

## CHANGES IN LIPOPROTEIN INDICATOR AND INDICATOR OF ENDOTHELIAL FUNCTION AFTER IMPLEMENTED CARDIOVASCULAR REHABILITATION PROGRAM

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Insufficient physical activity in the world annually is the cause of death of 1.9 million people. According to the data from the World Health Report, physical inactivity is about to become the global problem. Regular physical activity and good physical shape raise the functional capacity and the quality of patient's life. With physical activity it is possible to improve metabolic, endothelial, lateral-muscular, pulmonary and cardiovascular functions of an organism, but also the function of the autonomous nervous system. The endothelium has the important role in maintaining the normal cardiovascular tonus and blood fluidity by reducing the platelet activity and the adhesion of leukocytes, and also by restricting the reaction of vascular inflammation. The aim of this paper was to present the recent data about effects of cardiovascular rehabilitation and physical training on lipoproteins' status and markers of endothelial function.

The impact of physical activity on the lipid status is accomplished by affecting the enzymes of lipoprotein metabolism, including the lipoprotein and the liver lipase and the movable protein of cholesterol ester (11). The studies point out that aerobic physical activity result in increasing of HDL concentration and the decrease of the triglycerides value, total and LDL cholesterol. The connection, which is dose-dependant, exists between physical activity and the lipid level, as the arguments which suggest that the duration of physical activity is the key parameter in modification of the lipid metabolism.

Physical activity leads to the beneficial changes in the cardiovascular and lipid indicators and improves the endothelial function in the secondary prevention of coronary disease. Reduction of the lipid parameters by introducing physical rehabilitation and dietetic regime lie in the basis of secondary prevention of coronary disease. Furthermore, there is a constant improvement in NO biodisposability and therewith the improvement in endothelial function. *Acta Medica Medianae 2012;51(3):52-56.*

**Key words:** *carcinoid, gastrointestinal tract, neuroendocrine tumours, serotonin, carcinoid syndrome*

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### Introduction

Insufficient physical activity in the world annually is the cause of death of 1.9 million people. In 2002, the two-thirds of the grown-up population (15-year-olds and older) in the European Union did not achieve the recommended level of physical activity (1). According to the data from the World Health Report, physical inactivity is about to become the global problem, from the childhood to every age and social structure (2).

Literature review raises the question how much the changes in lipoprotein metabolism,

which are indicated by physical activity and appropriate diet, reduce the cardiovascular risk (3). Physical activity strongly influences the human health, especially in the pathogenesis of the diseases which constitute the metabolic syndrome (insulin resistance of, type 2 diabetes, hyperlipidaemia, hypertension, obesity, and cardiovascular diseases and osteoporosis) (4). Regular physical activity and good physical shape raise the functional capacity and the quality of patient's life (5).

The connection between the elevated values of total cholesterol and cholesterol in the low density lipoproteins (LDL-h), as well as the connection between low concentrations of cholesterol in the high density lipoproteins (HDL-h) with cardiovascular diseases was noticed long time ago (6). That is the main reason why the recommendations of the National Cholesterol Education Program (National Cholesterol Education Program – NCEP III) are based on the determination of these parameters' concentration, as the

basic parameters necessary for prediction and treatment of people having cardiovascular diseases (6).

Physical activity is generally categorized as low intensity (physical effort which requires less than 45% of the maximum oxygen consumption), moderate intensity (45% to 60% of the maximum oxygen consumption) and very high intensity (over 75% of the maximum oxygen consumption). Training of moderate intensity corresponds to about 60-70% of maximum heart frequency (7).

### Effects of physical activity on cardiovascular system

Regular physical activity is a well-known and accepted agent which reduces the global mortality and improves the outcome of many diseases (5). With physical activity it is possible to improve metabolic, lateral-muscular, pulmonary and cardiovascular functions of an organism, but also the function of the autonomous nervous system (8).

Physical activity affects the autonomous regulation of cardiovascular system in regard to reduced heart frequency and blood pressure, which brings about the reduction of needs for oxygen.

It has been proved that high value of blood pressure is negatively associated with the patient's age and the index of body mass (BMI); however, they are positively connected with the variability of blood pressure, which is, along with the variability of the heart frequency, the most valid identifier of an autonomous function and cardiovascular mortality (9).

Secco et al. proved that there is statistically relative correlation between the increase in the

physical activity duration and decrease in mortality. There is a large number of researches which indicate that regular physical activity and greater cardiorespiratory endurance reduce the global mortality related to the degree of achieved cardiorespiratory endurance, the duration and the intensity of physical load (10).

### Impact of physical activity on lipoprotein status

The impact of physical activity on the lipid status is accomplished by affecting the enzymes of lipoprotein metabolism, including the lipoprotein and the liver lipase and the movable protein of cholesterol ester (11). The studies point out that aerobic physical activity result in increasing of HDL concentration and the decrease of the triglycerides value, total and LDL cholesterol (11).

The connection, which is dose-dependant, exists between physical activity and the lipid level, as the arguments which suggest that the duration of physical activity is the key parameter in modification of the lipid metabolism. Physical activity is considered to be more effective when it comes to the reduction in body fat content in people with dyslipidaemia, compared to the people with normal lipid status. Physical activity modifies the lipid plasma concentration exerting effects on the key enzymes (12).

The effect of physical training on the lipoprotein parameter's value is shown in the following: it reduces the level of triglycerides and VLDL particles, considerably increases the level of HDL cholesterol especially on the account of HDL 3 subfraction, raises the level of apolipoprotein A-I, detects the positive effect on the level of total and LDL cholesterol (13,14).

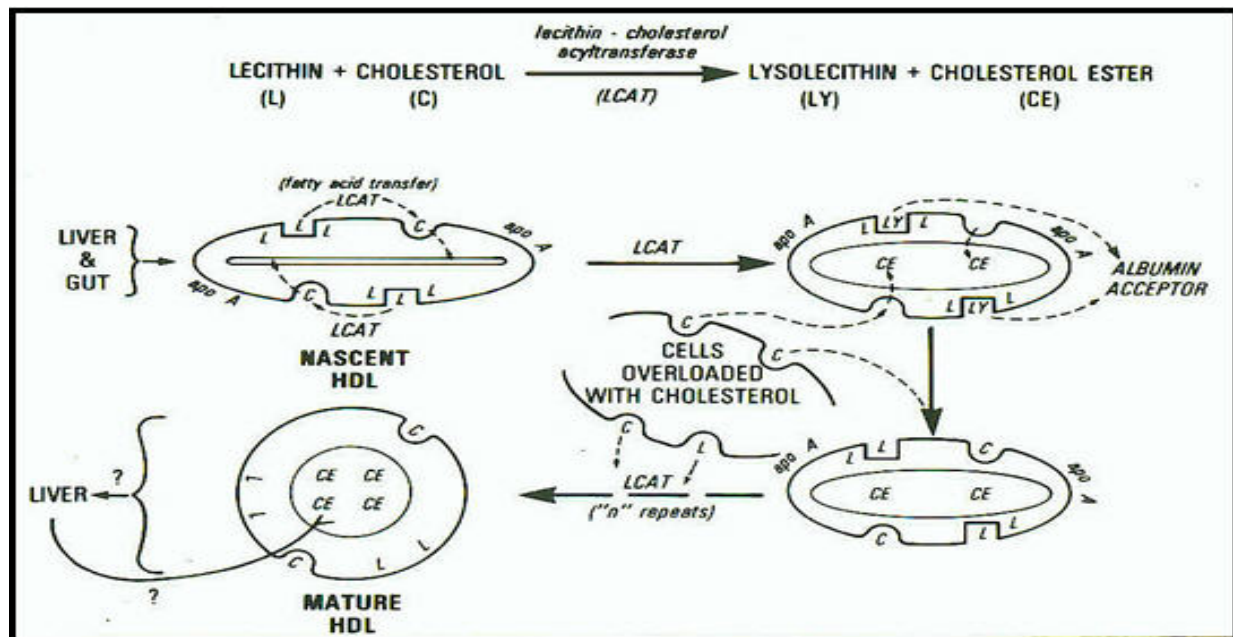


Figure 1. Lecithin- cholesterol acyl transferase (LCAT)

Physical activity increases the lipoprotein lipase level (LPL) and lecithin cholesterol acyl transferase (LCAT), decreasing the activity of liver lipase, with the consequential lowering of the level of triglycerides and increasing the concentration of HDL cholesterol (especially HDL2 subfractions). During triglyceride lipolysis in the VLDL particles, cholesterol, phospholipids and apolipoproteins are transferred to the nascent HDL particles, which are produced by the liver, increasing thus the plasma HDL cholesterol (13).

Physical activity strongly stimulates the activity of HDL receptors. Metabolism of fats is positively influenced by dynamic physical activity, aerobic exercises which activate many muscle groups (brisk walking, jogging, swimming), with the values of heart frequency i.e. pulse of about 40-85% of the maximum. The physical activity which demands very intensive but short-term effort is not recommended. Hence, it is more important to increase the physical endurance and less the strength itself (13,14).

While exercising, the physiological processes occur in the organism which contribute to the optimization of physical performances, whereby the efficiency and capacity are increased, contributing thus to the reduction of cardiovascular risk (14).

### Indicators of endothelial function

The endothelium has the important role in maintaining the normal cardiovascular tonus and blood fluidity by reducing the platelet activity and the adhesion of leukocytes, and also by restricting the reaction of vascular inflammation (15). The endothelium has autocrine, paracrine and endocrine roles (16). The important endothelial role is present in releasing the vasoactive substances, especially NO, endothelins, prostacyclin and angiotensinogen (16).

Abnormalities in peripheral endothelial function, detected by methods, such as brachial artery ultrasound and venous occlusion plethysmography, correlate with the presence of coronary vasomotor dysfunction (16). Furthermore, as with the coronary circulation, peripheral vasomotor function is diminished in subjects at risk for atherosclerosis, and medical interventions and lifestyle changes that reduce atherosclerotic risk are also associated with improved peripheral vascular function (17).

In addition to vascular imaging techniques, a number of even more novel techniques are being explored to assess the integrity of the endothelium. For example, cellular adhesion molecules, which play a key role in leukocyte adherence and transmigration, are expressed on the surface of damaged endothelial cells (16). Preliminary data suggest that these types of measurements may be the markers of increased cardiovascular risk. Similarly, elevated levels of C-reactive protein, a systemic marker of inflammation, have also recently been shown to

predict the presence of endothelial dysfunction, atherosclerosis, and the risk of future cardiovascular events. Metabolites of NO are excreted in the urine, thereby suggesting that measurements of levels of these compounds may also be reflective of endothelial function or dysfunction. Although urinary excretion of NO metabolites may be reduced in patients with atherosclerosis, this type of evaluation is complicated by the fact that many stimuli, such as exercise, regulate their release. Finally, in patients with coronary artery disease, vascular extracellular superoxide dismutase, an important antioxidant enzyme system, is substantially reduced, and thus this compound too is being evaluated as a marker of endothelial dysfunction (16).

Studies have identified a cell population termed endothelial progenitor cells that can be isolated from circulating mononuclear cells, bone marrow, and cord blood. Laboratory evidence suggests that these cells express a number of endothelial-specific cell-surface markers and exhibit numerous endothelial properties. In addition, when these cells are injected into animal models with ischemia they are rapidly incorporated into sites of neovascularization (18).

Low levels of circulating endothelial progenitor cells in patients with increasing cardiovascular risk could be a byproduct of a number of mechanisms. Presumably, risk factors, by modulating the levels of oxidative stress, nitric oxide activity, or other physiologic processes, could directly influence the mobilization or half-life of endothelial progenitor cells. Consistent with this explanation are observations demonstrating that the initiation of statin therapy increases the levels of circulating endothelial progenitor cells (18).

Raising the awareness of the importance of the endothelial function is now the main target in intervening therapy. Except for the pharmaceutical interventions with ACE inhibitors and statins, physical training is now accepted therapy for improving the endothelial function. The results show that regular moderate physical activity stimulates antioxidative state and preserves endothelial function, which means that exercising can have positive impact on developing cardiovascular diseases (19).

The disturbance of endothelial function can be detected in patients with diseases associated with vascular complications. The important functional consequence of endothelial dysfunction is impossibility to release azotes' monoxide (NO), the vasodilator of flat vascular muscle cells (19). The physical training is proved to be constantly improving the bioavailability of NO and the number of progenitor endothelial cells; it also reduces the level of inflammatory markers, i.e. the levels of proinflammatory cytokine and C-reactive protein (20).

### Conclusion

Timely identification of people suffering from cardiovascular diseases is very important,

not only because of the implementation of the proper treatment and reduction of the lethal outcome, but also because of the reduction of treatment costs. That is the reason why the existing cardiovascular markers are still the subject of research in many clinical studies and there is a need for introducing new, more efficient biochemical markers.

Physical activity leads to the beneficial changes in the cardiovascular and lipid indicators and improves the endothelial function in the

secondary prevention of coronary disease. Reduction of the lipid parameters by introducing physical rehabilitation and dietetic regime lie in the basis of secondary prevention of coronary disease. Furthermore, there is a constant improvement in NO biodisposability and there-with the improvement in endothelial function.

It can be concluded that moderate physical exercise comes before other therapeutic modalities in the secondary prevention of cardiovascular diseases.

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## PROMENE LIPOPROTEINSKOG I POKAZATELJA ENDOTELNE FUNKCIJE NAKON SPROVEDENOG PROGRAMA KARDIOVASKULARNE REHABILITACIJE

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Nedovoljna fizička aktivnost dovede do smrti oko 1,9 miliona ljudi godišnje u svetu. Prema podacima World Health Report-a, fizička neaktivnost pretili da postane globalni problem. Redovna fizička aktivnost je dobro poznati i prihvaćeni faktor koji smanjuje ukupan mortalitet i poboljšava ishod brojnih oboljenja (5). Pomoću fizičke aktivnosti moguće je poboljšati metaboličku, endotelnu, periferno-muskularnu, pulmonalnu, kardiovaskularnu funkciju organizma, ali i funkciju autonomnog nervnog sistema. Endotel igra važnu ulogu u održavanju normalnog vaskularnog tonusa i fluidnosti krvi smanjujući trombocitnu aktivnost i adheziju leukocita, kao i ograničavajući reakciju vaskularnog zapaljenja. Cilj rada bio je da se prikažu najnovija saznanja o efektima kardiovaskularne rehabilitacije fizičkom aktivnošću na promene lipoproteinskih frakcija i pokazatelje endotelne funkcije.

Uticaj fizičke aktivnosti na lipidni status ostvaruje se putem delovanja na enzime metabolizma lipoproteina, uključujući lipoproteinsku i jetrinu lipazu i transportni protein estara holesterola (11). Studije pokazuju da aerobna fizička aktivnost dovodi do povećanja koncentracije HDL holesterola i snižavanja vrednosti triglicerida, ukupnog i LDL holesterola. Postoji dozno-zavisna veza fizičke aktivnosti i nivoa lipida, kao i dokazi koji sugerišu da je trajanje fizičke aktivnosti ključni parametar u modifikovanju metabolizma lipida. Fizička aktivnost dovodi do povoljnih promena kardiovaskularnih i lipidnih pokazatelja i popravljaja endotelne funkcije u sekundarnoj prevenciji koronarne bolesti. Redukcija lipidnih parametara merama fizičke rehabilitacije i dijetalnim režimom leži u osnovi sekundarne prevencije koronarne bolesti, a osim toga, dolazi do konstantnog poboljšanja biorasploživosti NO, a samim tim i do poboljšanja endotelne funkcije. *Acta Medica Medianae 2012;51(3):52-56.*

**Ključne reči:** lipoprotein, dislipidemija, endotelna funkcija, fizička aktivnost, rehabilitacija