Review

Structural adaptations of the heart to physical exercises in the metabolic syndrome

Morvan, E.[1], Souza, RR.[1] and Maifrino, LBM.[1,2]*

[1]Biodinamic and Morphology Laboratory, São Judas Tadeu University
[2]Dante Pazzanese Institute of Cardiology, São Paulo, Brazil
*E-mail: lmaifrino@uol.com.br

Abstract

The objective of this investigation was to conduct a literature review on the structural adaptations of the heart to physical exercises in the Metabolic Syndrome. The search was conducted in the following electronic databases: *PubMed, Web of Sciences, LILLACS* and *MEDLINE* using keywords in English without time restrictions. The metabolic syndrome (MS) is characterized by a group of metabolic risk factors in a person. In Brazil, more than 300.000 people die every year of cardiovascular diseases. According to the Brazilian Ministry of Health, there are currently over 20 million hypertensive and 15 million have diabetes in the country, and this rate is increasing. Physical inactivity, in most individuals, leads to well characterized structural and functional cardiovascular alterations such as myocyte loss with subsequent hypertrophy of the remaining cells and reduction of the arterial complacency. However, the etiology of the cardiovascular alterations is still under investigation. The most likely mechanisms are related to the cumulative harm and several different aggressive factors. Oxidative stress, inflammations, and changes in cardiovascular gene expression seem to influence this system. The benefits of physical exercises have been studied combined with pharmacotherapy offering the opportunity of intervention in the process by using exercises and drugs that can reduce arterial rigidity, cardiac fibrosis, and ventricular hypertrophy.

Keywords: Metabolic Syndrome heart, exercise.

1 Introduction

The term metabolic syndrome (MS) has been used to relate coronary diseases, hypertension, diabetes type 2, upper body obesity, insulin resistance, and hyperinsulinemia (LAKKA, LAAKSONEM, LAAKA et al., 2003). There are several factors that characterize the MS: abdominal obesity, low HDL cholesterol, elevated triglycerides, elevated blood pressure, and elevated fasting glucose, which increase the risk of coronary diseases and diabetes (NIEMAN, 1999).

According to the Sociedade Brasileira de Cardiologia (2001), over 300.00 people die annually of cardiovascular diseases. According to the Brazilian Ministry of Health, there are currently over 20 million hypertensive and 15 million have diabetes in the country, and this rate is increasing. Despite the great number of studies demonstrating the protecting effects of physical exercises on health, great part of the population is still inactive (ORTIZ and MELLO, 2004; MELLO and TUFIK, 2004; CIOLAC and GUIMARÃES, 2004).

2 Material and methods

The PubMed, *Web of Sciences, LILLACS and MEDLINE* databases were used as search reference using keywords in English without time restrictions. In this systematization, papers were searched using the following keywords: “Metabolic Syndrome”, “heart”, ”exercise” by randomized combination until these terms were included.

3 Results

Through a structural point of view, the myocardium consists of myocytes and cardiac interstitial, which comprises the blood vessels and the conjunctive tissue (ROBINSON and COHEN-GOULD, 1983).

Although the volume of the myocardium is occupied almost entirely by the myocytes, they account for 25% of the total number of cells; the rest is represented by endothelial and conjunctive cells, manly fibroblasts. In the adult heart, the extracellular matrix consists of collagen type I (80%), III, IV, V, and VI, proteoglicans, and elastic fibers. This matrix is synthesized by fibroblasts distributed along the myocytes by endothelial and smooth muscle cells of the vessels (COTRAN, KUMAR and ROBBINS, 1994).

The heart undergoes a process of remodeling during the postnatal period with substantial alterations in the two compartments of the myocardium (MATTFELD and MALL, 1987; MANDARIM-DE-LACERDA and PESSANHA, 1995).

The development of new capillaries follows the progressive increase in the myocardial mass. Therefore, the maturation of the capillary coronary network is a dynamic process characterized mainly by accentuated capillary angiogenesis and subsequent increases in the capillary spacing homogeneity in relation to the myocytes in order to supply those cells adequately with oxygen and nutrients (ANVERSA, RICCI and OLIVETTI, 1986; RAKUSAN and NAGAI, 1994).

The heart structural alterations depend not only on the normal development, but also on the functional demands of the organ. On the other hand, with age and absence of

physical activity, the heart undergoes important alterations that affect its cells and the adjacent tissue and mainly the terminal vascular bed (ANVERSA, RICCI and OLIVETTI, 1986; RAKUSAN, CICUTTI and FLANAGAN, 1994; RAKUSAN and NAGAI, 1994).

The systematic exercises training results in changes in the skeletal muscle leading to an increase in the oxidative capacity and vascular conductance able to increase the oxygen arteriovenous difference (MARON, 1997). Dynamic regular exercises induce central and peripheral cardiovascular adaptations including induced bradycardia, tendency to low blood pressure, and increased muscular capillarity (COGGAN, SPINA, KING et al., 1992).

Some studies have shown that individuals with insulin resistance improve sensitivity in 22% after the first session of exercises and in 42% after six weeks of training (CIOLAC and GUIMARÃES, 2004). In view of this, fitness activities and physical exercises have been used as therapy to maintain the organ functions resulting in a better quality of life and low death rates associated to Metabolic Syndrome.

The heart alterations due to hypertrophy caused by pressure overload can be compared to those that occur with the metabolic syndrome aggravating factors. Studies have shown that the MS promotes cardiovascular and metabolic alterations in both sexes.

In the presence of the aggravating factors of the metabolic syndrome, the coronary arterioles become stiffer, the capillary density decreases, and there is an increase in the heterogeneity of capillary spacing. These capillary alterations can lead to a deficient tissue oxygenation predisposing the myocardium to ischemia (ANVERSA, RICCI and OLIVETTI, 1986; RAKUSAN, CICUTTI and FLANAGAN, 1994; RAKUSAN and NAGAI, 1994).

Comparing the heart of young and old sedentary animals, it can be seen that the myocardium of the old animals has lower number of cardiomyocytes and increased conjunctive tissue (MAIFRINO and SOUZA, 2006; MEIRELLES, VIANNA and MANDARIN-DE-LACERDA, 1998). The increase in the collagen fibers density can limit the cardiac muscle distension reflecting a rigidity of the complacency of the ventricular wall (DEBESSA, MAIFRINO and SOUZA, 2001) besides a myocardial hypertrophy and diastolic dysfunction (CARVALHO, SOUZA and FIGUEIRA, 1998).

The low number of cardiomyocytes results from death by apoptosis and/or necrosis (KAJSTURA, CHENG and SARANGARAJAN, 1996; DIEZ, 2000) whereas the increase in the myocardial conjunctive tissue is due to the occurrence of interstitial fibrosis and substitution fibrosis (MORENO JÚNIOR, METZE, BENTO et al., 2001; COELHO-FILHO, DE LUCA, TANUS-SANTOS et al., 2001; PACCA, AZEVEDO, OLIVEIRA et al., 2002).

In general, physical inactivity and aging, in most individuals, lead to well characterized structural and functional cardiovascular alterations such as myocyte loss (with subsequent hypertrophy of the remaining cells) and reduction of the arterial complacency. However, the etiology of the cardiovascular alterations is still under investigation. The most likely mechanisms are related to the cumulative harm and several different aggressive factors.

Oxidative stress, inflammations, and changes in cardiovascular gene expression seem to influence this system. The benefits of physical exercises have been studied combined with pharmacotherapy offering the opportunity of intervention in the process by using exercises and drugs that can reduce arterial rigidity, cardiac fibrosis, and ventricular hypertrophy (PUGH and WEI, 2001; FERRARI, 2002).

4 Conclusion

Physical inactivity and low fitness levels have been considered risk factors to dyslipidemia (high LDL cholesterol, high triglycerides, and low HDL cholesterol), hypertension, insulin resistance, hyperinsulinemia, diabetes, and abdominal obesity. The metabolic syndrome (MS) is characterized by the grouping of these risk factors (LAKKA, LAAKSONEM, LAAKA et al., 2003; HORTON et al., 1985 apud CIOLAC and GUIMARÃES, 2004).

This syndrome was also denominated X syndrome and civilization syndrome. It remains unknown the origin of this syndrome, but it was observed that the upper body obesity is associated to insulin resistance, which in turn is related to a higher risk of coronary diseases, hypertension, and diabetes type 2. It became an important subject of research in the 1990s, and the results can help us understand better the physiopathology of these diseases and their interrelations (ACSM, 2001).

The risk factors that characterize the MS are abdominal obesity, low HDL cholesterol, high triglycerides, elevated blood pressure, and elevated fasting glucose which increase the risk of coronary diseases and diabetes (NIEMAN, 1999).

This syndrome has become more prevalent in the last few years, and this is due to the everyday habits that encourage physical inactivity, unhealthy eating habits, and mainly due to the life expectancy increase, which in Brazil will increase from 4% of elderly in 1940 to 14.7% in 2020, i.e. within 80 years this age group will triplicate. This is one of the most important factors that deserve attention. People should reach this age in the best possible health conditions (MONTEIRO, DÁRIO and SOBRAL FILHO, 2004).

Given the strong association between visceral obesity and other MS risk factors, the International Diabetes Federation (IDF, 2005) and the National Cholesterol Education Program (NCEP, 2005) defined MS as the combination of metabolic complications that result from obesity. The obesity epidemic is the major factor responsible for the increased prevalence of MS. Overweight prevalence reached the incredible mark of 64.5% of the American population while obesity accounts for around 30.5% (FLEGAL et al., 2002 apud TROMBETTA, BRAGA and NEGRÃO, 2006).

In Brazil, the rates have been similar to those of most developed countries. This was evidenced by a government survey that included, the "Survey about risk behavior and reported morbidity of non-contagious diseases and damages" ("*Inquérito Domiciliar sobre Comportamento de Risco e Morbidade Referida de Doenças e Agravos Não Transmissíveis")*, conducted in 15 Brazilian capitals and in Brasília (District Capital). The survey revealed 40% of obesity prevalence, average rate, (IMC ≥ 25) in individuals over age 15 (WHO, 2002).

According to the Ministry of Health (DATASUS, 2003), in November alone, 325 cases of death by hypertension (high blood pressure) were registered in São Paulo, in addition to

37 due to diabetes type 1, 67 due to diabetes type 2, and 79 due to acute myocardial infarction (heart attack). This means that the metabolic syndrome can develop in more than 40% of adults aged over 60 and a lower rate but not insignificant in adults between 29 and 49 years old.

Several studies related to the MS show that physical activity is an important , if not the most important, factor that contributes to minimize the MS effects guaranteeing a healthier life. Thus, the protocols have to be followed adequately to reach satisfactory results (CIOLAC and GUIMARÃES, 2004).

Besides the sedentary habits such as watching television, working on the computer, and playing videogames among others, a reduction in the energetic expenditure is also observed with the reduction of physical activity at the workplace and in daily routine. The increased overweight and obesity prevalence is directly related to modernization as cause and effect (WANG, PARISE and LEVY, 2004).

Another interesting component which seems to be directly related to MS hormonal dysfunctions is leptin, an adipose derived hormone. The majority of obesity cases are associated to hypeleptinemia, which indicates an increase in the total body fat content and probable leptin resistance (CHEHAB, LIM and LU, 1996). Some effects of leptin in vitro include reduction of the insulin action on the hepatocytes, increase in fatty acid oxidation, and tryglicerides depletion; therefore, leptin is one of the factors responsible for controlling actions and insulin sensitivity (ZIMMET, BOYKO, COLLIER et al., 1999).

The authors state that changes in the life style can be important for the blood pressure control in hypertensive individuals contributing to the reduction of tensile strength levels and risk factors such as overweight, glucose tolerance, and blood lipid profile (APPEL et al., 1997 apud PINTO, MEIRELLES and FARINATTI, 2003).

Hypertension is characterized by the maintenance of elevated blood pressure levels, which can cause severe lesions in target organs (LATERZA, RONDON and NEGRÃO, 2007).

Hypertension can compromise the heart causing ventricular and arterial muscle hypertrophy (with an increase in the ventricular end-diastolic blood pressure), increasing the myocardial oxygen consumption, in addition to accelerating fat deposition in the vessels leading to atherosclerosis in both the coronary and systemic arteries (MCLENACHAN, HENDERSON, MORRIS et al., 1987).

Hypertensive patients with left ventricular hypertrophy present higher incidence of potentially serious ventricular arrhythmia that could result in ventricular fibrillation (MESSERLI, 1999; MCLENACHAN, HENDERSON, MORRIS et al., 1987).

The causes of ventricular arrhythmia vary and include: a) sub-endocardium ischemia caused by the disproportional growth of the coronary arteries in relation to the muscular growth; b) development of coronary failure; c) irregular pattern of muscular growth presenting eccentric hypertrophy more arrhythmic than the concentric hypertrophy; d) varied fibrosis intensity associated to the different levels of hypertension; e) microstructural alterations of the hypertrophied myocyte such as communicating junction and alterations in the potential propagation among cells; f) activation of ionic channels sensitive to cell stretching, which happens under fluctuating pressure levels conditions leading to ventricular ectopia due to the reduction in the cell electric activation; g) excessive activity of the sympathetic nervous system and probably of the renin-angiotensin system related to a higher development of tissue fibrosis; and h) hydroeletrolitic imbalance (MESSERLI, 1999).

Regular physical exercises have proved to prevent age-related hypertension increase even in individuals predisposed to develop hypertension, i.e., they reduce the systolic blood pressure in both hypertensive and normotensive individuals. Studies have shown that aerobic physical exercises represent an important benefit to the health of hypertensive individuals and discourage strength exercises (CIOLAC and GUIMARÃES, 2004).

The metabolic syndrome is frequently associated to obesity. It has been proved that obese patients are more vulnerable to hypertension and atrial fibrillation (WANG, PARISE and LEVY, 2004).

According to the literature, the majority of obese patients are more susceptible to suffer from atrial fibrillation as a consequence of insulin resistance. The increase in the sympathetic autonomic activity, already proved in obese individuals is another important factor in the origin of atrial fibrillation since the adrenergic hyperactivation reduces the atrial refractory period and increases the chances to ectopia and tachycardia which lead to atrial fibrillation. Weight loss can improve this situation since it causes the reduction of the sympathetic activity (BRINKWORTH, NOAKES, BUCKLEY et al., 2006). Specific inflammatory processes can also be activated in obese patients with respiratory apnea syndrome, which is an important cardiovascular risk. Moreover, such syndrome has been associated to the acceleration of the arteriosclerosis, higher hypertension risk, stroke, cardiac failure, atrial fibrillation, and sudden death (MCNICHOLAS and BONSIGGNORE, 2007).

The effects of physical exercises on the lipid and lipoprotein profiles in the event of dyslipidemia are well known. Physically active individuals have higher HDL cholesterol levels and lower tryglicerides, LDL and VDLL cholesterol levels if compared to sedentary individuals. These results are not related to sex, age, body weight, and diet (CIOLAC and GUIMARÃES, 2004).

For most individuals with diabetes type 1 and 2, regular physical exercises improve the glycemy control, reduce certain cardiac disease risk factors, improve the psychological state, and promote weight loss (NIEMAN, 1999).

Another important important factor mentioned is that flexibility exercises along with aerobic and strength, improve and maintain the physical fitness (moderate to high activity without excessive fatigue). Thus, they are recommended for the improvement and maintenance of physical fitness and for the rehabilitation of cardiovascular diseases in adults of all ages (CYRINO, OLIVEIRA, LEITE et al., 2004).

The increase in the volume load caused by aerobic exercises induces to an increase in the end-diastolic blood pressure, which will result in a ventricular wall stress. The myocytes grow longitudinally with the addition of new myofibrils, which will cause the cardiac chamber dilation, eccentric hypertrophy.

During the strength exercise, the overload will increase the systolic blood pressure. The higher blood pressure and the systolic stress induce a transverse myocyte growth with

a parallel addition of new myofibrils increasing the cardiac chamber (MARON, 1997).

For individuals with cardiopathies and diabetes, exercises that do not surpass 70% of the maximum cardiac rate (FC.max) are recommended. They can also perform exercises within the range of 40 to 60% of FC.max. From three to six times a week, aerobic exercises with 40 to 60% intensity (FCR or level 12 to 16 in the Borg scale) and duration of 20 to 60 minutes are recommended (IRIGOYEN, ANGELIS, SCHAAN et al., 2003).

Sedentary individuals with risk of cardiovascular diseases moderate intensity (FCR 50 to 70% and levels 12 to 13 in the Borg scale) and duration of 30 to 60 minutes exercises are recommended. The pre workout exercises (heating) before the actual exercises session or workout and the post exercise stretching should be emphasized (CIOLAC and GUIMARÃES, 2004).

Another point that should be taken into consideration is the correction of FC.max for hypertensive individuals who use beta blockers. It should be done according to the dosage of the medicine since it can interfere with some responses induced by the exercises leading to reductions in the myocardial contractility, cardiac rate, blood pressure, and double product (INBAR, OTEN, SCHEINOWITZ et al., 1994).

It is important to recommend some precautions when performing physical exercises for individuals with metabolic syndrome such as current clinical evaluation, ergometric test for cardiac evaluation, and adequate clothing and shoes.

The metabolic syndrome can cause morphologic alterations related to the volume and density in the cardiac tissue making it susceptible to complications such as hypertension and other degenerative diseases.

The present study shows the importance of physical exercises not only to control, but also to attenuate the effect of MS. Exercise programs can be personalized for individuals with hypertensive, diabetics, and obese in order to prevent MS aggravating factors.

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