in the ABCD study. (35, 36)

### 5. PLASMATIC LIPIDS

At the level of the general population, the concentration of the total cholesterol is a strong predictor for the coronary disease. An increase of 10% of the total cholesterol is associated to an increase of the incidence of the coronary disease with 27%. (37) On the other hand, the reduction with 10% of the plasmatic cholesterol is followed by a reduction with 25% of the incidence of the coronary disease 5 years after, while the reduction of the LDL-cholesterol with 4 mg/dl is accompanied by the reduction with 23% of the coronary disease, 19% reduction of the ischemic strokes and 21% reduction of the cardiovascular pathology. (38)

Before starting the pharmacologic treatment, the secondary causes of hyperlipidemia will be excluded (hypertiroidism, alcohol abuse, diabetes, Cushing disease, renal and hepatic diseases, obesity), especially those related of certain drugs (corticosteroids, cyclosporine).

The pharmacological therapy comprises more classes of drugs: HMG CoA reductase (statins) inhibitors, fibrates, bile acids sequestrants, nicotinic acid and selective inhibitors of the cholesterol absorption (ezetimib).

Statins represent the first line in the treatment of hypercholesterolemia, with angiographic arguments regarding the cessation of progression or even the regression of atherosclerosis; there are two studies with intravascular and ultrasound (IVUS) that registered good results; the same is valid for the LDL-cholesterol.

Statins are safe in administration, (38) easy to use and allow associations with classes of drugs without major interactions. (39)

Fibrates decrease the triglycerides and increase the HDL-cholesterol, but they decrease the LDL-cholesterol less than statins. Regarding the FIELD study, a trial that also comprises high risk diabetics, showed that phenobarbital reduced only the non-fatal infarctions and that the revascularizations did not influence the risk for fatal coronary events. (40)

Taking into account the clear benefices of the statins in diabetics, fibrates were not recommended as a first line treatment in the high risk groups, but only in those with persistent decrease of the HDL-cholesterol or in those with very large concentrations of triglycerides.

Nicotinic acid is another efficient agent in the decrease of lipidemia. It is difficult to be used because of its side effects (constipation, flushing). It is very useful in the increase of the HDL-cholesterol and certain data indicate the decrease of the general mortality.

Ezetimib has a mild effect on the decrease of the LDL-cholesterol in monotherapy and may be administered in those with side effects to statins or in the patients with hepatic active diseases. Its major part is related to the association of statins, there where these ones cannot reach the safe therapeutic targets.

The therapy of hyperglyceridemia requires special attention. Many times, the high level of triglycerides respond to the reduction of alcohol and of the weight, as a first management line. Bile acids sequestrants tend to increase the triglycerides and will not be administered when their plasmatic level exceeds 180 mg/dl.

Statins will be used when triglycerides exceed 450 mg/dl. When the level is of 450-900, fibrates or statins will be used as a first line treatment. Regarding levels above 900 mg/dl, medication becomes less useful, but fibrates will be used in the prevention of pancreatitis. The non-pharmacologic measures will be insisted on, as well as the reduction up to the forbiddance of alcohol consumption or insulin treatment etc. Mixed hyperlipidemia may also beneficiate from the combination between fibrates and ezetimib.

### 6. DIABETES AND THE METABOLIC SYNDROME

Randomized trials proved that a good medical check up prevents the microvascular complications, both in the patients with type 1 diabetes and in type 2. (34,41,42,43). Regarding the microvascular complications, this is not convincing yet, although UKPDS study strongly indicates this possibility.

Regarding the patients with types 1 diabetes, without nephropathy, the strict control of glycaemia helps in the maintenance of the plasmatic lipids at normal limits. In the patients with diabetic nephropathy, this is accompanied by multiple disorders of the plasmatic lipids that are not adjusted through the control of glycaemia. The high level of triglycerides and the reduced level of HDL-cholesterol that accompanies the diabetes type 2 are the only ones that are partially adjusted through a proper control of glycaemia. In type 1 diabetes, the control of glycaemia requires proper insulin therapy, associated to a professionally led diet. In type 2 diabetes, the diet will be accompanied by the oral hypoglycaemia treatment or insulin. In overweight people, metphormin seems to be the treatment that provides, besides the loss of weight, the delay in the occurrence of complications. Thiazolidinediones (commonly called glitazones) are more and more used in the type 2 diabetes, with impact on

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the increase of the insulin sensitivity of the peripheral tissues, being mainly represented by rosiglitazone and pioglitazone.

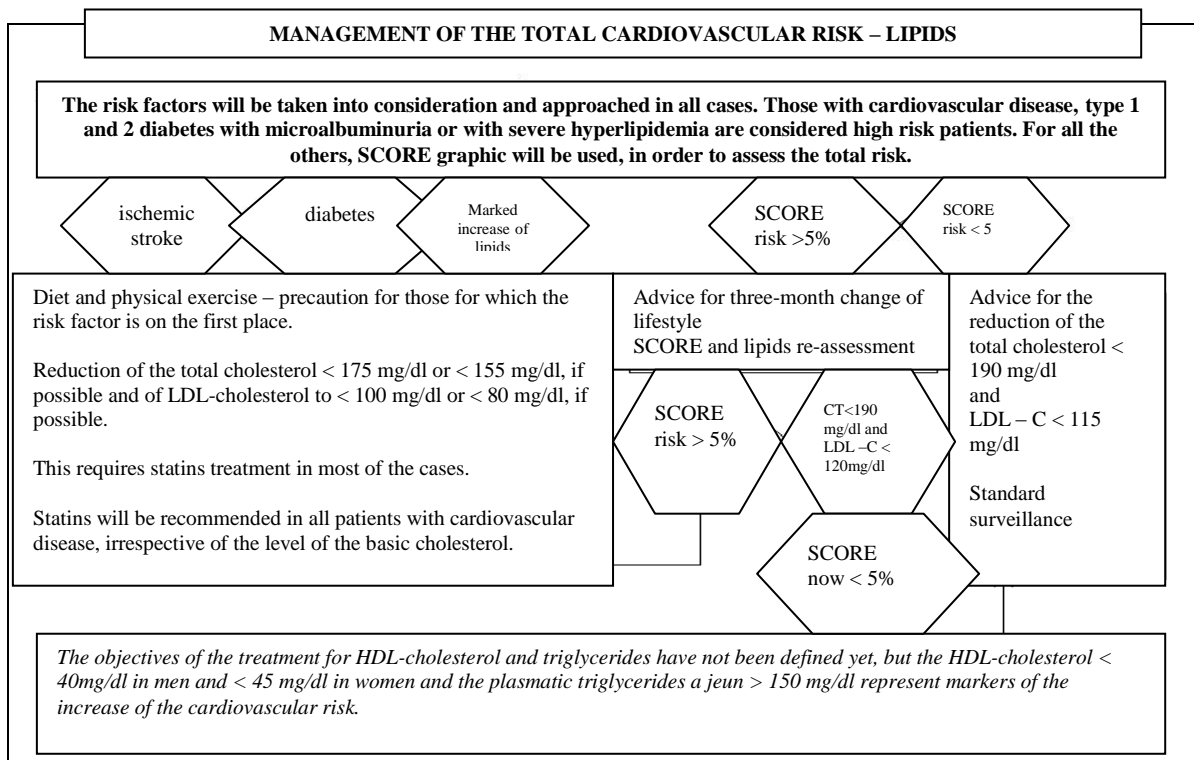
Self-monitoring is very useful in the treatment of type 1 diabetes, improving its quality and safety and avoiding hypoglycaemia. The same is to be found in type 2 diabetes.

There is a general consensus regarding the target of the glycaemia control (44,45,46) in the type 1 diabetes, that is glycosylated haemoglobin < 6,5% in the patients with established cardiovascular disease, microalbuminuria or nephropathy. In type 2 diabetes, different organizations propose HbA<sub>1c</sub> as a target of 7% or 6,5 %, but, it is

certain that cardiovascular prevention is accomplished below 6,5%.

As it was mentioned in the previous chapter, the decrease of the blood pressure in diabetics should be even higher, because this way, the development of the diabetic nephropathy and renal insufficiency will be prevented. (47,48,49,50,51) If it was said that the desired blood pressure in the diabetic patients should be below 130/80 mHg, it is important to note that in those with diabetic nephropathy, these values should be below 125/75 mmHg (55)

**Picture no. 1. Management of the total cardiovascular risk – lipids – according to the European guidelines on cardiovascular disease prevention in clinical practice, 2007.**



The type of medication is also important. The inhibitors of the conversion enzyme and of the angiotensin II receptors have benefic effects, especially in preventing the progression towards microproteinuria, in both types of diabetes. (47,48,49,50,51) and are preferred at the beginning of the treatment, even in combination. In the diabetic patients with hypertension and coronary disease, as in the case of those surviving after a myocardial infraction or angina, the use of beta-blockers is indicated. (52).

The therapy for decreasing the plasmatic lipids, in the absence of certain therapeutic targets, should provide values for the LDL-cholesterol <100 mg/dl and for the total cholesterol <175 mg/dl in the diabetic patients; recently, the CARDS study indicates even smaller targets for LDL-cholesterol < 80 mg/dl.

Prevention in the patients with metabolic syndrome, which may be a precursory condition of the types 2 diabetes and presents a risk for the development of the cardiovascular diseases, may also be made on the SCORE graphic. Taking into account the fact that changing the lifestyle has a great impact on all the elements of the metabolic syndrome, special attention will be paid on the importance of the weight decrease and of the physical exercise; disorders of the lipid metabolism will be carefully adjusted.

### 7. PSYCHOSOCIAL FACTORS

Besides the increase of the primary coronary event risk, the negative psychosocial factors act as a barrier in the patient's adherence to therapy and to the efforts of improving lifestyle and of promoting healthy customs.

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A low social status, the loss of the social support and isolation, work and family overstress, as well as the negative emotions worsen the clinical evolution and the prognostic of the coronary disease. There were identified certain physiopsychological and behavioural mediators. (53,54) Men and women with low social status, defined by reduced education, lower professional activity, residing in poor areas, register an increase of the risk due to cardiovascular mortality, which is only partly due to the traditional risk factors. (55) These mediators may be changed and all efforts should be oriented towards those with low social status, as they need such support mostly. Not recognizing the subjects with a low social status, when applying the SCORE standardized graphics, will lead to the underestimation of the social risk in the exposed individuals. (56) Insufficient preventing measures will lead to the increase of the cardiovascular morbidity in this unprivileged group of people.

Socially isolated subjects register a high risk of premature death due to the ischemic heart disease. (57,58) The social support has benefic effects on lifestyle and on a healthy behaviour, in the extend in which its loss is related to a bad prognostic to reduce survival in the patients with clinical manifestations of cardiovascular disease.

Long term exposure to an irregular timetable, including the night work will increase the cardiovascular risk after a period of certain years, both in men and in women. (60,61) Conflicts, crises, stress in the family life will lead to the increase of the cardiovascular risk, especially in women. (59,62) In the patients with manifested coronary disease, depression has its well documented cardiac symptoms, regarding the general quality of life and the healthy behaviour (including the increase of the use of the medical services, low adherence to the recommendations of changing the lifestyle, medication and low rate of resuming the professional activity. The prognostic is more reserved in those who combine the negative emotions with the social inhibition. (64,65)

Management of the psychosocial risk factors; clinical practice recommendations:

- The assessment of the psychosocial risk factors, such as depression and hostility, of the social and economic standard, of the social isolation and chronic stress will be made by clinical interview or by standardized questionnaires;
- Revealing, through discussions with patients, the life quality and the results of the medical interventions;
- Approaching a multimodal behavioural interventions integrating the individual or group counselling, in order to reduce the psychosocial risk factors and shaping the attitude towards stress and disease;
- Appealing to a specialist in case of emotional problems of clinical intensity.

Recognizing the psychosocial risks associated to depression, hostility, low socio-economic status, lack of social support or chronic psycho-social stress in the

patients and in the persons with risk factors may be crucial for the reduction of this risk.

**Table no. 3. Essential questions for the assessment of the psycho-social factors in clinical practice.**

DEPRESSION	Do you feel down, depressed, or helpless? Have you lost your interests and life enjoyment?
SOCIAL ISOLATION	Are you living alone? Do you need a companion (a trustful friend)? Do you have someone to care for you if you are ill?
WORK AND FAMILY STRESS	Do you have enough control in solving your working problems? Do you think the rewards are proportioned with your work? Do you have serious problems with your intimate partner?
HOSTILITY	Do you often get upset? If someone is annoying you, do you tell this to your partner? Are you nervous about the tics of those around you?
LOW SOCIO-ECONOMIC STANDARD	What is your socialization level? Is your work predominantly physical?
According to the European guidelines on cardiovascular disease prevention in clinical practice, 2007.	

If possible, the patients' approach will be made in a multimodal manner, with stress behavioural management measures and social integration. Depression and other negative feelings tend to accentuate the cardiovascular disease, the pharmacologic and psychotherapeutic treatment being necessary in all cases with significant intensity of the symptoms.

### REFERENCES

1. European guidelines on cardiovascular disease prevention in clinical practice, 2007 cap 7.1, pp. 121.
2. European guidelines on cardiovascular disease prevention in clinical practice, 2007 cap 7.1, pp. 125,126.
3. Manson J, Tosteson H, Ridker PM, Satterfield S, Hebert P, O'Connor GT, et al. The primary prevention of myocardial infarction. *N Engl J Med* 1992; 326:1406–1416.
4. European guidelines on cardiovascular disease prevention in clinical practice, 2007 cap 7.1, pp. 128,129.
5. Njolstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. *Circulation* 1996;93:450–456.
6. Crouse JD and Hagaman, AP. Smoking cessation in relation to cardiac procedures. *Am. J. Epidemiol.* 134:699, 1991.
7. Rigotti, NA, McKool KM and Shiffman S. Predictors of smoking cessation after coronary artery bypass

## CLINICAL ASPECTS

- graft surgery: Results of a randomized trial with 5-year follow-up. *Ann. Intern. Med.* 120:287, 1994.
8. [Abstract] Silagy C, Mant D, Fowler G and Lodge M. Meta-analysis on efficacy of nicotine replacement therapies in smoking cessation. *Lancet* 343:139, 1994.
  9. Fiore MC, Smith SS, Jorenby DE and Baker TB. The effectiveness of the nicotine patch for smoking cessation: A meta-analysis. *JAMA* 271:1940, 1994.
  10. [Abstract] Hurt RD, Dale LC, Fredrickson PA et al. Nicotine patch therapy for smoking cessation combined with physician advice and nurse follow-up: One-year outcome and percentage of nicotine replacement. *JAMA* 271:595, 1994.
  11. European guidelines on cardiovascular disease prevention in clinical practice, 2007, p. 25.
  12. [en.wikipedia.org/wiki]
  13. Kris-Etherton P, Etherton TD, Carlson J, Gardner C. Recent discoveries in inclusive food-based approaches and dietary patterns for reduction in risk for cardiovascular disease. *Curr Opin Lipidol* 2002; 13:397–407.
  14. Serra-Majem L, Roman B, Estruch R. Scientific evidence of interventions using the Mediterranean diet: a systematic review. *Nutr Rev* 2006;64:S27–S47.
  15. Wajchenberg B. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. *Endocrine Rev* 2000; 21:697–738.
  16. Carr M, Brunzell JD. Abdominal obesity and dyslipidemia in the metabolic syndrome: importance of type 2 diabetes and familial combined hyperlipidemia in coronary artery disease risk. *J Clin Endocrinol Metab* 2004;89:2601–2607.
  17. Despres J, Moorjani S, Lupien PJ, Tremblay A, Nadeau A, Bouchard C. Regional distribution of body fat, plasma lipoprotein, and cardiovascular disease. *Arteriosclerosis* 1990;10:497–511.
  18. Vikram N, Pandey RM, Misra A, Sharma R, Devi JR, Khanna N. Non-obese (body mass index < 25 kg/m<sup>2</sup>) Asian Indians with normal waist circumference have high cardiovascular risk. *Nutrition* 2003;19:503–509.
  19. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. *Lancet* 2005; 366:1640–1649.
  20. Reieski W, Brawley LR, Ambrosius WT, Brubaker PH, Focht BC, Foy CG, et al. Older adults with chronic disease: benefits of group-mediated counseling in the promotion of physically active lifestyles. *Health Psychol.*
  21. Carlson J, Norman GJ, Feltz DL, Franklin BA, Johnson JA, Locke SK. Self-efficacy, psychosocial factors, and exercise behaviour in traditional versus modified cardiac rehabilitation. *J Cardiopulm Rehabil* 2001;21:363–373.
  22. Klein S, Burke LE, Bray GA, Blair S, Allison DB, Pi-Sunyer X et al. Clinical implications of obesity with specific focus on cardiovascular disease: a statement for professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation* 2004; 110:2952–2967.
  23. Berkel L, Poston WSC, Reeves RS, Foreyt JP. Behavioral interventions for obesity. *J Am Diet Assoc* 2005;105:S35–S43.
  24. Collins R, Peto R, MacMahon S, Hebert P, Fiebach NH, Eberlein KA et al. Blood pressure, stroke, and coronary heart disease. Part 2, Short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. *Lancet* 1990; 355:827–838.
  25. Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively-designed overviews of randomised trials. Blood pressure lowering treatment trialists' collaboration. *Lancet* 2003;362:1527–1535.
  26. Staessen J, Gasowski J, Wang JG, Thijs L, Den Hond E, Boissel JP, et al. Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials. *Lancet* 2000;355:865–872.
  27. Collins R, MacMahon S. Blood pressure, antihypertensive drug treatment and the risk of stroke and of coronary heart disease. *Br Med Bull* 1994; 50:272–298.
  28. Lindholm L, Ibsen H, Borch-Johnsen K, Olsen MH, Wachtell K, Dahlof B et al. For the LIFE study group. Risk of new-onset diabetes in the Losartan Intervention for Endpoint reduction in hypertension study. *J Hypertens* 2002;20:1879–1886.
  29. Kjeldsen S, Julius S, Mancia G, McInnes GT, Hua T, Weber MA, et al. VALUE Trial Investigators. Effects of valsartan compared to amlodipine on preventing type 2 diabetes in high-risk hypertensive patients: the VALUE trial. *J Hypertens* 2006; 24:1405–1412.
  30. Mancia G, Grassi G, Zanchetti A. New-onset diabetes and antihypertensive drugs. *J Hypertens* 2006;24:3–10.
  31. Weber M, Julius S, Kjeldsen SE, Brunner HR, Ekman S, Hansson L et al. Blood pressure dependent and independent effects of antihypertensive treatment on clinical events in the VALUE Trial. *Lancet* 2004; 363: 2049–2051.
  32. Pepine C, Kowey PR, Kupfer S, Kolloch RE, Benetos A, Mancia G, Coca A, et al., INVEST Investigators. Predictors of adverse outcome among patients with hypertension and coronary artery disease. *J Am Coll Cardiol* 2006;47:547–551.
  33. Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. *Lancet* 1998; 351:1755–1762.



## CLINICAL ASPECTS

34. UKPDS. UK Prospective Diabetes Study. Tight blood pressure control and risk of microvascular and macrovascular complications in type 2 diabetes: UKPDS 38. *BMJ* 1998;317:703–713.
35. Schrier R, Estacio RO, Esler A, Mehler P. Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and stroke. *Kidney Int* 2002;61:1086–1097.
36. Estacio R, Jeffers BW, Hiatt WR, Biggerstaff SL, Gifford N, Schrier RW. The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin independent diabetes and hypertension. *N Engl J Med* 1998; 338:645–652.
37. Law M, Wald NJ, Thompson SG. By how much and how quickly does reduction in serum cholesterol concentration lower risk of ischemic heart disease? *BMJ* 1994; 308:367–372.
38. Baigent C, Keech A, Kearney PM, Blakwell L, Buck G, Pollicino et al. Cholesterol Treatment Trialist'(CTT) collaborators. Efficacy and safety of cholesterol - lowering treatment: prospective meta-analysis of data from 90.056 participants in 14 randomised trials of statins. *Lancet* 2005;366:1267–1278.
39. Reiner Z, Galic M, Hanzevacki M, Tedeschi-Reiner E. Concomitant use of statins and cytochrome P 450 inhibitors. *Lijec vjesn* 2005;127:65–68.
40. Keech A, Simes RJ, Barter P, Best J, Scott R, Taskinen MR, et al.; FIELD study investigators. Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. *Lancet* 2005;366:1849–1861.
41. UKPDS. UK Prospective Diabetes Study. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; 352:837–853.
42. UKPDS. UK Prospective Diabetes Study. Effect of intensive blood glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS34). *Lancet* 1998;352:854–865.
43. Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long term complications in insulin dependent diabetes mellitus. *N Eng J Med* 1993;329:977–986.
44. Ryden L, Standl E, Bartnik M, Van den Berghe G, Betteridge J, de Boer MJ et al. Guidelines on Diabetes, pre-diabetes and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD). *Eur Heart J* 2007; 28: 88–136.
45. American Diabetes Association Position Statement. Standard of medical care in diabetes. *Diabetes Care* 2007;30(Suppl 1):S4–S40.
46. National Collaborating Centre for Chronic Diseases. Type 1 diabetes in adults. National clinical guideline for diagnosis and management in primary and secondary care. London (UK): Royal College of Physicians; 2004 <http://www.rcplondon.ac.uk/pubs/books/DIA/index.asp>.
47. Lewis E, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;345:851–860.
48. Brenner B, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001; 345:861–869.
49. Parving H, Lehnert H, Brochner-Mortensen J, Gomis R, Andersen S, Arner P. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med* 2001;345:870–878.
50. HOPE. Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and micro-HOPE substudy. *Lancet* 2000;355:253–259.
51. Ravid M, Savin H, Jutrin I, Bental T, Katz B, Lishner M. Long term stabilizing effect of angiotensin-converting enzyme inhibition on plasma creatinine and on proteinuria in normotensive type II diabetic patients. *Ann Intern Med* 1993;118:577–581.
52. European guidelines on cardiovascular disease prevention in clinical practice, 2007.
53. De Backer G, Ambrosioni E, Bort-Johnsen K, Brotons C, Cifkova R, Dallongeville J et al. European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of eight societies and by invited experts). *Eur J Cardiovasc Prev rehab* 2003; 10 (Suppl 1):S1–S78.
54. Rozanski A, Blumenthal JA, Davidson KW, Saab PG, Kubzansky L. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioral cardiology. *J Am Coll Cardiol* 2005; 45:637–651.
55. Steptoe A, Marmot M. The role of psychobiological pathways in socioeconomic inequalities in cardiovascular disease risk. *Eur Heart J* 2002; 23:13–25.
56. Woodward M, Brindle P, Tunstall-Pedoe H; SIGN group on risk estimation. Adds social deprivation and family history to cardiovascular risk assessment: the ASSIGN score from the Scottish Heart Health Extended Cohort (SHHEC). *Heart* 2007;93:172–176.

57. Orth-Gomer K, Rosengren A, Wilhelmsen L. Lack of social support and incidence of coronary heart disease in middle-aged Swedish men. *Psychosom Med* 1993;55:37–43.
58. Penninx B, van Tilburg T, Kriegsman DM, Deeg DJ, Boeke AJ, van Eijk JT. Effects of social support and personal coping resources on mortality in older age: the Longitudinal Aging Study Amsterdam. *Am J Epidemiol* 1997;146:510–519.
59. Rosengren A, Hawken S, Ounpuu S, Sliwa K, Zubaid M, Almahmeed WA, et al. INTERHEART investigators. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364:953–962.
60. Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Speizer FE, et al. Prospective study of shift work and risk of coronary heart disease in women. *Circulation*
61. Tuschsen F. Working hours and ischemic heart disease in Danish men: a 4-year cohort study of hospitalization. *Int J Epidemiol* 1993;22:215–221.
62. Orth-Gomer K, Wamala SP, Horsten M, Schenck-Gustafsson K, Schneiderman N, Mittleman MA. Marital stress worsens prognosis in women with coronary heart disease: The Stockholm Female Coronary Risk Study. *JAMA* 2000;284:3008–3014.
63. Herrmann-Lingen C, Buss U. Angst und Depressivität im Verlauf der koronaren Herzkrankheit. Frankfurt/Main: VAS Verlag; 2003.
64. Denollet J, Sys SU, Brutsaert DL. Personality and mortality after myocardial infarction. *Psychosom Med* 1995;57:582–591.
65. Denollet J, Vaes J, Brutsaert DL. Inadequate response to treatment in coronary heart disease: adverse effects of type D personality and younger age on 5-year prognosis and quality of life. *Circulation* 2000;102:630–6.