Arch. Biol. Sci., Belgrade, 61 (3), 367-374, 2009 DOI:10.2298/ABS0903367P

EFFECTS OF THREE TYPES OF PHYSICAL ACTIVITY ON REDUCTION OF METABOLIC PARAMETERS INVOLVED IN CARDIOVASCULAR RISK

GORDANA PETROVIĆ-OGGIANO[1], VLASTA DAMJANOV[2], VESNA VUČIĆ[1],
JASMINA DEBELJAK-MARTAČIĆ[1], MIRJANA PAVLOVIĆ[1], and MARIJA GLIBETIĆ[1]

[1]*Institute for Medical Research, Department of Nutrition and Metabolism, University of Belgrade,* 11000 Belgrade, Serbia
[2]*Faculty of Medicine, University of Kragujevac,* 34000 Kragujevac, Serbia

Abstract — The aim of present study was to investigate the effects of three different types of physical activity on reduction of the metabolic parameters mainly responsible for cardiovascular diseases. This prospective-intervention study was performed at the «ČIGOTA» Thyroid Institute on Mt. Zlatibor (Serbia) between August 2004 and June 2006. Sixty-eight overweight/obese patients aged 40-70 years with hyperlipidemia were divided into three groups according to their weight and overall health. The program of physical workout included: group I – fast walking; group II – gymnastic exercises and specially chosen exercises in the swimming pool; and group III – combined physical training of higher intensity and greater length. All patients were also on a special reduced diet of 1000 kcal per day, the AHA step-2 diet. We monitored the body mass index, body composition, glucose, cholesterol (total, LDL-, and HDL-), and triglycerides before, during, and after the intervention. After 2 and particularly 12 weeks of intervention, a significant improvement of all metabolic parameters was achieved in all three groups of patients. Although most patients completed the study with normal values of all parameters, the most desirable results were achieved in group III (combined exercises with an average energy expenditure of 900 kcal per day). Our research indicates that a specially conceived program of physical activity and diet intervention resulted in significant reduction of cardiovascular risk factors.

Key words: Physical activity, lipid status, cardiovascular risk, AHA step-2 diet program

UDC 616.1-036:613.72:612.015.3

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of mortality worldwide (Tavridou et al., 2008). Alteration of life habits, particularly diet and physical activity, is the primary therapeutic approach for persons with increased risk of CVD (Pettman et al., 2008). There are numerous different mechanisms through which physical activity modifies the risk of CVD, including its effects on lipid metabolism (Lee et al., 1999; Thompson et al., 2003); blood pressure and vasodilatation (Hu et al., 2000; Lee et al., 2003); function of endothelium (Pate et al., 1995); coagulation and fibrinolysis (Kokkinos et al., 1995; Endres et al., 2003); insulin sensitivity (Kohrt et al., 1993); and body composition (Dylewicz et al., 1999). Recent studies showed that moderate physical activity reduced risk of CVD by 20%, and even by 27% in people who are more physically active (Williams et al., 2002).

Physical training influences lipid status through its effects on the enzymes involved in lipoprotein metabolism, including lipoprotein and hepatic lipases, and transport proteins of cholesterol esters (Mackinnon et al., 1999; Kraus et al., 2002). Epidemiological studies showed that individually customized and programmed physical activity, i.e., implementation of primarily aerobic exercises, led to an increase in concentration of HDL cholesterol and reduction of triglycerides (TG) and total and LDL cholesterol (Kokkinos et al., 1999; Leon et al., 2001). In view of all these data, the aim of this study was to investigate the effect of different types of physical activity on reduction of the metabolic parameters mainly involved in cardiovascular risk and to determine which type of physical activity gives the most desirable results. Accordingly, we studied the effects of different forms of physical activity (fast, powerful, or brisk walking; gymnastic exercises in the gym or swimming pool; and combined physical training), together with a diet reduction regime, on the values of several metabolic risk factors (lipid status, glucose, body mass, and body composition) in controlled research conditions.

SUBJECTS AND METHODS

This prospective-intervention study was performed in the period between August 2004 and June 2006 at the "ČIGOTA" Thyroid Institute on Mt. Zlatibor (Serbia). The study involved 68 overweight/obese patients, 49 women and 19 men, aged 40-70 years, with BMI of 28-45 kg/m^2 and severe hyperlipidemia (total cholesterol > 5.2 mmol/l, triglycerides > 1.7 mmol/l, LDL cholesterol > 3.4 mmol/l, HDL-cholesterol < 1.68 mmol/l, in men and < 1.45 mmol/l in women). Exclusion criteria included the presence of active liver disease, hepatic or renal dysfunction, unstable angina pectoris, and myocardial infarction within the previous 6 months. None of the patients were taking insulin, lipid-lowering drugs, immunosuppressive medication, anticoagulants, hormone substitutes, beta-blockers, or diuretics. Out of 68 patients selected at the beginning of the program, eight dropped out in the first week (five women and three men), and 60 patients finished the study. All study participants provided written informed consent, which was approved by the Ethical Review Boards of the participating institutions in accordance with the principles of the Declaration of Helsinki.

Study design

All study participants had a complete physical examination, anthropometric measurements, ergometric measurements, and biochemical analyses at the beginning, after 2 weeks, and at the end of the study.

The subjects were divided into three groups depending on their overall health and weight, and a program of physical workout was adapted as follows:

* **Group I** – fast walking, i.e., powerful or brisk walking and an aerobic type of physical activity lasting 45 minutes with energy expenditure of 300 kcal (path length 4-5 km, activity of moderate intensity and moderate length);

* **Group II** – gymnastic exercises and specially chosen swimming pool exercises of greater intensity and moderate length (60 minutes daily) with energy expenditure of 600 kcal daily;

* **Group III** – combined physical training (activities from groups I and II) of high intensity and greater length (105 minutes daily) with energy expenditure of 900 kcal daily.

All three groups were on a diet reduction regime of 1000 kcal per day, the American Heart Association (AHA) step-2 diet, which is compatible with dietary recommendations of WHO concerning the prevention of chronic diseases (WHO, 1998).

Analytical methods

Total cholesterol (TC) and triglyceride (TG) concentrations were measured in serum after a 12 h fast using automated enzymatic methods with cholesterol oxidase and glycerol oxidase, respectively (EliTech Diagnostic, Sees, France). Serum HDL-C was determined by measuring cholesterol concentration in the supernatant liquid after precipitation of other classes of lipoproteins with phosphotungstic acid and magnesium chloride (Lopes-Virella et al., 1977). Estimation of LDL cholesterol was performed using the Friedwald formula (Friedwald et al., 1972).

Statistical analysis

All results are expressed as means±SD. Normality was tested using the Shapiro-Wilks test. Comparisons between two groups were performed using the parametric Student t-test and the Mann Whitney U test for non-normally distributed variables. The differences were considered significant at $p \leq 0.05$.

RESULTS

Out of 68 patients, 60 (88%) completed the study. In all three groups, significant changes in life habits were achieved through the program ($p<0.05$).

Table 1. BMI values and body composition at the beginning of the study and after 90 days of intervention. All data are presented as means±SD. **p < 0.01, ***p < 0.001- compared to baseline values after 90 days of intervention. Signific.: *p < 0.1, **p < 0.01, ***p < 0.001.

	Group I		Group II		Group III	
	Start	90. d.	Start	90. d.	Start	90. d.
BMI	36.4±2.2	** 28.48±2.6	34.5±4.6	*** 26.8±4.3	35.4±2.8	*** 27.2±2.93
Body fat (%)	40.8±6.4	** 38.0±8.1	40.4±5.4	*** 36.3±7.3	39.8±6.7	*** 34.0±8.9
Fat mass (kg)	36.9±6.2	*** 32.6±8.0	35.5±5.7	*** 29.5±7.5	36.7±7.1	*** 31.3±9.3
Muscle mass (kg)	53.6±11.1	54.2±10.6	51.6±9.4	52.8±9.3	54.2±9.5	* 55.4±9.4
Waist circumferen. (cm)	104.0±9.5	*** 92.0±9.5	103.0±10.5	*** 90.0±10.3	105.0±8.4	*** 89.0±9.2

The pulse values in all study participants were measured at the beginning, in the middle and at the end of the training. The initial values (0 min) in all three groups were within the limits of allowed values (68-93). During the physical activity period, participants in all three groups achieved pulse values near the maximum of allowed heart frequency (up to 132 beats per minute), but did not exceed it, while at the end of training heart frequency dropped to an average of 100 beats per minute (data not shown).

Changes of BMI values and body composition in all three groups of participants after 90 days of dietary intervention and physical activity are shown in Table 1. The percentage of fat, fat mass, BMI, and waist circumference were significantly reduced in all study participants. The greatest reduction of all parameters was found in patients of group III, who practiced the most intensive exercises. Their fat reduction was also accompanied by a significant increase in muscle mass, which can be considered as another positive effect of the treatment.

Glucose concentrations and lipid parameters were determined at the beginning, after 15 days, and after 90 days of the study. Alterations of the glucose level in group I were slight but significant after three months of training, while in patients of groups II and III, who practiced more intensive exercises, the decrease was significant already after 15 days. Although a significant reduction in total cholesterol concentration was found in all groups, a surprisingly great decrease (from 8.1 to 5.66 mmol/l) was found in group III after only two weeks of the intervention. Levels of LDL cholesterol also significantly decreased after two weeks, and even more after three months of treatment. To be specific, LDL cholesterol values in patients of group III, who underwent combined physical training, fell to a half of the baseline concentrations. On the contrary, levels of HDL cholesterol significantly increased in all study groups, especially in group I of participants, who exercised by fast walking. These results confirm that even moderate physical activity is a key factor in achieving desirable concentrations of HDL in sera. Finally, values of triglycerides (TG) were also significantly reduced during and after the intervention period ($p<0.05$), even though these changes were not as remarkable as changes in total and LDL cholesterol.

The TC/HDL and LDL/HDL ratios, representing the atherogenic index, are also presented in Table 2. They showed a tendency toward reduction in all three groups, particularly group III ($p<0.001$). Although a significant reduction of atherogenic risk was detected after only 2 weeks, the most prominent reduction in all three groups was achieved after 90 days of physical activity and dietary intervention ($p<0.001$).

Table 2. Serum glucose and lipids at baseline and changes induced by three types of physical activity and dietary intervention. All data are presented as means ± SD. *p < 0.05, **p < 0.01, ***p < 0.001 - compared to baseline values after 15 or 90 days of intervention. Signific.: *p < 0.1, **p < 0.01, ***p < 0.001.

	Group I			Group II			Group III		
	Start	15. d.	90. d.	Start	15. d.	90. d.	Start	15. d.	90. d.
Glucose	4.7±0.0	4.0±1.0	4.5±0.0***	4.9±1.6	3.7±0.9***	3.1±0.7***	4.5±1.2	3.9±0.2***	3.6±0.6***
TC	7.3±0.5	6.6±0.5*	5.2±0.3***	7.6±1.1	6.3±1.1***	4.7±0.5***	8.1±1.1	5.6±1.0***	4.5±0.6***
HDL	0.9±0.3	13±0.1*	1.7±0.1***	1.2±0.3	1.3±0.3*	1.6±0.2***	1.1±0.3	1.3±0.2**	1.6±0.1***
LDL	5.1±0.5	4.8±0.6*	3.2±0.3**	5.4±0.8	4.3±0.5***	2.9±0.5***	5.9±1.1	3.8±1.0***	2.0±0.6***
TG	2.4±1.1	1.8±0.9*	1.5±0.3*	1.8±1.3	1.4±0.7*	0.9±0.3*	2.2±1.6	1.4±0.5**	1.2±0.0**
LDL/HDL	5.5±0.8	3.7±0.8*	1.9±0.3**	4.9±1.1	3.5±1.7*	1.7±0.5***	5.6±2.6	3.0±0.8***	1.5±0.4***
TC/HDL	8.1±1.3	5.3±0.8**	3.1±0.4***	7.1±2.0	5.2±2.5*	2.9±0.5***	8.0±3.5	4.4±1.0***	2.6±0.4***

DISCUSSION

The focus of our study was to examine the extent to which different types of physical activity contribute to reduction of hyperlipidemia and cardiovascular risk. A program of diet and exercises at the «ČIGOTA» Institute on Mt. Zlatibor (Serbia) was adapted to the individual health conditions of the patients. Their average energy expenditure was 300-900 kcal per day, depending on the types of training (brisk or powerful walking, gymnastic exercises in the gym and swimming pool, or combined physical treatment).

The program was primarily accepted by women. Women generally were more disciplined and prepared to accept healthier life habits, which is in compliance with similar intervention studies conducted all over the world (Alexander et al., 1995; Meyer et al., 1996).

Most of our participants in all three groups at the beginning of the treatment had BMI higher than 30, which indicates the presence of first-degree obesity. Obesity is considered as an independent risk factor in cardiovascular disease, but it is often associated with several other leading risk factors, including dyslipidemia, hypertension, and diabetes (Manson et al., 1995; Fontaine et al., 2003). In particular, the abdominal type of obesity with primarily visceral accumulation of fat tissue contributes to alteration of lipids and lipoproteins (Weil et al., 2002) and an increased risk of cardiovascular complications (Dey et al., 2002; Suk et al., 2003). It is well known that physical activity increases energy expenditure and together with dietary intervention leads to reduction of fat tissue and body mass (WHO, 1998; Shephard et al., 1999). The reduction of body mass in our treatment comprised an average of 2.5 kg weekly. There was also a significant decrease in the percentage of fat in the body, as well as in the mass of fat tissue, followed by a slight increase of muscle tissue, which is in agreement with the results of other studies (Rexrode et al., 1997; Turcato et al., 2000). In view of the relation of abdominal-visceral obesity with CVD, the reduction of waist by 12-16 cm achieved in our study was of great importance as well.

Physical activity can reduce the risk of diabetes, and it is thus an important component in the treatment of diabetes patients (Gautier et al., 1995). To be specific, it has been shown that exercises increased insulin sensitivity by 25%, and that circulating concentrations of insulin and adrenalin were significantly lower in physically active persons, primarily due to formation of more insulin receptors on the membranes of trained muscle cells (DeFronzo et al., 1991; Dey et al., 2002). Training also increases insulin effects on peripheral tissues (skeletal muscles) through activation of enzymes involved in the deposition and oxidation of glucose, while an increase of muscle mass contributes to larger glucose deposits. These processes lower insulin resistance, increase clearance of glucose in the liver, and reduce its production (Borghouts et al., 2000). We found significantly reduced glucose levels in sera of all three groups of participants after the intervention period.

The changes in levels of total cholesterol in our patients showed that the duration of physical activity was of greater importance than the intensity of training. However, the greatest reduction of LDL cholesterol, which is recognized as one of the most important risk factors for CVD, together with a low level of HDL cholesterol, was found in group III, suggesting that more exhausting physical effort leads to a better lipid profile. This is particularly important for postmenopausal women, which represented the majority of our patients. During the premenopausal period, women are protected by estrogens as natural cardioprotective agents that stimulate formation of LDL receptors, reduce the activity of lipoprotein lipase (e.g., conversion of VLDL to LDL particles), act as inhibitors on the oxidation of LDL particles, and thereby reduce LDL cholesterol levels in the plasma. Results of the "Framingham Heart Study" (Vasan et al., 2005) indicate that postmenopausal females 50-59 years old have four times higher incidence of cardiac events in comparison with women in the pre-menopausal period. Moreover, a low concentration of protective HDL cholesterol, which is responsible for reverse transport of cholesterol to the liver and then into gall acids (Gordon et al., 1989), additionally contributes to the development of CVD (Calabresi et al., 2003). Training contributes to increased activity of lipoprotein lipase in fat tissue and muscles, which lowers VLDL and chylomicron triglyceride levels and enhances clearance of cholesterol-rich VLDL and chylomicron remnants (Thompson et al., 2001; Tall, 2002). The physical activity in our study resulted in a desirable level of lipid parameters, not only in decreased TC, LDL, and TG, but also in significantly increased HDL, with considerably reduced risk of CVD in the patients.

Concerning values of the atherogenic risk indexes TC/HDL and LDL/HDL, our research shows that at the beginning of the study, the TC/HDL index in all three groups significantly exceeded the limit value of 4.5 (7.18-8.09). However, after only 15 days, the TC/HDL ratio was significantly reduced ($p<0.05$) in the groups with types I and II of physical activity, whereas in group III the atherogenic index was even normal. As for the second atherogenic indicator, the LDL/HDL ratio, we note that at the beginning of the treatment all three groups had values highly above the allowed value of 2.31 (4.94-5.61). After a 15-day period of active training, the values of this cardiovascular risk indicator were noticeably decreased, while after a 90-day intervention period the values of both atherogenic indicators were brought down to the standard level in all three groups.

In analyzing lipid parameters according to Fredrickson's classification of hyperlipidemia (Frederickson, 1965), we note that participants in all thee groups had a combined type of hyperlipidemia at the beginning of the program, while after a 15-day intervention period, all three groups of participants had isolated hypercholesterolemia. After a 90-day period, a normal lipid status in all three groups of participants was achieved due to disciplined physical training and a diet reduction regime. The positive benefits regarding lipid status in our study are consistent with results reported by other authors, although there are not many studies which addressed this topic (Donnelly et al., 2003; Ruiz et al., 2004; Aloys et al., 2005; Kiefer et al., 2005). For instance, Poirier et al. (2001) showed that body mass reduction of 5% in patients with the abdominal type of obesity can lead to reduction in hyperlipidemia, hypertension, and hyperglycemia.

The outcomes achieved in our study are a consequence not only of the program of specially conceived physical activity, but also of the significantly reduced fat and calory intake. By adhering to the AHA step-2 diet, fats were reduced to less than 25% of the total energetic intake, with an average daily intake of 4.6 g of fats per day. In particular, the intake of saturated fats was decreased, while the intake of plant fibers was increased. Since all participants had the same dietary intervention, the differences in achieved outcomes are obviously the results of different physical activity. Even though all study participants showed significantly reduced BMI, less fat tissue, and improved lipid status, the more strenuous trainings performed in group II and especially group III led to more desirable results. However, patients in group I, who practiced fast walking only, achieved the highest values of beneficial HDL cholesterol.

Our results showed that all three types of different physical activity, together with the AHA step-2 diet reduction regime, achieved significant success in reduction of proatherogenic risk factors, which were radically improved after a 3-month period. They prove that specifically designed and customized programs, such as that in effect at the «ČIGOTA» Thyroid Institute on Mt. Zlatibor, achieve excellent results in reduction of body mass and improvement of lipid status through the modification of behavioral life habits.

Acknowledgment — This study was supported by the Ministry of Science Republic of Serbia (Project No. 145071).

REFERENCES

Alexander, J. M., and *B. J. Tepper* (1995). Use of reduced-calorie/reduced-fat foods by young adults: influence of gender and restraint. *Appetite* **25,** 217-230.

Aloys, B., Ingrid, F., and *U. Landmann* (2005). Gewichtsreduktion durch Lebensstilintervention-Einjahresergebnisse einer klinisch kontrolierten, randomisierten Studie mit übergewichtigen Erwachsenen. *Ernährungs-Umschau* **52,** 8.

Borghouts, L. B., and *H. A. Keizer* (2000). Exercise and insulin sensitivity: a review. *Int. J. Sports Med.* **21,** 1-12.

Calabresi, L., Gomaraschi, M., and *G. Franceschini* (2003). Endothelial protection by high-density lipoproteins: from bench to bedside. *Arter. Thromb. Vasc. Biol.* **23,** 1724-1731.

DeFronzo, R. A., and *E. Ferrannini* (1991). Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diab. Care* **14,** 173-194.

Dey, D. K., Rothenberg, E., Sundh, V., Bosaeus, I., and *B. Steen* (2002). Waist circumference, body mass index, and risk for stroke in older people: a 15 year longitudinal population study of 70-year-olds. *J. Am. Geriatr. Soc.* **50,** 1510-1518.

Donnelly, J. E., Hill, J. O., Jacobsen, D. J., Potteiger, J., Sullivan, D. K., Johnson, S. L., Heelan, K., Hise, M., Fennessey, P. V., Sonko, B., Sharp, T., Jakicic, J. M., Blair, S. N., Tran, Z. V., Mayo, M., Gibson, C., and *R. A. Washburn* (2003). Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women: the Midwest Exercise Trial. *Arch. Intern. Med.* **163,** 1343-1350.

Dylewicz, P., Przywarska, I., Szcześniak, L., Rychlewski, T., Bieńkowska, S., Dlugiewicz, I., and *M. Wilk* (1999). The influence of short-term endurance training on the insulin blood level, binding, and degradation of 125I-insulin by erythrocyte receptors in patients after myocardial infarction. *J. Cardiopulm. Rehab.* **19,** 98-105.

Endres, M., Gertz, K., Lindauer, U., Katchanov, J., Schultze, J., Schröck, H., Nickenig, G., Kuschinsky, W., Dirnagl, U., and *U. Laufs* (2003). Mechanisms of stroke protection by physical activity. *Ann. Neurol.* **54,** 582-590.

Fontaine, K. R., Redden, D. T., Wang, C., Westfall, A. O., and *D. B. Allison* (2003). Years of life lost due to obesity. *J. Am. Med. Assoc.* **289,** 187-193.

Frederickson, D. S., and *R. S. Lee* (1965). A system for phenotyping hyperlipidemia. *Circulation* **31,** 321-327.

Friedewald, W. T., Levy, R. I., and *D. S. Frederickson* (1972). Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of the ultracentrifuge. *Clin. Chem.* **18,** 449-502.

Gautier, J. F., Scheen, A., and *P. Lefebvre* (1995). Exercise in managment of non-insulin-dependent (type 2) diabetes mellitus. *Intern. J. Obesity* **19,** 458-461.

Gordon, D. J., Probstfield, J. L., Garrison, R. J., Neaton, J. D., Castelli, W. P., Knoke, J. D., Jacobs, D. R. Jr., Bangdiwala, S., and *H. A. Tyroler* (1989). High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation* **79,** 8-15.

Hu, F. B., Stampfer, M. J., Colditz, G. A., Ascherio, A., Rexrode, K. M., Willett, W. C., and *J. E. Manson* (2000). *J. Am. Med. Assoc.* **283,** 2961-2967.

Kiefer, I., and *M. Kunze* (2005). Änderungen des Ernährungsverhaltens und des Körpergewichts im Rahmen des Gewichtsreduktions Programmes "Schlank ohne Diät". *Aktuel Ernaehr. Med.* **30,** 23-28.

Kohrt, W. M., Kirwan, J. P., Staten, M. A., Bourey, R. E., King, D. S., and *J. O. Holloszy* (1993). Insulin resistance in aging is related to abdominal obesity. *Diabetes* **42,** 273-281.

Kokkinos, P., and *B. Fernhall* (1999). Physical activity and high density lipoprotein cholesterol levels: what is the relationship? *Sports Med.* **28,** 307-314.

Kokkinos, P. F., Narayan, P., Colleran, J. A., Pittaras, A., Notargiacomo, A., Reda, D., and *V. Papademetriou* (1995). Effects of regular exercise on blood pressure and left ventricular hypertrophy in African-American men with severe hypertension. *New Eng. J. Med.* **333,** 1462-1467.

Kraus, W. E., Houmard, J. A., Duscha, B. D., Knetzger, K. J., Wharton, M. B., McCartney, J. S., Bales, C. W., Henes, S., Samsa, G. P., Otvos, J. D., Kulkarni, K. R., and *C. A. Slentz* (2002). Effects of the amount and intensity of exercise on plasma lipoproteins. *New Eng. J. Med.* **347,** 1483-1492.

Lee, C. D., Folsom, A. R., and *S. N. Blair* (2003). Physical activity and stroke risk: a meta-analysis. *Stroke* **34,** 2475-2481.

Lee, I. M., Hennekens, C. H., Berger, K., Buring, J. E., and *J. E. Manson* (1999). Exercise and risk of stroke in male physicians. *Stroke* **30,** 1-6.

Leon, A. S., and *O. A. Sanchez* (2001). Response of blood lipids to exercise training alone or combined with dietary intervention. *Med. Sci. Sports Exercise* **33,** S502-515, discussion S528-529.

Lopes-Virella, M. F., Stone, P., Ellis, S., and *J. A. Colwell* (1977). Cholesterol determination in high-density lipoproteins separated by three different methods. *Clin. Chem.* **23,** 882-886.

Mackinnon, L. T., and *L. M. Hubinger* (1999). Effects of exercise on lipoprotein(a). *Sports Med.* **28,** 11-24.

Manson, J. E., Willett, W. C., Stampfer, M. J., Colditz, A., et al. (1995). Body weight and mortality among women. *New Eng. J. Med.* **333,** 677-685.

Meyer, P. C., and *O. Jeanneret* (1996). Umwelt-Sozialstrukturelle Determinanten der Gesundheit, In: *Sozial- und Praventivmedizin* (Eds. G. Gutywiller and O. Jeanneret), 480-489. Verlag Hans Huber, Bern.

Pate, R. R., Pratt, M., Blair, S. N., Haskell, W. L., Macera, C. A., Bouchard, C., Buchner, D., Ettinger, W., Heath, G. W., and *A. C. King* (1995). Physical activity and public health: a recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *J. Am. Med. Assoc.* **273,** 402-407.

Pettman, T. L., Misan, G. M., Owen, K., Warren, K., Coates, A. M., Buckley, J. D., and *P. R. Howe* (2008). Self-management for obesity and cardio-metabolic fitness: description and evaluation of the lifestyle modification program of a randomised controlled trial. *Intern. J. Behav. Nutr. Phys. Activity* **5,** 53.

Poirier, P., and *J. P. Despres* (2001). Exercise in weight management of obesity. *Cardiol. Clinics* **19,** 459-470.

Rexrode, K. M., Hennekens, C. H., Willet, W. C., Colditz, G. A., Stampfer, M. J., Rich-Edwards, J. W., Speizer, F. E., and *J. E. Manson* (1997). A prospective study of body mass index, weight change, and risk of stroke in women. *J. Am. Med. Assoc.* **277,** 1539-1545.

Ruiz, J. R., Mesa, J. L., Mingorance, I., Rodriguez-Cuartero, A., and *M. J. Castillo* (2004). Deportes con alto grado de estrés físico afectan negativamente el perfil lipídico plasmático. *Rev. Espan. Card.* **57,** 499-506.

Shephard, R. J., and *G. J. Balady* (1999). Exercise as cardiovascular therapy. *Circulation* **99,** 963-972.

Suk, S. H., Sacco, R. L., Boden-Albala, B., Cheun, J. F., Pittman, J. G., Elkind, M. S., and *M. C. Paik* (2003). Abdominal obesity and risk of ischemic stroke: the Northern Manhattan Stroke Study. *Stroke* **34,** 1586-1592.

Tall, A. R. (2002). Exercise to reduce cardiovascular risk-how much is enough? *New Eng. J. Med.* **347,** 1522-1524.

Tavridou, A., and *V. G. Manolopoulos* (2008). Novel molecules targeting dyslipidemia and atherosclerosis. *Curr. Methods Chem.* **15,** 792-802.

Thompson, P. D., Buchner, D., Pina, I. L., Balady, G. J., Williams, M. A., Marcus, B. H., Berra, K., Blair, S. N., Costa, F., Franklin, B., Fletcher, G. F., Gordon, N. F., Pate, R. R., Rodriguez, B. L., Yancey, A. K., and *N. K. Wenger* (2003). Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention), and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation* **107,** 3109-3116.

Thompson, P. D., and *D. J. Rader* (2001). Does exercise increase HDL cholesterol in those who need it the most? *Arter. Thromb. Vasc. Biol.* **21,** 1097-1098.

Turcato, E., Bosello, O., Di Francesco, V., Harris, T. B., Zoico, E., Bissoli, L., Fracassi, E., and *M. Zamboni* (2000). Waist circumference and abdominal sagittal diameter as surrogates of body fat distribution in the elderly: their relation with cardiovascular risk factors. *Intern. J. Obesity* and *Rel. Metab. Disorders* **24,** 1005-1010.

Vasan, R. S., Pencina, M. J., Cobain, M., Freiberg, M. S., and *R. B. D'Agostino* (2005). Estimated risks for developing obesity in the Framingham Heart Study. *Ann. Int. Med.* **143,** 473-480.

Weil, E., Wachterman, M., McCarthy, E. P., Davis, R. B., O'Day, B., Iezzoni, L. I., and *C. C. Wee* (2002). Obesity among adults with disabling conditions. *J. Am. Med. Assoc.* **288,** 1265-1268.

Williams, M. A., Fleg, J. L., Ades, P. A., Chaitman, B. R., Miller, N. H., Mohiuddin, S. M., Ockene, I. S., Taylor, C. B., and *N. K. Wenger* (2002). Secondary prevention of coronary heart disease in the elderly (with emphasis on patients > or = 75 years of age): an American Heart Association scientific statement from the Council on Clinical Cardiology Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention. *Circulation* **105,** 1735-1743.

World Health Organization (1998*). Obesity: Preventing* and *Managing the Global Epidemic*. Report of a WHO Consultation on Obesity. WHO/NUT/NCD/981, WHO, Geneva.