Overview article

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Physical activity and dyslipidemia

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Abstract

Dyslipidemia is a condition associated with increased cholesterol and/or lipids in the blood, and is one of the risk factors leading to cardiovascular disease and stroke. Besides drug treatment, non-pharmacological interventions such as diet and physical activity are the main keys in both prevention and treatment.

The rationale for physical activity to improve dyslipidemia through a mechanism of reducing inflammation. Many studies that have focused on the relationship between aerobic exercise and cholesterol found that HDL-C levels are more sensitive to aerobic exercise than both LDL-C and TG. Moreover, non-HDL-C is also an index of current concern and is the treatment target after LDL-C. Of course, aerobic also helps reduce this index.

This article gives an overview of the mechanism and the correlation between the intensity of physical activity and detailed blood lipids. Physical activity is still an important non-pharmacological treatment, even for people with disabilities, or with chronic diseases.

Key words: Dyslipidemia, non-HDL-C, physical activity, aerobic exercise.

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1. INTRODUCTION

Dyslipidemia is a condition associated with inherited and acquired disorders characterized by elevated plasma lipid levels. Specifically, increased low-density lipoprotein (LDL-C), total cholesterol (TC), triglycerides (TG) or decreased high-density lipoprotein (HDL-C)[1].

High levels of LDL-C in the blood was the 15th leading risk factor of death in 1990, increasing to 11th in 2007 and 8th in 2019. The global burden of dyslipidemia has increased for 30 years[2]. The complications include atherosclerosis, coronary artery disease, myocardial infarction, and cerebral infarction[3]. Treatment initially focuses on dietary and lifestyle modifications, with the addition of drugs if needed[4]. WHO defines physical activity (PA) as any bodily activity that is produced by skeletal muscles and expends energy. PA refers to all recreational activities, moving from one place to another, or while working. Both moderate and high levels of PA improve health[5].

PA is recommended to everyone to improve their health as an obvious fact. However, did we know all about the topic? Whether or not the new evidence presented in the research, it would have changed the outcome of the original beliefs. This review is aiming to provide an overall view about PA, including definition, how to measure the level of PA or their effects on both lipidemia and dyslipidemia. The mechanisms of aerobic exercise and non-aerobic exercise on lipidemia are also described.

2. REVIEWS

Methods of assessing the level of physical activity

• Self - report method

These methods included questionnaires and PA diaries, identifying participants' perceptions and concerns about PA. These tools can also be viewed as a subjective assessment method because they rely on the person's ability to interpret and recall the level of PA. Information about frequency, intensity, duration, type of PA, and PA context (e.g. indoor or outdoor) converted into energy units (e.g. kcals). Some methods such as Previous Day Physical Activity Recall (1d-PAR), the 3-day Physical Activity Recall (3d-PAR) and the Youth Activity Profile (YAP), International Physical Activity Questionnaire (IPAQ).[6]

• Monitor - based reporting method

Monitors provide accuracy and practicability, and are therefore widely used in fitness research applications. In the past, monitors were usually worn on the waist, but recently, wrist-worn types have been more popular.

Heart Rate Monitor: Heart rate monitors are uncommon in athletic studies, but are popular in exercise apps and for determining exercise intensity. Monitor beats per minute (bpm), which is (assumed to be) linear in relation to oxygen consumption. This relationship is fundamental to estimating energy expenditure in kcal/day or kJ and can be used to distinguish between different intensities of activity.[7-9]

Pedometer Monitor: is an objective monitoring device designed to quantify the number of steps in motion.[10,11]

• Standard method: Difficult to implement in practice

Calorimeter: A calorimeter is a method based on measuring the amount of heat released by chemical processes that occur in the metabolism of various body substrates (e.g. carbohydrates, fats or proteins). The energy breakdown associated with these chemical processes can be inferred by determining the amount of heat radiating from the body and using direct or indirect heat. Estimates of heat produced are based on the relationship between oxygen consumed and carbon dioxide produced, commonly known as the respiratory exchange rate. This method is based on the assumption that 1 liter of oxygen consumed is equivalent to a known kcal depending on the substrate to be metabolized. For simplicity, it is generally assumed that a respiratory exchange rate of 1.0 and calories equals 5.0 kcal per liter of oxygen consumed.[12]

• Direct Observation: The Gold Standard

This method includes System for Observing Fitness Instruction (SOFIT), Behaviors of Eating and Activity for Children's Health: Evaluation System (BEACHES), System for Observing Play and Leisure Activity in Youth - System for Observing Play and Active Recreation in Youth (SOPLAY) and System for Observing Play and Active Recreation in Communities (SOPARC). Standardization, cost, time, and subjectivity of the observer are the disadvantages of this method.[13,14]

Aerobic and anaerobic physical exercise

The American College of Sports Medicine (ACSM) defines aerobic exercise as any activity that uses large muscle groups that can be maintained continuously and rhythmically[15]. As the name, the muscle groups activated by this exercise rely on aerobic metabolism for energy in the form of adenosine triphosphate (ATP) from amino acids, carbohydrates, and fatty acids. Examples of aerobic exercise include cycling, dancing, hiking, jogging/running, swimming. These activities require oxygen supply by the cardiovascular system and the ability of skeletal muscles to use oxygen[16]. The criterion for measuring aerobic capacity is maximum oxygen consumption (VO2). The value of peak VO2 can be highly recommended by a study conducted by Vaitkevicius et al.[17], in which, VO2max is calculated along with other metrics.

Aerobic exercise has been shown to have a positive effect on coronary heart disease risk factors. Several studies have shown that aerobic exercise improves lipid composition, especially increasing HDL-C[18]. In an Australian study, aerobic exercise reduced TC, LDL-C and TG by between 0.08 mmol/L and 0.10 mmol/L, which is small but statistically significant. Simultaneously increase HDL-C by about 0.05 mmol/L[19]. Similar results have also been observed in children and adolescents[20]. In a meta-analysis performed by Kelley et al[21], demonstrated that aerobic exercise contributed to a statistically significant 9% increase in HDL-C and 11% decrease in TG, but no statistically significant change in TC and LDL-C.

Anaerobic exercise defined by the ACSM as very brief, intense PA that is generated by energy sources during muscle contraction and does not depend on the use of oxygen as an energy source[16]. Without the use of oxygen, cells revert to ATP formation through glycolysis and fermentation. This process produces less ATP than the aerobic process and leads to the accumulation of lactic acid. Exercises that are generally considered anaerobic include weight training, sprinting, high-intensity interval training. Anaerobic metabolism causes lactate elevation and metabolic acidosis and this transition point is called the anaerobic threshold (AT)[22].

Similar to aerobic exercise, anaerobic activity benefits the cardiovascular system. In a Turkish study completed by Akseki Temür et al[23], the effects of anaerobic exercise were evaluated with a family of sodium diuretic peptides, known as C-type diuretic sodium peptides (CNPs). CNP is synthesized by the endothelium and exerts protective effects through effects on vascular tone, as well as antifibrotic and antiproliferative effects, producing a hyperpolarizing effect on vascular smooth muscle, causing vasodilation[24] . CNP has also been reported to have an antiproliferative effect on cardiofibroblasts that helps prevent myocardial aging through the cyclic guanosine monophosphate (cGMP) pathway[25]. In this study, 12 healthy young male study participants were divided into two groups based on their previous exercise habits. After being classified into groups, subjects were asked to participate in a program of intense exercise, which included anaerobic exercise. Blood samples were obtained from subjects before exercise and then one minute, five minutes, and thirty minutes after exercise and checked for levels of aminoterminal proCNP (NT-proCNP), a biologically inactive peptide. of the CNP. The results showed that NT-proCNP levels increased statistically significantly at 5 min after exercise in the PA group after anaerobic exercise.

Similar to aerobic, beneficial effects of anaerobic activity and lipid metabolism were found. A small European study including 16 obese subjects was able to show the increased benefits of aerobic training followed by anaerobic training, compared with aerobic training alone. In which, the amount of non-esterified fatty acids decreased more. This group was also found to have the greatest decrease in body mass index (BMI)[26].

However, there are predictions about the disadvantages of such an exercise program. An Iranian study published by Manshouri et al[27], showed that anaerobic exercise resulted in a significant decrease in human growth hormone (GH), a hormone from the pituitary gland. It has been previously hypothesized that long-term GH deficiency may cause coronary morbidity and mortality through the development of early atherosclerosis. GH deficiency has been shown to lead to higher BMI and TG, lower HDL-C levels, as well as the development of hypertension.[28] Furthermore, cardiac structure is affected in GH-deficient subjects, as demonstrated by reduced left ventricular posterior wall thickness, smaller left ventricular mass index, and compromised left ventricular ejection fraction (LVEF).[29] The mechanism of action has not been exactly determined.

Benefits of physical activity on lipid profile

The rationale for PA to improve dyslipidemia through a mechanism of reducing inflammation. Lipids have an important role in activating the inflammatory cascade, increasing the production of cytokines, mainly TNF-alpha factor, interleukin 6 and 1. On the other hand, cytokines disrupt lipid metabolism, transport reverse cholesterol, and are associated with the development of atherosclerosis.

Regular PA helps to control the appropriate weight[30,31], improve lipid profile[32] and relates to reducing mortality[33]. The benefits of PA for improving the status of lipid profile have also been demonstrated[34,35], can be used to partially explain its protective effect. The change in blood lipid during exercise is due to the impact of exercise on inflammatory and anti-inflammatory factors related to insulin resistance[35,36]. Despite the obvious benefit, there are no established and widely accepted standards (eg, intensity, volume, and duration) for the goal of dyslipidemia control[32].

Epidemiological studies have shown that higher rates of dyslipidemia and hypertension in people with cardiopulmonary inactivity are related to certain genetic segments[37-39]. It is believed that the benefits of exercise still beneficial in carriers of this gene are due to methylation in the target tissue[40]. Aerobic or anaerobic physical exercise increases the activity of lecithin-cholesterol aciltransferase (L-CAT), an enzyme responsible for converting cholesterol esters to HDL-C; reduces the activity of cholesterol plasmatic ester transfer protein (CETP), the enzyme that converts esters of HDL-C to other lipoproteins[41].

However, some data have been collected showing that exercise in young people sometimes leads to no or only small changes in blood lipids[42]. This can be explained by the normal lipid test in young people initially. However, in all surveys in the elderly and middle-aged people, there was a significant improvement. Dyslipidemia in overweight and obese subjects with type 2 diabetes and male participants responded best to PA[42].

The recommendations on the level of PA among the associations often focus on aerobic exercise. Therefore, within the scope of this article, we also focus on aerobic exercise on blood lipids.

Not only is it associated with an increase in HDL-C and a decrease in TG, recent studies show that aerobic and high-intensity exercise lowers TC and LDL-C immediately after training sessions[43-47].

Aerobic exercise and HDL-C

Many studies that have focused on the relationship between aerobic exercise and HDL-C have found that HDL-C levels are more sensitive to aerobic exercise than both LDL-C and TG. Furthermore, all studies focusing on this association seem to indicate that there is a greater or lesser increase in HDL-C, whether in humans or in mice[48-51].

However, the question was made whether exercise is often accompanied by dietary changes and this may affect the results. To avoid this problem, author Kodama performed a meta-analysis of 25 randomized controlled trials, which participants only exercised, without medication or diet. As a result, they found a 2.53 mg/dL increase in HDL-C during aerobic exercise of 5.3 MET (64.8% maximal aerobic capacity)[52].

Recently, researchers have begun to focus on the relationship between aerobic exercise and the more HDL-C and HDL2-C segments than HDL3-cholesterol (HDL3-C)[53]. Because of the evidence that HDL2-cholesterol (HDL2-C) provides greater protection against coronary heart disease, Author Kelley et al studied the effects of aerobic exercise on HDL2-C in adults. using a meta-analysis, which included 19 randomized controlled trials, and resulted in an approximately 11% increase in HDL2-C in the above subjects. In addition, even when individual studies were removed from the model, the results remained statistically significant. In addition, the exercise-induced increase in HDL2-C did not appear to be associated with changes in body weight, body mass index, and body fat composition[54].

Aerobic and LDL-C

Unlike HDL-C, the effects of aerobic exercise on LDL-C have been inconsistent across studies and have even produced contradictory results[48-51]. The results of these different studies may be due to differences in the participants' body weights. Some studies have shown that exercise alone does not change LDL-C levels, unless weight is also changed during this period. In addition, research statistics show that each kilogram of body weight loss results in a decrease in LDL-C of about 0.8 mg/dL.[55]

Although current results on LDL-C changes in PA are conflicting, studies still show significant cardioprotective improvements in LDL-C subunits. LDL-Cs are classified according to their size and density. The LDL-C particles directly associated with cardiovascular events are the smaller, denser LDL particles[56]. In some patients with mild to moderate dyslipidemia, researchers found that after a few months of aerobic exercise, LDL-C did not change significantly, but the density of small LDL particles caused atheroma decreased, and the size of the average LDL particles increased[57]. Therefore, the impact of PA on LDL-C should not be limited to total LDL-C but must consider the small fractions of LDL-C. However, Varady's study found that LDL particle volume decreased in patients with hypercholesterolemia after exercise. Therefore, they worry that exercise might reduce LDL particle mass and increase the risk of coronary heart disease[57]. In contrast, the study of the author Elosua showed that PA did not affect the LDL particle diameter.[58]. Given these divergent results, additional studies on this correlation are needed in the future.

Plasma Lp(a) is another LDL subunit containing Apo(a). However, unlike other low-density lipoprotein subunits, Lp(a) is genetically influenced, is not affected by exercise, and cannot be improved by any form of exercise[59].

ApoB which is a major component of LDL particles is essential for elimination in the blood. Approximately 95% of apoB is bound to LDL particles, and each LDL particle is bound to only one apoB molecule[60]. Therefore, apoB concentration indirectly reflects LDL-C concentration to a certain extent. Elevated apoB levels may reflect increased cardiovascular risk[61]. The effect of PA on apoB levels has not been clearly defined. Both Crouse et al[62] and Laaksonen et al[63] found that after a few months of PA, apoB levels in men diagnosed with dyslipidemia decreased. However, there is controversy over these findings. For example, Leon's study found that 20 weeks of exercise had no effect on apoB levels[64]. Other studies found no change in apoB levels with long (48 weeks) or short (3 weeks) aerobic exercise. Therefore, more research is needed on PA and apoB.

Aerobic and TG

Physical activity can reduce plasma TG levels[48-51]. However, many studies show that sedentary people have no change in TG levels after a single exercise session[65]. This difference may be due to the requirement of regular maintenance of PA. Meanwhile, TG reduction in sedentary subjects was achieved regardless of low or moderate energy consumption[66]. Thus, the level of exercise is not the most important factor, but the maintenance of PA. The researchers showed that while participants with lower baseline TG levels experienced only a slight decrease in TG after exercise, high baseline TG levels decreased significantly. Thus, basal TG levels may be a key factor influencing the effects of exercise on TG reduction[67].

The researchers also noted an increase in HDL-C but not a concomitant decrease in TG levels in the subjects after exercise. Many studies have shown that a decrease in TG is always accompanied by an unchanged HDL-C, or an increase in HDL-C without a clear improvement in TG levels[67]. However, many authors still agree that there is both an increase in HDL-C and a decrease in TG in sedentary people after exercise training. For example, Peter et al. reported that after 2 days of aerobic exercise, TG decreased with an increase in HDL-C of about 14%[68]. Currently, there is still a lot of controversy. Body weight, fat, cardiovascular status, exercise level, current blood lipid levels, diet and genetic factors all contribute.

Aerobic and postprandial blood lipids

Most studies on PA and blood lipids before eating. However, this may only reflect the effect of PA on fasting lipids. Just a few hours before breakfast can be called fasting, whereas most of the day after a meal is longer than in a fasted state. Therefore, the researchers speculate that postprandial lipids may be more significant in lipid metabolism than preprandial lipids and have a greater role than fasting lipids in predicting cardiovascular risk factors. In addition, this hypothesis was validated by finding that postprandial blood triacylglycerol better predicts cardiovascular events than fasting triacylglycerol (TAG) concentrations[69]. Mestek et al observed that exercise significantly lowers postprandial TG on a high-fat diet in individuals with metabolic syndrome.[70]. The reduction in postprandial blood lipids for PA does not only occur immediately after exercise but also lasts into the next day. In addition, there was no significant difference between continuous exercise and a single session in reducing postprandial TG levels[71]. Sabaka et al found that a 4-days exercise resulted in significant changes in postprandial TG, LDL-C and VLDL. However, there were no significant changes in postprandial HDL-C, but some HDL-C molecules were altered. For example, the authors noted a significant reduction in small and medium HDL particles in the post-exercise state[72]. Therefore, PA has an effect on lipid distribution after meals.

Another important finding was that just 4 days of exercise could lead to significant positive changes in postprandial blood lipids,

Aerobic and non-HDL-C

In addition to the normal blood lipid profile, some other valuable additional lipid parameters are of interest such as apolipoprotein, particle size, LDL concentration, but most of these parameters serve mainly in studies.

Non-HDL-C is now concerned in clinical evaluation. Several studies point to the clinical benefit and even superiority of non-HDL-C as a comprehensive solution to indicate atherosclerotic lipoprotein levels. Non-HDL-C is accepted as one of the primary secondary goals of treatment in the National Cholesterol Education Program Adult Treatment Panel III national lipids *(NCEP/ATPIII)* and the American Diabetes Association *(ADA)* and the American College of Cardiology (ACC).

Non-HDL-C is a better indicator of cardiovascular disease risk than traditional lipids such as HDL-C, LDL-C, and TG. Studies have also shown that, as a predictor of future cardiovascular risk, non-HDL-C is to some extent more convincing than LDL-C. Indeed, non-HDL-C has an advantage over LDL-C because of its similar accuracy when measured fasting or postprandial. In contrast, the conventional measurement of LDL-C is imprecise in the postprandial sample, as it is a calculated value based on the triglyceride concentration according to the Friedewald equation:[73]

LDL-C = TC – HDL-C – triglyceride/5

Non-HDL-C is based primarily on total cholesterol levels, a well-standardized and precisely calibrated parameter with little biological or laboratory variation. Although non-HDL-C is secondarily dependent on HDL-C, HDL-C is less severely affected by fasting or postprandial, non-HDL-C is shown to be accurate and useful when measuring particles containing apoli poprotein-B in postprandial samples, compared with most other lipid parameters, such as TG. Furthermore, HDL-C levels are often much lower than TC, minimizing the possibility of variation in the non-HDL-C measurement. A final advantage of non–HDL-C is that it can easily be calculated from the values obtained on a regular lipid bilan file.[74].

	Non-HDL-C goal (mg/dL)	
	NCEP ATP III	**ADA/AHA**
Patients at very high/high risk (CVD, high risk diabetes)	< 130 mg/dL Tối ưu: <100 mg/dL*	< 100 mg/dL
High-risk patients (Framingham 10-year CVD risk 20%/10 years, diabetes without other risk factors)	< 130 mg/dL	< 130 mg/dL
Moderate/high risk patients (2 CVD risks, Framingham 10-year CVD risk 10%-20%)	< 160 mg/dL Tối ưu: <130 mg/dL	< 130 mg/dL

Table 1: Non-HDL-C treatment goals 74

(*) Optimal treatment when risk factors are not controlled: still smoking; TG > = 200 mg/dL; low HDL-C less than 40 mg/dL; or acute coronary syndrome

Previous reports indicate that walking reduces non-HDL-C by 4% in adults 75. Meta-analysis was used to examine the effects of aerobic exercise on non-HDL-C in children and adolescents. However, the study showed that non-HDL-C in the exercise group did not change significantly compared with the control group. It is possible that children and adolescents subjects had essentially normal TC and HDL-C levels, and both are important factors in the calculation of non-HDL-C, therefore not achieve the desired results. Studies on this correlation are not many and need to be conducted more in the future.

Recommendations on the level of physical activity

• World Health Organization - World Health Organization (WHO) Physical Activity Level Recommendations 5 76

In addition to the multiple health benefits of physical activity, societies that are more active can generate additional returns on investment including a reduced use of fossil fuels, cleaner air and less congested, safer roads. These outcomes are interconnected with achieving the shared goals, political priorities and ambition of the Sustainable Development Agenda 2030.

The new WHO global action plan to promote physical activity responds to the requests by countries for updated guidance, and a framework of effective and feasible policy actions to increase physical activity at all levels. It also responds to requests for global leadership and stronger regional and national coordination, and the need for a whole-of-society response to achieve a paradigm shift in both supporting and valuing all people being regularly active, according to ability and across the life course.

The action plan was developed through a worldwide consultation process involving governments and key stakeholders across multiple sectors including health, sports, transport, urban design, civil society, academia and the private sector.

WHO makes recommendations on the general level of PA for the population depending on age (infants, children, adolescents, adults, the elderly) and special populations such as people with disabilities, people with diseases chronic disease, malignancy, pregnant women. For the most part there is no difference. For special subjects, there is no difference in frequency and duration of exercise; pay attention to exercises depending on the context and conditions of the patient (on-site exercises, wheelchair exercises,…)

• Centers for Disease Control and Prevention (CDC) Physical Activity Level Recommendations 77

Adults need 150 minutes of moderate-intensity physical activity each week and 2 days of muscle-strengthening activity. With 150 minutes/week, it can be divided into 30 minutes/day, 5 days/week or can be broken down and spread over the days of the week.

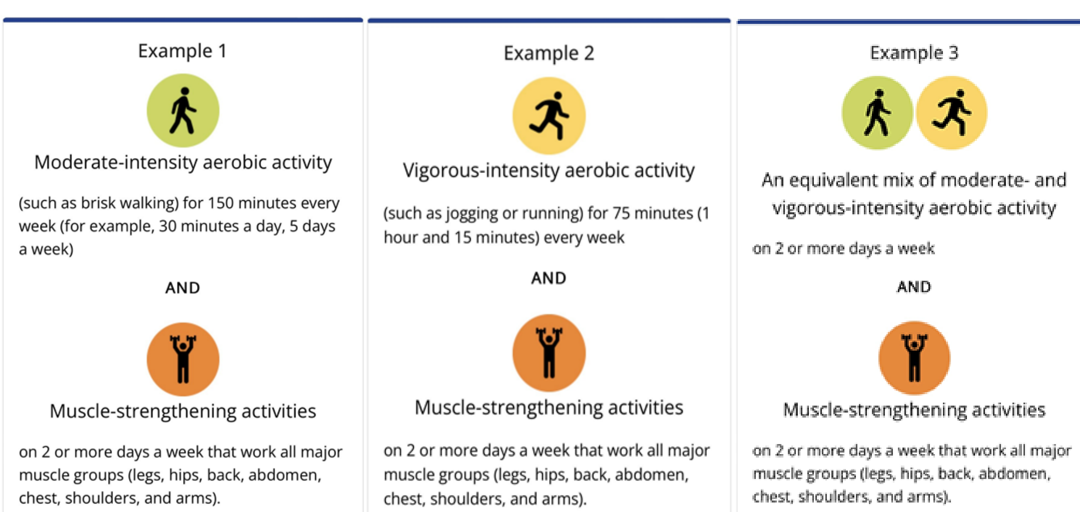

Figure 1: Example of physical activity for a week - CDC 77

• American Heart Association (AHA) Physical Activity Level Recommendations

These recommendations are based on the Physical Activity Guidelines for Americans, 2nd edition, published by the U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. They recommend how much physical activity we need to be healthy. The guidelines are based on current scientific evidence supporting the connections between physical activity, overall health and well-being, disease prevention and quality of life. 78

- Get at least 150 minutes per week of moderate-intensity aerobic activity or 75 minutes per week of high-intensity aerobic activity, or a combination of both, preferably spread throughout the week.

- Add moderate to high intensity muscle-strengthening activity (such as resistance or weightlifting) at least 2 days per week.

- Reduce passive time, sit in one place. Even light-intensity activity can be beneficial.

- Increasing number and intensity gradually over time.

3. CONCLUSIONS

In general, “direct observation” method is currently still the gold standard in assessing physical activity levels. non-HDL-C added in addition to LDL-C play a role in assessing and predicting cardiovascular risks. Aerobic and anaerobic exercises both have benefits in improving blood lipid profiles, especially HDL-C and TG. An exercise program that combines both aerobic and anaerobic exercise is considered as the most effective non-pharmacological control method, besides dietary modification. Research shows that the effectiveness of exercise and improving blood lipid status comes from maintaining a moderate exercise frequency rather than too high intensitive, that the associations' recommendations also indicate that 150 minutes/week of moderate-intensity aerobic exercise or 75 minutes/week of high-intensity aerobic exercise combined with 2 days of anaerobic exercise. Moreover, the frequency and requirement of PA for special populations such as people with disabilities, people with chronic diseases (cancer, HIV, high blood pressure, diabetes) do not differ much from healthy people.

REFERENCES

1. FREDRICKSON DS. An international classification of hyperlipidemias and hyperlipoproteinemias. American College of Physicians; 1971. p. 471-472.
2. Pirillo A, Casula M, Olmastroni E, Norata GD, Catapano AL. Global epidemiology of dyslipidaemias. *Nature Reviews Cardiology.* 2021;18(10):689-700.
3. Shattat GF. A review article on hyperlipidemia: types, treatments and new drug targets. *Biomedical*. 2015;7(1):399-409.
4. *JAMA*. The Lipid Research Clinics Coronary Primary Prevention Trial results. II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. JAMA. Jan 20 1984;251(3):365-74.
5. Organization WH. Physical activity: World Health Organization. 2018.
6. Welk G, Morrow J, Saint-Maurice P. Measures registry user guide: Individual physical activity. *National Collaborative on Childhood Obesity Research: Washington, DC, USA*. 2017.
7. Engström E, Ottosson E, Wohlfart B, Grundström N, Wisén A. Comparison of heart rate measured by Polar RS400 and ECG, validity and repeatability. *Adv Physiother.* 2012;14(3):115-122.
8. Lee CM, Gorelick M. Validity of the Smarthealth watch to measure heart rate during rest and exercise. *Measurement in Physical Education Exercise Science.* 2011;15(1):18-25.
9. Porto LGG, Junqueira Jr LF. Comparison of time-domain short-term heart interval variability analysis using a wrist-worn heart rate monitor and the conventional electrocardiogram. *Pacing Clinical Electrophysiology*. 2009;32(1):43-51.
10. Laurson KR, Eisenmann JC, Welk GJ, Wickel EE, Gentile DA, Walsh DA. Evaluation of youth pedometer-determined physical activity guidelines using receiver operator characteristic curves. *Prev Med.* 2008;46(5):419-424.
11. Tudor-Locke C, McClain JJ, Hart TL, Sisson SB, Washington TL, sport. Pedometry methods for assessing free-living youth. *Research quarterly for exercise.* 2009;80(2):175-184.
12. Bassett Jr DR, Rowlands AV, Trost SG. Calibration and validation of wearable monitors. *Medicine science in sports.* 2012;44(1 Suppl 1):S32.

13. McKenzie TL, Van Der Mars H. Top 10 research questions related to assessing physical activity and its contexts using systematic observation. *Research quarterly for exercise sports.* 2015;86(1):13-29.
14. McKenzie TL. 2009 CH McCloy lecture seeing is believing: Observing physical activity and its contexts. *Research quarterly for exercise sports* 2010;81(2):113-122.
15. Wahid A, Manek N, Nichols M, et al. Quantifying the association between physical activity and cardiovascular disease and diabetes: a systematic review and meta-analysis. *Journal of the American Heart Association.* 2016;5(9):e002495.
16. Medicine *ACoS. ACSM's guidelines for exercise testing and prescription.* Lippincott williams & wilkins; 2013.
17. Vaitkevicius PV, Fleg JL, Engel JH, et al. Effects of age and aerobic capacity on arterial stiffness in healthy adults. *Circulation.* 1993;88(4):1456-1462.
18. Blumenthal JA, Emery CF, Madden DJ, et al. Effects of exercise training on cardiorespiratory function in men and women > 60 years of age. *The American journal of cardiology.* 1991;67(7):633-639.
19. Halbert J, Silagy C, Finucane P, Withers R, Hamdorf PJEjocn. Exercise training and blood lipids in hyperlipidemic and normolipidemic adults: a meta-analysis of randomized, controlled trials. 1999;53(7):514-522.
20. Tolfrey K, Jones AM, Campbell IG. The effect of aerobic exercise training on the lipid-lipoprotein profile of children and adolescents. *Sports Med*. 2000;29(2):99-112.
21. Kelley GA, Kelley KS, Franklin B. Aerobic exercise and lipids and lipoproteins in patients with cardiovascular disease: a meta-analysis of randomized controlled trials. *J Cardiopulm Rehabil Prev.* 2006;26(3):131.
22. Kara M, Gokbel H, Bediz C, Ergene N, Ucok K, Uysal H. Determination of the heart rate deflection point by the Dmax method. *Journal of sports medicine physical fitness.* 1996;36(1):31-34.
23. Temür HA, Vardar SA, Demir M, et al. The alteration of NTproCNP plasma levels following anaerobic exercise in physically active young men. *Anatolian journal of cardiology.* 2015;15(2):97.
24. Chauhan SD, Nilsson H, Ahluwalia A, Hobbs AJ. Release of C-type natriuretic peptide accounts for the biological activity of endothelium-derived hyperpolarizing factor. *Proceedings of the National Academy of Sciences.* 2003;100(3):1426-1431.
25. Sangaralingham SJ, Huntley BK, Martin FL, et al. The aging heart, myocardial fibrosis, and its relationship to circulating C-type natriuretic peptide. *Hypertension.* 2011;57(2):201-207.
26. Salvadori A, Fanari P, Marzullo P, et al. Short bouts of anaerobic exercise increase non-esterified fatty acids release in obesity. *Eur J Nutr.* 2014;53(1):243-249.
27. Manshouri M, Ghanbari-Niaki A, Kraemer RR, Shemshaki A. Time course alterations of plasma obestatin and growth hormone levels in response to short-term anaerobic exercise training in college women. *Applied Physiology, Nutrition, Metabolism: Clinical and Experimental.* 2008;33(6):1246-1249.
28. Rosén T, Edén S, Larson G, Wilhelmsen L, Bengtsson B-Å. Cardiovascular risk factors in adult patients with growth hormone deficiency. *European Journal of Endocrinology*. 1993;129(3):195-200.
29. Merola B, Cittadini A, Colao A, et al. Cardiac structural and functional abnormalities in adult patients with growth hormone deficiency. *The Journal of Clinical Endocrinology*. 1993;77(6):1658-1661.
30. Lee I-M, Djoussé L, Sesso HD, Wang L, Buring JE. Physical activity and weight gain prevention. *Jama.* 2010;303(12):1173-1179.
31. Friedenreich CM, Woolcott C, McTiernan A, et al. Adiposity changes after a 1-year aerobic exercise intervention among postmenopausal women: a randomized controlled trial. *Int J Obes*. 2011;35(3):427-435.
32. Kraus WE, Slentz CA. Exercise training, lipid regulation, and insulin action: a tangled web of cause and effect. *Obesity.* 2009;17(S3):S21-S26.
33. Moore SC, Patel AV, Matthews CE, et al. Leisure time physical activity of moderate

to vigorous intensity and mortality: a large pooled cohort analysis. *PLoS Med*. 2012;9(11):e1001335.

34. Zaros PR, Pires CE, Bacci M, Moraes C, Zanesco A. Effect of 6-months of physical exercise on the nitrate/nitrite levels in hypertensive postmenopausal women. *BMC Womens Health*. 2009;9(1):1-5.
35. Balducci S, Zanuso S, Nicolucci A, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. *Nutrition, Metabolism*. 2010;20(8):608-617.
36. Teixeira-Lemos E, Nunes S, Teixeira F, Reis FJCd. Regular physical exercise training assists in preventing type 2 diabetes development: focus on its antioxidant and anti-inflammatory properties. *Cardiovasc Diabetol*. 2011;10(1):1-15.
37. Malagrino PA, Sponton CH, Esposti RD, et al. Prevalence of dyslipidemia in middle-aged adults with NOS3 gene polymorphism and low cardiorespiratory fitness. *Arquivos Brasileiros de Endocrinologia Metabologia*. 2013;57:33-43.
38. Kimura T, Yokoyama T, Matsumura Y, et al. NOS3 genotype–dependent correlation between blood pressure and physical activity. *Hypertension*. 2003;41(2):355-360.
39. Xi B, Cheng H, Shen Y, et al. Physical activity modifies the associations between genetic variants and hypertension in the Chinese children. *Atherosclerosis*. 2012;225(2):376-380.
40. White AJ, Sandler DP, Bolick SC, Xu Z, Taylor JA, DeRoo LA. Recreational and household physical activity at different time points and DNA global methylation. *Eur J Cancer*. 2013;49(9):2199-2206.
41. Lira F, Rosa Neto J, Antunes B, Fernandes R. The relationship between inflammation, dyslipidemia and physical exercise: from the epidemiological to molecular approach. *Curr Diabetes Rev*. 2014;10(6):391-396.
42. Doewes RI, Gharibian G, Zaman BA, Akhavan-Sigari R. An updated systematic review on the effects of aerobic exercise on human blood lipid profile. *Curr Probl Cardiol*. 2023:101108.
43. Lira FS, Rosa JC, Lima-Silva AE, et al. Sedentary subjects have higher PAI-1 and lipoproteins levels than highly trained athletes. *Diabetology Metabolic Syndrome*. 2010;2(1):1-5.
44. Lira FS, Koyama CH, Yamashita AS, et al. Chronic exercise decreases cytokine production in healthy rat skeletal muscle. Cell Biochemistry Function: *Cellular biochemistry its modulation by active agents or disease*. 2009;27(7):458-461.
45. Madge LA, Pober JS. TNF signaling in vascular endothelial cells. *Experimental molecular pathology*. 2001;70(3):317-325.
46. Collins T, Read MA, Neish AS, Whitley MZ, Thanos D, Maniatis T. Transcriptional regulation of endothelial cell adhesion molecules: NF-κB and cytokine-inducible enhancers. *The FASEB Journal*. 1995;9(10):899-909.
47. Manuela Crispim Nascimento C, Rodrigues Pereira J, Pires de Andrade L, et al. Physical exercise in MCI elderly promotes reduction of pro-inflammatory cytokines and improvements on cognition and BDNF peripheral levels. *Current Alzheimer Research*. 2014;11(8):799-805.
48. LeMura LM, von Duvillard SP, Andreacci J, Klebez JM, Chelland SA, Russo J. Lipid and lipoprotein profiles, cardiovascular fitness, body composition, and diet during and after resistance, aerobic and combination training in young women. *Eur J Appl Physiol*. 2000;82(5):451-458.
49. Nybo L, Sundstrup E, Jakobsen MD, et al. High-intensity training versus traditional exercise interventions for promoting health. *Med Sci Sports Exerc*. 2010;42(10):1951-8.
50. Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med*. 2002;347(19):1483-1492.
51. O'Donovan G, Owen A, Bird SR, et al. Changes in cardiorespiratory fitness and coronary heart disease risk factors following 24 wk of moderate-or high-intensity exercise of equal energy cost. *J Appl Physiol*. 2005;98(5):1619-1625.

52. Kodama S, Tanaka S, Saito K, et al. Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis. *Arch Intern Med.* 2007;167(10):999-1008.
53. Morgan J, Carey C, Lincoff A, Capuzzi D. High-density lipoprotein subfractions and risk of coronary artery disease. *Current atherosclerosis reports*. 2004;6(5):359-365.
54. Kelley GA, Kelley K. Aerobic exercise and HDL2-C: a meta-analysis of randomized controlled trials. *Atherosclerosis.* 2006;184(1):207-215.
55. Goldberg AC, Hopkins PN, Toth PP, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients: clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. *J Clin Lipidol.* 2011;5(3):133-140.
56. Davidson MH, Ballantyne CM, Jacobson TA, et al. Clinical utility of inflammatory markers and advanced lipoprotein testing: advice from an expert panel of lipid specialists. *J Clin Lipidol.* 2011;5(5):338-367.
57. Varady K, St-Pierre A, Lamarche B, Jones P. Effect of plant sterols and endurance training on LDL particle size and distribution in previously sedentary hypercholesterolemic adults. *Eur J Clin Nutr.* 2005;59(4):518-525.
58. Elosua R, Molina L, Fito M, et al. Response of oxidative stress biomarkers to a 16-week aerobic physical activity program, and to acute physical activity, in healthy young men and women. *Atherosclerosis.* 2003;167(2):327-334.
59. Durstine JL, Grandjean PW, Cox CA, Thompson PDJJoCR. Lipids, lipoproteins, and exercise. *Journal of Cardiopulmonary Rehabilitation Prevention.* 2002;22(6):385-398.
60. Shelness GS, Sellers JA. Very-low-density lipoprotein assembly and secretion. *Curr Opin Lipidol*. 2001;12(2):151-157.
61. Lamarche B, Moorjani S, Lupien PJ, et al. Apolipoprotein AI and B levels and the risk of ischemic heart disease during a five-year follow-up of men in the Que´bec cardiovascular study. *Circulation.* 1996;94(3):273-278.
62. Crouse SF, O'Brien BC, Grandjean PW, Lowe RC, Rohack JJ, Green JS. Effects of training and a single session of exercise on lipids and apolipoproteins in hypercholesterolemic men. *J Appl Physiol.* 1997;83(6):2019-2028.
63. Laaksonen DE, Atalay M, Niskanen LK, et al. Aerobic exercise and the lipid profile in type 1 diabetic men: a randomized controlled trial. *Medicine science in sports exercise.* 2000;32(9):1541-1548.
64. Leon AS, Rice T, Mandel S, et al. Blood lipid response to 20 weeks of supervised exercise in a large biracial population: the HERITAGE Family Study. *Metabolism.* 2000;49(4):513-520.
65. Kantor MA, Cullinane EM, Sady SP, Herbert PN, Thompson PD. Exercise acutely increases high density lipoprotein-cholesterol and lipoprotein lipase activity in trained and untrained men. *Metabolism.* 1987;36(2):188-192.
66. Crouse SF, O'Brien BC, Rohack JJ, et al. Changes in serum lipids and apolipoproteins after exercise in men with high cholesterol: influence of intensity. *J Appl Physiol.* 1995;79(1):279-286.
67. Wang Y, Xu D. Efectos del ejercicio aeróbico sobre lípidos y lipoproteínas. *Lipids Health Dis.* 2017;16:132.
68. Grandjean PW, Crouse SF, Rohack JJ. Influence of cholesterol status on blood lipid and lipoprotein enzyme responses to aerobic exercise. *J Appl Physiol.* 2000; 89(2):472-480.
69. Bansal S, Buring JE, Rifai N, Mora S, Sacks FM, Ridker PM. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. *Jama.* 2007;298(3):309-316.
70. Mestek ML, Plaisance EP, Ratcliff LA, Taylor JK, Wee S-O, Grandjean PW. Aerobic exercise and postprandial lipemia in men with the metabolic syndrome. *Medicine science in sports exercise.* 2008;40(12):2105-2111.
71. Li J, Siegrist J. Physical activity and risk of cardiovascular disease-a meta-analysis of prospective cohort studies. *International journal of environmental research public health.* 2012;9(2):391-407.

72. Sabaka P, Kruzliak P, Balaz D, et al. Effect of short term aerobic exercise on fasting and postprandial lipoprotein subfractions in healthy sedentary men. *Lipids in health.* 2015;14(1):1-8.
73. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972;18(6):499-502.
74. Blaha MJ, Blumenthal RS, Brinton EA, Jacobson TA. The importance of non–HDL cholesterol reporting in lipid management. *J Clin Lipidol.* 2008;2(4):267-273.
75. Kelley GA, Kelley KS, Tran ZV. Walking and non-HDL-C in adults: a meta-analysis of randomized controlled trials. *Prev Cardiol.* 2005;8(2):102-107.
76. Organization WH. Global action plan on physical activity 2018-2030: more active people for a healthier world. 2018.
77. Control CfD, Prevention. How much physical activity do adults need. 2011;11:2013.
78. Association AH. American Heart Association recommendations for physical activity in adults and kids. 2018;23:2020.

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Dr My: find the materials, references, previous research and publishments, arrange into the whole overview.

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