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Review

Exercise training-induced modification in autonomic nervous system: An update for cardiac patients

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ABSTRACT

Patients with cardiovascular disease show autonomic dysfunction, including sympathetic activation and vagal withdrawal, which leads to fatal events. This review aims to place sympathovagal balance as an essential element to be considered in management for cardiovascular disease patients who benefit from a cardiac rehabilitation program. Many studies showed that exercise training, as non-pharmacologic treatment, plays an important role in enhancing sympathovagal balance and could normalize levels of markers of sympathetic flow measured by microneurography, heart rate variability or plasma catecholamine levels. This alteration positively affects prognosis with cardiovascular disease. In general, cardiac rehabilitation programs include moderate-intensity and continuous aerobic exercise. Other forms of activities such as high-intensity interval training, breathing exercises, relaxation and transcutaneous electrical stimulation can improve sympathovagal balance and should be implemented in cardiac rehabilitation programs. Currently, the exercise training programs in cardiac rehabilitation are individualized to optimize health outcomes. The sports science concept of the heart rate variability (HRV)-vagal index used to manage exercise sessions (for a goal of performance) could be implemented in cardiac rehabilitation to improve cardiovascular fitness and autonomic nervous system function.

1. Introduction

According to recent epidemiological studies, cardiovascular disease (CVD) is the most common cause of death among Europeans: more than 4 million people die of CVD every year in Europe (~45% of all deaths) [1,2]. Disorders of the autonomic nervous system (ANS) have a key pathophysiological role in early stages of essential hypertension [3,4], myocardial infarction [5,6], and chronic heart failure (CHF) [7–10], producing coronary vasoconstriction, increasing cardiac oxygen consumption and leading to fatal events [11–13]. The clinical importance and prognostic implications of the exaggerated sympathetic nervous system (SNS) are well documented in CVD [14,15] in that it is a known trigger of cardiac arrhythmias and sudden death [16–19]. The activity of the central nervous system also seems to play a role in sympathetic hyperactivity [20,21] and is accompanied by humoral overactivity of the renin–angiotensin–aldosterone system (RAAS) [9,22]. In the long term, sympathetic chronic stimulation is deleterious [14,23]. In the periphery, tubular fluid level and sodium reabsorption increase in response to RAAS activation [24] and peripheral arterial resistance increases [25], thereby increasing cardiac pre- and postload. In addition, sympathetic hyperactivity alters myocardial calcium cycling, which is responsible for reduced myocardial contractility [26]. The spontaneous activity of certain slow calcium channels (L-type) could explain in part ventricular arrhythmias and cardiac sudden death [17].

Pharmacological treatments for CVD need to decrease the overactivity of the SNS (β blockers, angiotensin-converting enzyme inhibitors, etc.) [27,28] and to increase the activity of the parasympathetic nervous system (adenosine, cholinesterase inhibitors, statins) [29]. Additionally, different non-pharmacological techniques have the same goal, such as vagal stimulation, renal denervation and carotid baroreceptor stimulation, and were well described in a recent review [30]. Among the non-pharmacological techniques, ET is of growing interest in major

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CVD guidelines. With an IA level of evidence for the latest recommendations from the European Society of Cardiology and an IB level from the American Heart Association, ET has become one of the pillars of CHF treatment and coronary heart disease (CHD) [31–35]. The therapeutic potential of restoring or enhancing the cardiac vegetative balance with ET is very promising [36–38], but the underlying mechanisms are still unclear.

This review aims to summarize some of the beneficial effects of aerobic ET on CVD and place sympathovagal balance as an essential element to be considered in management for patients who benefit from a cardiac rehabilitation program.

2. Effect of ET on the autonomic nervous system

2.1. Muscle sympathetic nerve activity

Muscle sympathetic nerve activity (MSNA) is a neurophysiological method (microneurography) that allows for recording sympathetic nerve traffic. MSNA is markedly increased in patients with CHD [39,40] (45 ± 2.3 vs. 31 ± 1 bursts/min; $p < 0.001$), hypertension [41,42] (33.3 ± 1.7 vs. 23.9 ± 1.6 bursts/min; $p < 0.01$ respectively), and CHF [43] (62 ± 4 vs. 39 ± 4 bursts/min; $p < 0.01$) as compared with healthy subjects, but MSNA can be decreased by ET [44,45]. The research team from the Heart Institute of University of Sao Paulo has spent more than 10 years investigating the effects of ET on MSNA in CHF and CHD patients [46–51]. The team demonstrated that regular ET can normalize the basal overactivation of the sympathetic nerve (Table 1). After 4–6 months of ET (3 supervised 60-min exercise sessions/week of cycling and strengthening), baseline values of MSNA (about 45 bursts/min for CHF patients) decreased significantly to within normal values relative to healthy participants (about 30 bursts/min) [46–51], with no change in untrained groups. Furthermore, ET had no gender- or age-specific effect on MSNA.

2.2. Heart rate variability (HRV)

HRV is a non-invasive reproducible measure of ANS function corresponding to the balance between sympathetic and parasympathetic effects on the sinoatrial node rate [52–54]. HRV indexes are highly decreased in CVD patients and predict poorer outcomes, such as reduced left-ventricular function and sudden cardiac death [38,55–58]. The risk of all-cause and progressive heart failure death was increased with a standard deviation of normal to normal R-R intervals (SDNN) of <67 ms (relative risk [RR] 2.5; 95% CI 1.5–4.2) [56]. In a retrospective analysis of 1284 CHD patients, SDNN values <70 ms significantly and independently predicted cardiac mortality (RR 3.2; 95% CI 1.6–6.3) [59]. According to Bilchick et al. [58], each increase of 10 ms in SDNN conferred a 20% decrease in risk of mortality ($p = 0.0001$) with an increase in vagal tone and a decrease in sympathetic activity [38,60–65]. In a recent randomized controlled, single-blinded trial, Murad et al. [64] included 66 CHF patients (mean age 69 years, New York Heart Association [NYHA] class II–III) with preserved or reduced ejection fraction.

Table 1
Effect of exercise training on muscle sympathetic nerve activity (MSNA) in patients with chronic heart failure (CHF) and post-acute coronary syndrome (post-ACS) from the literature.

References	No. of patients	Patient characteristics	Training protocol	MSNA basal values	MSNA post-training values
CHF patients					
Antunes-Correa, 2012	52	45–59 years Trained ($n = 16$) vs. untrained ($n = 17$) 60–75 years Trained ($n = 11$) vs. untrained ($n = 8$)	4 months 3×60 min/week Stretching Cycling Strengthening Intensity: anaerobic threshold up to 10% below the respiratory compensation point	43–50 bursts/min according to the group with no difference between them	In trained groups: 27–29 bursts/min ($p < 0.001$) Unchanged in untrained groups No age effect ($p = 0.69$)
Antunes-Correa, 2010	40	57–60 years Men exercise-trained ($n = 12$) Men untrained ($n = 10$) Women exercise-trained ($n = 9$) Women untrained ($n = 9$)		43–50 bursts/min according to the group with no difference between them	In trained groups: 30 bursts/min ($p < 0.001$) Unchanged in untrained groups No gender effect
Roveda, 2003	16	35–60 years Exercise-trained ($n = 7$) Sedentary control ($n = 9$)		40–50 bursts/min	In reply to: trained groups ~30 bursts/min ($p < 0.001$) Unchanged in untrained groups HF trained group did not differ from trained healthy control group after training
Fraga, 2007	27	Exercise training ($n = 15$) Untrained control ($n = 12$)		45 bursts/min	In trained group: 35 bursts/min ($p = 0.001$) Unchanged in untrained groups
Mello Franco, 2006	29	Untrained control ($n = 12$) Exercise trained ($n = 17$)		43–45 bursts/min	In trained group: 35 bursts/min ($p = 0.007$) Unchanged in untrained groups
Post-ACS patients					
Martinez, 2011	28	Exercise trained ($n = 14$) Untrained control ($n = 14$)	6 months/3×60 min/week Stretching/cycling/strengthening/anaerobic threshold	42–45 bursts/min	In trained group: ~20 bursts/min ($p < 0.001$) (similar to healthy control group) Unchanged in untrained groups

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