Review
article

Impact of exercise training and detraining after myocardial infarction: a literature review

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Abstract

Despite the advances in the treatment and prevention, myocardial infarction (MI) remains the leading cause of morbidity and mortality worldwide. Different degrees of ventricular dysfunction, changes in hemodynamic and molecular mechanisms, as well as neurohumoral derangements, are substantially associated with increased mortality rate in MI patients. Cardiovascular, metabolic and autonomic benefits of acute and chronic exercise training (ET) have led many researchers to suggest ET as an important tool in the management of coronary artery disease and after MI. Regarding cardiovascular rehabilitation, several factors, such as illness, injury, travel, vacation or even rehabilitation program discharge may often interfere with the ET process, leading to a disruption in physical activity patterns by either decreasing training level or frequency or interrupting the training program altogether. Thus, it is necessary to identify the impact of ET after MI, as well as the possible consequences of such disruption in infarcted individuals.

Keywords: myocardial infarction, exercise training, detraining.

1 Introduction

Coronary artery disease with subsequent myocardial infarction (MI) afflicts nearly one million people in the United States each year and accounts for tens of billions of dollars in hospital costs (ROGER, LLOYD-JONES, BENJAMIN et al., 2012). MI is defined by pathology as myocardial cell death due to prolonged ischemia. Cell death is categorized pathologically as coagulation and/or contraction band necrosis, which usually evolves through oncosis, but can result to a lesser degree from apoptosis (ALPERT, THYGESEN, JAFFE et al., 2008).

Since the classical studies by Sullivan, Higginbotham, and Cobb (1989) in the late 1980s, evidence has accumulated supporting the beneficial effects of exercise training (ET) as a key intervention for preventive cardiology. ET in patients with cardiovascular disease increases exercise capacity, reduces cardiac ischemia (HAMBRECHT, WALTHER, MÖBIUS-WINKLER et al., 2004; THOMPSON, 2005), delays the onset of or eliminates angina pectoris (THOMPSON, CULLINANE, LAZARUS et al., 1981), improves endothelial (VONA, ROSSI, CAPODAGLIO et al., 2004; VONA, CODELUPPI, IANNINO et al., 2009) and autonomic function (LA ROVERE, BERSANO, GNEMMI et al., 2002); and also improves overall and cardiovascular-related mortality (HAYKOWSKY, SCOTT, ESCH et al., 2011).

Detraining has been redefined as the partial or complete loss of training-induced anatomical, physiological, and performance adaptations, as a consequence of training reduction or cessation (MUJIKA and PADILLA, 2000). However, little is known about the effects of detraining in patients after MI. Considering the importance of ET in the management of MI, as well as the clinical implication of detraining in these individuals, the present review aims to exhibit the impact of ET and detraining after myocardial infarction.

2 Material and methods

The PubMed (www.pubmed.nl) and MEDLINE databases were used to conduct a literature search using keywords without restrictions. In this systematization, a search was conducted using the keywords: myocardial infarction, exercise training and detraining.

3 Results

3.1 Myocardial infarction: pathophysiology and clinical implications

Since the 1950s, when cardiovascular disease overcame the threshold of 50% as cause of death, with MI becoming truly a nightmare, a search for risk factors was started with the Framingham Study. Cigarette smoking, hypertension, hypercholesterolemia, diabetes mellitus, physical inactivity, and obesity were identified as major threats, and prevention strategies were initiated (THIENE and BASSO, 2010).

In the United State of America it has been estimated that about 86,000,000.00 individuals have one or more types of cardiovascular disease, and 24,200,000.00 presents coronary artery and/or MI (ROGER, LLOYD-JONES, BENJAMIN et al., 2012). In Brazil, these estimates are not different, cardiovascular disease accounts for about 32% of total mortality, and prevalence of coronary artery disease has been estimated as a range of 5% to 8% in adults over 40 years, providing a high rate of mortality due to MI of about 48/100.000 individuals (POLANCZYK and RIBEIRO, 2009).

Coronary atherosclerosis is a chronic disease with stable and unstable periods in which, during the unstable periods, the activation of inflammatory factors in the vascular wall induces the development of MI, which may be the first manifestation of coronary artery disease or may occur repeatedly, in patients with established disease (THYGESEN, ALPERT, WHITE et al., 2007). The partial or complete occlusion of epicardial coronary artery, from the vulnerable plaque rupture or erosion is the most common cause of MI, accounting for about 70% of fatal events. After plaque rupture or erosion, exposure to substances of platelet activation and aggregation, thrombin generation and a thrombus formation, usually occurs (LIBBY, 2001).

Myocardial ischemia, with or without reperfusion, induces the production of reactive oxygen species and inflammatory cytokines. These changes are responsible, at least in part, by cardiac depression, especially regarding to the loss of Ca^{+2} homeostasis; imbalance of metaloproteinases matrix; and the signaling cascade of tissue necrosis (HORI and NISHIDA, 2009). This final pathway is mediated by the time-dependent oncosis processes, and in a lesser extent, to apoptosis itself. The complete myocardial necrosis in the affected area requires 2-4 hours or more, depending on the presence of collateral circulation in the ischemic area, myocardial sensitivity, preconditioning and, finally, nutrients and oxygen demands (THYGESEN, ALPERT, WHITE et al., 2007).

Among the determinants of left ventricular (LV) function after an ischemic event, some of them deserve attention: the MI size and localization, myocardium contractility, ventricular compliance, aortic impedance, venous capacitance (pre-load), and others (COHN, JOHNSON, SHABETAI et al., 1993). If a large ventricular mass is subjected to ischemic injury, the pump function of LV becomes depressed; cardiac output, stroke volume, blood pressure and peak dP/dt decrease. In contrast, the LV end-diastolic pressure increases (PFEFFER, PFEFFER, FISHBEIN et al., 1979; JORGE, RODRIGUES, ROSA et al., 2011). The depression of cardiac function after MI is directly related to the extent of the ischemic lesion in the LV and the degree of increase in the LV end-diastolic pressure, one of the biggest predictors of mortality rate after an ischemic event. However, the clinical parameter most widely used in the chronic phase of MI is the LV ejection fraction, which is applied to evaluate the patient's systolic function and cardiovascular risk (DUTCHER, 2007).

MI initiates a ventricular remodeling process, which is characterized by progressive LV dilatation, rearrangement of the ventricular wall architecture, and hypertrophy (YOUSEF, REDWOOD and MARBER, 2000). However, at the cellular level, the precise pathophysiological changes associated with LV remodeling are not completely understood. Innumerous molecular and cellular processes appear to be particularly important, including apoptosis of the cardiac myocytes, particularly in the peri-infarct zone, autophagy and reduced proliferative capacity of new cardiomyocytes (SHIH, SHAU, HSIEH et al., 2011). Loss of cells and the inability to replace them, may contribute to deterioration of cardiac function.

MI-induced heart failure in experimental animals has been widely used by several researchers in order to better understand the evolution of MI and its complications. Due to clinical relevance and applicability, permanent coronary artery ligation is one of the most widely used models of MI in small animals (ELSER and RIEGGER, 1995). Many researchers have determined the hemodynamic changes in rats at different times of MI. Decrease of LV systolic pressure and velocity of contraction (+dP/dt of the LV), hypotension, and increase of LV end-diastolic pressure are constantly observed in this experimental model (FLETCHER, PFEFFER, PFEFFER et al., 1981; JORGE, RODRIGUES, ROSA et al., 2011).

Previous data from our group have shown that MI caused a series of ventricular and hemodynamic dysfunctions, such as reduction of systolic and diastolic function, decrease of cardiac output, blood pressure, and expression of the SERCA2 from the sarcoplasmic reticulum in rats after 90 days of coronary artery ligation (JORGE, RODRIGUES, ROSA et al., 2011). In fact, the decrease in cardiac cell performance in heart failure seems to be determined by biochemical and molecular alterations of cardiomyocytes, mainly expression of proteins that participate in the regulation of the excitation-contraction and relaxation process (BALKE and SHOROFSKY, 1998).

Besides the functional and molecular changes, peripheral manifestations of heart failure, endothelial dysfunction, changes in morphological and metabolic profile of skeletal muscles, as well as disturbances in the ventilatory control are crucial for the appearance of symptoms such as exercise intolerance and reduced maximum oxygen consumption (VO_2 max), resulting from peripheral perfusion and cellular metabolism impairment (LA MONTE and BLAIR, 2006).

It is well known that MI initiates a cascade of neurohumoral changes in order to minimize the consequences of reduced ventricular function caused by obstruction of blood flow in the coronary artery of infarcted patients. Considerations regarding the autonomic dysfunction in patients after an ischemic event are not new. In fact, Webb, Adgey and Pantridge (1972) observed that 92% of MI patients with autonomic imbalance displayed bradycardia and hypotension, and these functional alterations were associated with inferior and posterior LV ischemia. In patients with LV anterior wall ischemia, there was a higher incidence of hypotension and tachycardia, suggesting that the action of the sympathetic nervous system was predominant.

Recently, the reflex control of circulation (baroreflex) has been recognized as an important predictor of risk after a cardiovascular event. The ATRAMI study (Autonomic Tone and Reflexes After Myocardial Infarction) provided clinical evidence of the prognostic value of baroreflex sensitivity and heart rate variability (HRV) in cardiac mortality after MI, regardless of LV ejection fraction and ventricular arrhythmias (LA ROVERE, BIGGER JUNIOR, MARCUS et al., 1998). Furthermore, Kleiger, Miller, Bigger Junior et al. (1987), studying patients of a Multicenter Post Myocardial Infarction Program, observed a relative risk of mortality five times greater in those patients with reduced HRV, a marker of cardiac autonomic modulation, compared to those who had increased levels of this variable.

In this sense, in the experimental setting, several authors have demonstrated autonomic dysfunction after coronary artery ligation in animals. Lacerda, Consolim-Colombo, Moreira et al. (2007) observed that acutely, 8 hours after MI, animals presented renal sympathetic nerve hyperactivity, as well as decrease of the arterial and cardiopulmonary baroreflex. In fact, our group have consistently shown that after chronic MI, baroreflex dysfunction, HRV reduction,

high frequency and low frequency bands of HRV were reduced in comparison with non-infarcted animals (MOSTARDA, RODRIGUES, VANE et al., 2010; JORGE, RODRIGUES, ROSA et al., 2011).

In view of cardiac and autonomic consequences of MI that usually lead to morbidity and mortality, interventions in order to improve cardiac function, baroreflex sensitivity, and the participation of the parasympathetic nervous system in the control of circulation and heart rate, have been seen as a new strategy in the management of cardiovascular diseases.

3.2 Role of exercise training in the management of myocardial infarction

The cardiovascular, metabolic and autonomic benefits of ET have led many researchers to suggest that ET is an important non-pharmacological tool to treat different cardiovascular diseases which culminate in heart failure (LA ROVERE, BERSANO, GNEMMI et al., 2002, PEDERSEN and SALTIN, 2006). The evidence that aerobic ET is a great tool in the treatment of patients with coronary artery disease, with or without MI, is quite significant. A meta-analysis, based on 48 randomized controlled trials (8940 patients) showed that cardiac rehabilitation programs based on aerobic ET, reduced the overall mortality rate by 20%, cardiovascular mortality by 26%, while reduced total cholesterol, triglycerides and blood pressure levels in patients after MI, angina pectoris and/or coronary artery disease (TAYLOR and MONEER, 2004).

Moreover, experimental studies have been effective in order to demonstrate the benefits of ET on cardiac function after MI in animals, complementing clinical information with molecular evidence. Chen, Hsu, Lee et al. (2010) recently demonstrated that four weeks of aerobic ET were effective in improving ventricular function of rabbits after descending coronary artery ligation. These authors suggest that this improvement in the ventricular function occurred in consequence of changes in autophagic function and fatty acids use of trained animals. Additionally, Xu, Wan, Ji et al. (2008) observed that cardiac function was significantly preserved and collagen volume fraction was reduced in trained infarcted rats compared with sedentary.

Corroborating previous data from the literature, our group recently demonstrated that three months of aerobic ET in MI rats caused an improvement in ventricular function, assessed invasively and noninvasively, associated with increased expression of SERCA2 and reduced LV infarcted area in trained animals. Furthermore, increased maximum oxygen consumption, cardiac output, gene expression of vascular endothelial growth factor (VEGF) and regional blood flow, were also displayed as benefits of ET in infarcted animals (JORGE, RODRIGUES, ROSA et al., 2011).

One of the most striking results achieved by ET in heart failure patients (after MI) is the reduction in sympathetic nerve activity. Coats, Adamopoulos, Radaelli et al. (1992) were the first to report that ET caused significant changes in cardiac parasympathetic/sympathetic balance. Increased parasympathetic control of heart rate with a shift away from sympathetic dominance was found in exercise-trained heart failure patients (RADAELLI, COATS, LEUZZI et al., 1996). In addition, these investigators described that whole-body radiolabeled norepinephrine spillover was 16% reduced by ET. Similar results were reported by other investigators where the power sympathetic component was evaluated by means analysis of heart rate variability (KIILAVUORI, TOIVONEN, NÄVERI et al., 1995; TOEPFER, MEYER, MAIER et al., 1996). More recently, Pliquett, Cornish, Patel et al. (2003) found that ET decreased norepinephrine levels in a rabbit model of MI.

Thus, ET as a non-pharmacologic intervention in preventing and/or attenuate cardiac autonomic changes and LV dysfunction has been seen as an important strategy in the management of cardiovascular diseases, especially after MI. On the other hand, exercise prescription essentially describes the process whereby a person's recommended regimen of physical activity is designed in a systematic and individualized manner. An "individualized manner" implies specific strategies to optimize return to work or activities of daily living, reduction of risk factors for future cardiac events, and maximization of the patient's capacity to maintain an active lifestyle. The development of an appropriate exercise prescription to meet the individual patient's needs has a sound scientific foundation, but there is also an art to set up an effective exercise programming.

3.3 Impact of physical detraining

Despite the physiological adaptations of the ET after MI are being extensively studied, the literature about the detraining is less consistent. Detraining has been redefined as the partial or complete loss of training-induced anatomical, physiological, and performance adaptations, as a consequence of training reduction or cessation (MUJIKA and PADILLA, 2000). Previous studies have demonstrated that highly trained athletes submitted to 7-10 days of detraining displayed reduction of glucose tolerance (ARCIERO, SMITH and CALLES-ESCANDON, 1998). In contrast to this result, it was found that 2 months detraining in young dancers did not affect glucose tolerance. However, insulin levels in fasting and postprandial periods were substantially higher. This result suggests that despite the insulin sensitivity was reduced with short-term cessation of physical activity; this metabolic alteration may not reflect on glucose tolerance in individuals that are not highly trained (CHEN, CHEN, CHANG et al., 2006).

Regarding musculoskeletal adaptations, several studies examining detraining have reported a decrease or no change (HOUSTON and GAMBAL, 1979; COYLE, MARTIN, SINACORE et al., 1984) in skeletal muscle capillarity after different periods of detraining. A possible reason for the lack of consistency among the studies may be different aerobic capacity of the studied subjects. For example, Coyle, Martin, Sinacore et al. (1984) reported that capillary density was maintained after 84 days of detraining in athletes (VO_2 max = 62.1 ± 3.3 mL/kg^{-1}/min^{-1}), while Klausen, Andersen, and Pelle (1981) reported that the increase in capillary density induced by eight weeks of resistance training in a sedentary group was reduced after four weeks of detraining. Furthermore, Hernández, Torres and Rivas (1997) reported that an increase in exercise-induced muscle capillary was reduced in the gastrocnemius muscle of cats only after 20 weeks of detraining.

Studying streptozotocin-diabetic rats our group previously demonstrated that aerobic ET improved baroreflex sensitivity, heart rate variability, parasympathetic tonus, blood glucose levels, and mortality rate. After 3 weeks

of detraining, these ET beneficial changes were maintained in diabetic rats (MOSTARDA, ROGOW, SILVA et al., 2009). Regarding the cardiovascular adaptations of ET, Kemi, Haram, WislØff et al. (2004), using preparations of isolated rats myocytes, have described that fractional shortening regressed with only 2 weeks of detraining. Also, Bocalini, Carvalho, De Sousa et al. (2010) have shown that inotropism and lusitropism parameters, studied on papillary muscles, regressed to control values after 2 weeks of detrained in female rats. In humans, it has been reported that after detraining, ventricular adaptations returned to conditions similar to those prior to training (GIANNATTASIO, SERAVALLE, CATTANEO et al., 1992; GIADA, BERTAGLIA, DE PICCOLI et al., 1998; PELLICCIA, MARON, DE LUCA et al., 2002).

Regarding cardiovascular rehabilitation, several factors, such as illness, injury, travel, vacation or even rehabilitation program discharge may often interfere with the ET process, leading to a disruption in physical activity patterns by either decreasing training level or frequency or interrupting the training program altogether. Therefore, it is necessary to identify the consequences of such disruption and its underlying mechanisms particularly to MI subjects, for whom ET is a highly recommended therapeutic tool. Vona, Rossi, Capodaglio et al. (2004) have found that 3 months of aerobic ET improved endothelium-dependent vasodilation in post-MI patients, but this beneficial effect disappears after 1 month of detraining. In addition, in patients with recent acute MI, ET was associated with improved endothelial function regardless of the type of training (1 month of aerobic, resistance or aerobic + resistance), but this effect also disappears after 1 month of detraining (VONA, CODELUPPI, IANNINO et al., 2009). However, the effects of detraining in the LV remodeling, autonomic function and survival rate after MI remains poorly understood and require further elucidation.

4 Conclusions

A wealth of data published over the last two decades has documented the ventricular, autonomic, physiological, psychosocial, and outcome benefits of exercise training programs in patients after MI. However, as demonstrated by some of the studies, it is important that exercise becomes a habit, since the interruption may promote the regression of the ET benefits. Therefore, it is necessary to educate the patient during cardiac rehabilitation programs, so the patient understands that physical exercises should be adopted as a lifestyle. Furthermore, it is important to find ways to extend the benefits of this practice. For it to happen, it is important to study new public policies of monitoring these patients after a period of supervised rehabilitation, as well as new approaches and methodologies of ET for these MI patients. A possible solution to the adherence of these individuals would be accumulation of training in small session during a day. This method of training might increase the patient adherence, since exercises will not be continuous, which is even safer for the participant in the unsupervised practice. However, the question that arises is: is cumulative ET capable of promoting the same benefits of continuous ET in patients after MI? Thus, further studies are necessary for such practice to be carried through into cardiac rehabilitation programs and during the critical period of post-rehabilitation period.

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