The Effect of Aerobic Interval Training and Massage Therapy on C-Reactive Protein and Cardiorespiratory Fitness in Cardiovascular Patients after Coronary Artery Bypass Graft

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ABSTRACT

The purpose of this study was to investigate the effects of an 8 week period of aerobic interval training and massage therapy on changes in C-reactive protein (CRP) level and cardiorespiratory fitness in cardiovascular patients after coronary artery bypass graft. The study population consisted of patients who had undergone a coronary artery bypass graft and at least one month had passed since their surgery. 60 patients met the study inclusion criteria and were willing to cooperate; they were divided randomly into three groups (n = 20) as follows; interval, massage therapy and a control. Subjects in groups taking interval training and massage therapy were administered three sessions per week for eight weeks. 48 hours before and after eight weeks of exercise, subjects were measured for peak oxygen consumption and blood samples were taken. Results of the present study show that 8-week programs of regular exercise and massage therapy resulted in significant reduction of CRP of 42% and 25% respectively (P<0.05). Peak oxygen consumption values after eight weeks of regular exercise showed a significant increase (22% in interval exercise and 17% in massage therapy (P<0.05). In general, these findings show that 8-week programs of aerobic interval training and massage therapy significantly reduced serum CRP value and caused a significant increase in peak oxygen consumption in patients with coronary artery bypass graft. These changes can be effective for prevention of sudden death and cardiovascular problems after bypass surgery. Also, interval training was more effective on reducing CRP and increasing peak oxygen consumption than massage therapy.

INTRODUCTION

Cardiac rehabilitation is an important component of a comprehensive program of secondary prevention of cardiovascular diseases that can reduce age-related cardiovascular mortality by about 50 percent. The World Health Organization considered treating the symptoms of a disease and improving quality of life as the main purpose of modern rehabilitation (1). It is widely accepted that cardiac rehabilitation can have a great effect on extending life span. Studies have shown that such programs reduce total mortality by about 20-25% and reduction in mortality from cardiovascular disease after a 3-year follow-up by about 22-25% (2). Rehabilitation has been considered as a factor that helps to control risk factors in individuals by slowing down the development of disease (3).

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Massage is a systematic form of mechanical manipulation of soft tissues of the body applied by hands; it is applied as a therapy to improve health and welfare. Massage is used as an intervention in many areas such as treatment, rehabilitation and recovery from injury or exercise (4). Studies also have shown that proper design of an interval training program causes less physiological pressure in patients than does conventional aerobic training and causes no sign of abnormal heart rate or blood pressure or abnormal function of the left ventricle. Interval training program has shown no added clinical damage, even in patients that were not on awaiting a heart transplant, so interval training is a potential tool for widespread application in cardiovascular patients (5).

C-reactive protein (CRP) is a sensitive and non-specific index of inflammation that has been widely studied. CRP is attached to a wide variety of microbial polysaccharide and phosphatide choline substances and it causes damage to cell membrane. CRP also increases activity of phagocytic cells and activates the complement classical pathway. CRP has also been obtained from human atherosclerotic lesions (5, 6). In addition, various studies have shown that CRP predicts increased risk of myocardial infarction, stroke or peripheral vascular disease in those who have no known symptoms of coronary artery disease. Also, a meta-analysis study demonstrated a significant positive correlation between CRP and coronary heart disease (6, 7). It has been reported that atherosclerosis and peripheral vascular changes reduced levels of cardiorespiratory fitness (7, 8). A positive correlation has been reported between cardiorespiratory fitness and aerobic fitness by reducing coronary artery disease (7). Also, it has been stated that those with high cardiorespiratory fitness had lower CRP levels than those with low cardiorespiratory fitness (8, 9). Cardiovascular fitness is defined as a person's ability to participate in aerobic exercise activity and is related to low clinical factors such as stroke, metabolic syndrome symptoms, myocardial infarction and other cardiovascular diseases (9, 10) and can be determined by Vo2max (8). Vo2max can be used to predict exercise capacity of an individual and is used as a strong predictor of cardiovascular function (8). Theoretically, low cardiovascular fitness can cause changing peripheral or coronary artery atherosclerotic (9).

Also, Kullo, Khaleghi, and Hensrud (2007) reports that adult inflammatory indices were inversely related to level of aerobic fitness (11). Few studies have investigated the effect of cardiovascular rehabilitation on inflammatory indices and cardiorespiratory fitness of patients after coronary artery bypass graft. Kim *et al.* (2008) examined the positive effects of cardiac and exercise rehabilitation on inflammatory factors after coronary bypass graft. The 60 Subjects were divided into two equal groups; 30 male and 30 female (12). The results of this study showed that CRP level was significantly reduced in the experimental group as well as a significant increase in amount of Vo2max among them (12). Onishi *et al.* (2009) studied the effects of cardiac rehabilitation program on patients after coronary artery bypass graft (13). Patients were given 6 months of aerobic and resistance training and treadmill exercise. CRP level was not significantly reduced and the amount of Vo2max in this study showed a significant reduction (13). According to patient condition, aerobic interval training to inflammatory indices and cardiorespiratory fitness received less research attention. This study addresses the question of whether or not aerobic training and massage therapy can reduce serum levels of CRP and increase cardiorespiratory fitness in cardiovascular patients after coronary artery bypass graft. And which treatment, aerobic interval training or massage therapy, had the greatest effect on indices?.

MATERIALS AND METHODS

This research was conducted as a semi-experimental study, carried out as field tests for the purpose of obtaining applicable results.

Subjects. The study population consisted of cardiac patients in Isfahan province; 60 patients met the inclusion criteria and were willing to cooperate. The patients had undergone coronary artery bypass graft in 2010 in Chamran, Sina and Sepahan hospitals in Isfahan, and at least 1 month had passed since their surgery. 60 subjects were selected randomly and divided into three groups; interval (n = 20), massage therapy (n = 20) and a control (n = 20) group. The control group did not participate in any intervention while the interval and massage therapy groups had intervention three times a week for eight weeks. All subjects underwent echocardiography and 75 patients with

evaluations higher than 40% were selected and were willing to participate in the study. 15 patients were excluded from each group for reasons such as lack of regular training, chest pain and shortness of breath during exercise tests and echocardiography or hospitalization. All participants received written information about the study including an explanation of the risks of doing the training. Patients read and signed written consent. Ethical approval for the study was obtained from Tapesh rehabilitation center in Isfahan. This study was performed under supervision of a specialist and exercise physiology specialists, and the condition of each subject was confirmed by a physician as clear from diabetes, kidney and liver diseases affecting CRP level and immune system.

Study Design. A meeting was held to familiarize subjects with exercise activities and the blood sampling technique. To reduce some confounding factors affecting results of the study and to reduce the effects of food type on inflammatory and immune indices, subjects were asked at the meeting for at least 24 hours before the training program and blood sampling to ensure abstenance from fast food consumption and caffeine drinks (13, 14). Blood samples were taken from subjects in 2 steps, 48 hours before training (stage 1) and 48 hours after the last training session (session 24) (step 2). In each step, 5 cc of blood was collected. Exercise activities and massage therapy were only given to experimental groups and the control group received no exercise intervention.

Training Protocol. The interval training and massage therapy intervention were selected by the researchers according to the physical condition of subjects and with consideration that at least 1 month had passed since their surgery. The program for subjects in the interval group was as follows; treadmill for 5 min with intensity of 50-70% of maximum heart rate (50-60% of maximal oxygen uptake) in order to warm up, then exercise in four intervals of 4 min with intensity of 85-95 percent of maximum heart rate (80-90% of maximal oxygen uptake) and 3 intervals of 3 min between four-minute intervals with 50-70 percent of maximum heart rate (50-60% of maximal oxygen uptake) and at the end of three minutes they exercised at the intensity of 50-70% of maximum heart rate to cool off. Therefore, total training time was 33 minutes (4, 14, 15). Patients in the massage therapy group were asked to lie down on a bed to receive their massage intervention. Massage was applied by a masseur for 15 minutes to lower and upper organs using a combination of conventional methods (Table 1).

Table 1. Massage techniques

Massage techniques	Procedure	Grade
Stroking	With both hands towards the center	Starts with a few caresses grade 1(superficial contacts) and then a few caresses Grade 2 (a bit depth to impact superficial vessels)
Effleurage	With both hands towards the center and multidirectional	Starts with grade 1(with proper depth to influence blood flow in superficial vessels and continues with grade 2 (impact on the deeper veins) and finishes with grade 3
Petrissage	With both hands towards and outward the center and multidirectional	Starts with grade 1(with proper depth to influence tissues and the blood flow in superficial vessels) then grade 2 (influences deeper veins and tissues)
Wringing	With both hands towards and outward the center and multidirectional	grade 1(with proper depth to influence tissues and the blood flow in superficial vessels)
Rolling	With both hands towards the center	Grade 2(Rolling and Lifting the muscle to influence the deeper structures)
Compression	With one hand in the direction of the distal to proximal and with both hands outward the center	Grade 2(puts Pressure on muscle tissue in order to influence the deeper structures)
Effleurage	With both hands towards the center	Grade 2

Massage Protocols were performed by 3 experts who had sports massage certificate. All techniques were performed in distal to the proximal direction

Massage program with caresses was used (grades 1 and 2) and gradually deep EFFLEURAGE (Levels 1, 2 and 3). Then, the technique of kneading (Petrissage) was used to work on vessels, tissues and structures deep within the muscle. The effleurage technique was used (grade 2) at the end of the program. For more massage and to avoid inconvenience, vegetable oil was used (15, 16). Blood samples were taken on completion of interventions (massage or relax). It is worth noting that using questionnaires and interviews, control group subjects did not participate in any rehabilitation program and continued with their routine daily activity.

Measurements. Height of subjects was measured by a height meter with accuracy of 0.01 and weight was measured on scales with an accuracy of 0.1 kg. Body Mass Index (BMI) was obtained by dividing weight (kg) by height (m). For the measurement of oxygen consumption, the peak of Rockport walk test was used, using Polar pulse meter and equation at the start and end of the period (10). Oxygen consumption as maximal oxygen uptake of subjects was considered in ml/kg/min. It should be noted that to determine training intensity, heart rate was randomly measured in 7 subjects by pulse meter.

$$Vo_{2peak} = 88.768 - [0.0957 \times weight\ (pond)] + (8.892 \times gender) - (1.4537 \times time) - (0.1194 \times heart\ rate)$$

Level of CRP was measured in subjects 48 hours before and 48 hours after the start of training after 8-10 hours of fasting from blood samples taken in rest in supine position. Blood samples were centrifuged at 1500 RPM for 10 minutes to separate serum and the obtained serum was distributed and immediately frozen at -80°C for later analysis. High-sensitivity CRP levels were measured using ELISA kit (Randox Biosciences, England). The minimum functional sensitivity of the kit was 0.01 mg per deciliter and coefficient of variation was between 1.5 and 2.5, respectively.

Statistical Analysis. To describe data obtained for each of the study variables, frequency, mean and standard deviation were used (Table 1). Smirnov test was used to determine data distribution. Given normal distribution of data, the paired t-test was used to compare intergroup variations for intergroup comparison covariance (ANCOVA) and for the significance; the post hoc test was used. Statistical analysis was performed by software SPSS 16 at significant level $P < 0.05$.

RESULTS

Preliminary data obtained from experimental and control subjects including age, height, weight, body mass index (BMI) and aerobic fitness are summarized in Table 2.

Table 1. Statistics related to the items constituting evoked nostalgia

Variables	Massage Therapy	Aerobic Interval Training	Control	p
Age (year)	51.5 ± 2.07	47.83 ± 2.05	53.83 ± 2.06	0.42
Weight (kg)	67.88 ± 11.00	77.12 ± 11.72	73.15 ± 11.6	0.37
Height (cm)	159.0 ± 5.26	169.50 ± 6.00	164.83 ± 5.8	0.11
BMI (kg/m^2)	27.07 ± 1.06	26.72 ± 1.00	26.91 ± 1.01	0.98
RSBP (mm/Hg)	136.13 ± 11.14	114.00 ± 10.14	128.0 ± 11.0	0.23
RDBP (mm/Hg)	84.0 ± 0.7	85.0 ± 0.8	81.0 ± 0.6	0.74
HRrest (bpm)	81.0 ± 7.5	67.0 ± 0.7	79.0 ± 7.2	0.1
Ejection Fraction	45.0 ± 2.08	44.0 ± 2.09	46.0 ± 2.4	0.59
VO$_{2peak}$	34.45 ± 2.15	35.0 ± 2.16	35.76 ± 1.86	0.21

BMI: Body Mass Index. **RSBP:** Resting Systolic Blood Pressure. **RDBP:** Resting Diastolic Blood Pressure. **HRrest:** Resting Heart Rate.

Results of the t-test on comparison of variables before and after tests in massage therapy between the interval and control groups are presented in Table 3. CRP values in massage therapy group and interval group were reduced significantly compared to pre-training (p<0.05). VO2peak in the massage therapy group and the interval group were

significantly increased compared to pre-   training (p<0.05).

Table 3. paired sample t test for comparison of pretest and posttest

Variable	Sampling Time	Massage Therapy			Aerobic Interval Training			Control		
		Mean±SD	t	p	Mea ±SD	t	p	Mean±SD	t	p
CRP	preTest	270.8 ± 5.4	33.4	0.001**	271.4 ± 4.1	65.8	0.001**	270.8 ± 3.2	1.65	0.11
	postTest	205.6 ± 6.8			159.5 ± 7.4			269.4 ± 7.4		
VO$_{2peak}$	preTest	34.5 ± 2.1	-22.3	0.001**	35.0 ± 2.2	-19.7	0.001**	35.8 ± 1.9	0.11	0.9
	postTest	41.4 ± 2.5			44.7 ± 3.9			35.7 ± 4.7		
Weight	preTest	67.8 ± 0.3	8.6	0.001**	77.1 ± 2.1	12.2	0.001**	73.2 ± 0.2	1.1	0.28
	postTest	66.1 ± 0.7			73.9 ± 2.3			73.0 ± 0.2		

CRP: C-Reactive Protein. ***:** Significant at p<0.01.

Results of analysis of covariance (ANCOVA) for intergroup comparison of variables with the control pretest was presented in massage therapy, interval and control groups, shown in Table 4. Values of CRP in interval group showed greater reduction than other groups (p<0.05). Also maximal oxygen uptake in interval group showed a greater increase than other groups (p<0.05).

Table 4. ANCOVA Statistics

Variables	Massage Therapy	Aerobic Interval Training	Control	F	p
		Adjusted Means ± SE			
CRP	205.6 ± 6.80	159.45 ± 7.47	269.35 ± 3.39	1603.89	0.001**
VO$_{2peak}$	41.40 ± 2.52	44.71 ± 3.9	35.66 ± 4.71	206.047	0.001**
Weight	66.11 ± 0.71	73.85 ± 2.32	73.00 ± 0.20	388.25	0.001**

CRP: C-Reactive Protein. ****:** Significant at p<0.01.

DISCUSSION

This study aimed to investigate the effect of interval aerobic training and massage therapy on changes in C-reactive protein and cardiorespiratory fitness in cardiovascular patients after coronary artery bypass graft. Results showed that intergroup values of serum CRP were reduced in the interval aerobic group (0.05> p). However, findings related to intergroup differences suggest that changes in the index in subjects after participating in a course of 24 sessions of interval aerobic training were statistically significant (P = 0.0001). The findings of this study were consistent with those of other researchers on reduced CRP subsequent interval aerobic training (17-19). But they showed inconsistency with the results of other research (13, 20). This inconsistency may be related to inadequate intensity and duration of the training. In one study it was reported that inadequate intensity of the training may have caused metabolic changes (13). Lower initial or pre-training CRP level will result in its reduction by training (13). Milani, Lavie, and Mehra (2004) reduced CRP through rehabilitation programs and exercise activity in patients with coronary artery bypass graft. Results showed that CRP level was reduced according to measurements taken at 3-months, from 3.4 to 2 mg/c (19). Pluss *et al.* (2008) examined the effects of rehabilitation programs developed for patients with heart attack and coronary artery bypass graft. Patients exercised on a bike ergometer and were asked to maintain a speed of 60 rounds per minute during training. Work load was 30-50 watts to begin with and based on work load maximum per minute; its intensity was increased to 10-20 watts (20). Results of the study showed that after three months' training and after a year's training, there was no significant change in CRP level in the group that received the more intense rehabilitation program compared to the control that received common program of rehabilitation (45 minutes of physical activity and 15 minutes of relaxation, two

days a week) (20). This lack of difference between the groups may have been caused by uncontrolled research because of the length of training. Increased serum level of CRP indicates increased trend of inflammation especially atherosclerosis that probably shows that patients remained at risk of cardiovascular disease post surgery (14). Also, by increasing the amount of oxygen peak in the study subjects, it might be concluded that training by strengthening the cardiovascular system reduced production of pre-inflammatory cytokines from mononuclear cells (17, 21). It is also likely that antioxidant effects of exercise activity can reduce inflammation (CRP) (18, 22). In short, it is probable that interval training caused reduced CRP both directly; by reducing the production of cytokines in adipose tissue, muscle and mononuclear cells and indirectly; by increasing insulin sensitivity, improving the functioning of endothelial cells as well as weight loss and lower body fat percentage (18, 22).

The results of the present study show reduced intergroup serum CRP values in the massage group. However, the findings on intergroup difference indicate that changes in the index in subjects after participating in an interval massage period was statistically significant. Other research has mostly tested the effect of massage therapy on on IgA, cortisol, CD4/CD8, lymphocytes, cells of NK, dopamine, serotonin and alpha amylase (23). No study was found for tests on the effect of massage therapy on CRP. However, findings of other researchers demonstrated a positive effect of massage therapy on biochemical indices such as cortisol, serotonin, glucose and inflammatory cytokines (IL-6 and TNF-alpha) (12, 16, 24-27). However, Billhult *et al.* (2008) reports that massage therapy had no effect on biochemical indices (28). Perhaps this was due to a lack of difference after rehabilitation of subjects and accuracy of laboratory instruments. Hernandez-Reif *et al.* (2004) reports on examination of immune system improvement and performance of nervous hormones of women with breast cancer after surgery was performed over a period of massage therapy. The results showed that massage caused a reduction on cortisol and increased levels of dopamine, serotonin and the number of NK cells and lymphocytes (16). The present study can be considered as consistent with those showing that massage therapy caused increased levels of NK cells, and the number of

lymphocytes, reducing levels of cortisol, neutropenia, insulin and glucose after the massage (21-24, 26). Research results show that improved mental state was associated with biochemical changes such as blood CRP level. Massage therapy can reduce post operative stress that can cause a reduction in CRP level. Massage may stimulate pressure receptors and affect nerves in internal organs such as liver and vascular wall and limbic system reduces sympathetic activity and increases parasympathetic activity and finally reduces inflammation and CRP (25).

Results of the present study show, Vo2peak intergroup values increased in the interval group. On the other hand, findings on intergroup difference suggest that changes in the index in subjects in the interval group after participation were statistically significant. Findings of the present study are consistent with findings of some other research (17, 27, 29) but were inconsistent with the results reported in Onishi *et al.* (2009), (13). Changes in coronary and peripheral vascular atherosclerosis also reduce cardiorespiratory fitness. A positive correlation was recorded between cardiorespiratory fitness and high aerobic fitness by reducing coronary artery disease (11). In the present study, VO_{2peak} showed an increase before exercise activity, this can be considered as a result of fit of cardiovascular, muscular and metabolic system with interval exercise activities including an increase in total hemoglobin, and fat metabolism and reduced glycolysis, increased end-diastolic volume (cardiac preload), end-systolic volume reduction and an increase in pulse volume (22). Results of the present study show that intergroup Vo2peak values increased in the massage group. On the other hand, findings on intergroup difference suggest that changes in the index in subjects after participation in a period of massage intervention were statistically significant. Findings of the present study are consistent with those of other research (17, 30, 31) and inconsistent with the results reported in Cox and Hayes (1999), (32). Rahmani Anarak *et al.* (2011) examined the effect of back massage on some physiological parameters of patients. Results showed that artery oxygen saturation was increased after massage (31). They examined the effect of foot massage on patients with stroke arterial oxygen saturation percentage. In general, it can be concluded that foot massage increased the

percentage of arterial oxygen saturation (31). The mechanism that causes VO_{2peak} increase is yet unknown, but it is possible that massage caused separation of the particles coagulated in tissues, lymph return acceleration, spread and increase in capillary active, contributing to better functioning of the heart and ability to withstand pressure, better transmission of blood and oxygen to tissues, stimulating the return of waste from tissues, stimulation of blood flow of the limbs and internal organs to the skin and muscles leading to increased VO_{2max}, also massage increases elasticity of muscles and joints and increases the amount of oxygen supplied to muscles (17, 30, 31).

CONCLUSION

Levels of inflammatory indices in patients after bypass surgery are high and aerobic interval activity and massage therapy served to significantly reduce serum CRP levels. Also, interval activity and massage therapy increased cardiovascular fitness in patients post surgery. Aerobic interval training to massage had the greatest influence. Reduction of inflammation factors and increased cardiovascular fitness can probably prevent sudden mortality and cardiovascular disorders. In general, this study can be applied as a proper and regular rehabilitation program (with respect to training intensity and duration) for distribution among health centers to serve this growing class of patients. The results of this research can be clarified further with more tests to evaluate the effects long-term and under different training intensities as well as nutrition control on changes in rest levels of the index.

APPLICABLE REMARKS

- The interval training could be an appropriate alternative instead of traditional training schemes for CABG patients for increase in VO2peak and enhancement of patient's heart.

- High intensity interval training (HIIT) did not cause any cardiac events for those patients who had gone under the surgery 4 months before the training program. Therefore; there is no ban for CABG patients to do these sorts of trainings.

- The massage therapy could be a reliable effective method in decreasing inflammatory factors like C-reactive protein and thus increasing aerobic capacity of the CABG patients, therefore rehabilitation centers could consider that for a better recovery in CABG patients especially high risk ones.

REFERENCES

1. Lie I, Arnesen H, Sandvik L, Hamilton G, Bunch EH. Predictors for physical and mental health 6 months after coronary artery bypass grafting: a cohort study. European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology. 2010;9(4):238-43.
2. Williams MA, Ades PA, Hamm LF, Keteyian SJ, LaFontaine TP, Roitman JL, et al. Clinical evidence for a health benefit from cardiac rehabilitation: an update. American heart journal. 2006;152(5):835-41.
3. Muto T, Yamauchi K. Evaluation of a multicomponent workplace health promotion program conducted in Japan for improving employees' cardiovascular disease risk factors. Preventive medicine. 2001;33(6):571-7.
4. Galloway SD, Watt JM. Massage provision by physiotherapists at major athletics events between 1987 and 1998. British journal of sports medicine. 2004;38(2):235-6; discussion 7.
5. Helgerud J, Hoydal K, Wang E, Karlsen T, Berg P, Bjerkaas M, et al. Aerobic high-intensity intervals improve VO2max more than moderate training. Med Sci Sports Exerc. 2007;39(4):665-71.
6. Aronson D, Sheikh-Ahmad M, Avizohar O, Kerner A, Sella R, Bartha P, et al. C-Reactive protein is inversely related to physical fitness in middle-aged subjects. Atherosclerosis. 2004;176(1):173-9.
7. Witkowska AM. Soluble ICAM-1: a marker of vascular inflammation and lifestyle. Cytokine. 2005;31(2):127-34.
8. Gaeini A-A, Fallahi A-A, Abdolreza Kazemi A, Kordi R. Association between Cardiovascular Fitness and Inflammatory Markers in Boys Aged 11-14 Years. Iranian Journal of Pediatrics. 2009;19(3):262-70.
9. Church TS, Barlow CE, Earnest CP, Kampert JB, Priest EL, Blair SN. Associations between cardiorespiratory fitness and C-reactive protein in men. Arteriosclerosis, thrombosis, and vascular biology. 2002;22(11):1869-76.

10. Medicine ACoS, Pescatello LS. ACSM's Guidelines for Exercise Testing and Prescription. 9th ed: Wolters Kluwer/Lippincott Williams & Wilkins Health; 2013. 456 p.
11. Kullo IJ, Khaleghi M, Hensrud DD. Markers of inflammation are inversely associated with VO2 max in asymptomatic men. Journal of applied physiology (Bethesda, Md : 1985). 2007;102(4):1374-9.
12. Kim YJ, Shin YO, Bae JS, Lee JB, Ham JH, Son YJ, et al. Beneficial effects of cardiac rehabilitation and exercise after percutaneous coronary intervention on hsCRP and inflammatory cytokines in CAD patients. Pflugers Archiv : European journal of physiology. 2008;455(6):1081-8.
13. Onishi T, Shimada K, Sunayama S, Ohmura H, Sumide T, Masaki Y, et al. Effects of cardiac rehabilitation in patients with metabolic syndrome after coronary artery bypass grafting. Journal of cardiology. 2009;53(3):381-7.
14. Blake GJ, Ridker PM. Novel clinical markers of vascular wall inflammation. Circulation research. 2001;89(9):763-71.
15. Adachi H, Koike A, Obayashi T, Umezawa S, Aonuma K, Inada M, et al. Does appropriate endurance exercise training improve cardiac function in patients with prior myocardial infarction? Eur Heart J. 1996;17(10):1511-21.
16. Hernandez-Reif M, Ironson G, Field T, Hurley J, Katz G, Diego M, et al. Breast cancer patients have improved immune and neuroendocrine functions following massage therapy. Journal of psychosomatic research. 2004;57(1):45-52.
17. Choo J, Burke LE, Pyo Hong K. Improved quality of life with cardiac rehabilitation for post-myocardial infarction patients in Korea. European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology. 2007;6(3):166-71.
18. Lavie CJ, Milani RV. Cardiac rehabilitation and exercise training in secondary coronary heart disease prevention. Progress in cardiovascular diseases. 2011;53(6):397-403.
19. Milani RV, Lavie CJ, Mehra MR. Reduction in C-reactive protein through cardiac rehabilitation and exercise training. Journal of the American College of Cardiology. 2004;43(6):1056-61.
20. Pluss CE, Karlsson MR, Wallen N, Billing E, Held C. Effects of an expanded cardiac rehabilitation programme in patients treated for an acute myocardial infarction or a coronary artery by-pass graft operation. Clinical rehabilitation. 2008;22(4):306-18.
21. Blake GJ, Ridker PM. Inflammatory bio-markers and cardiovascular risk prediction. J Intern Med. 2002;252(4):283-94.
22. Duncan GE, Perri MG, Theriaque DW, Hutson AD, Eckel RH, Stacpoole PW. Exercise training, without weight loss, increases insulin sensitivity and postheparin plasma lipase activity in previously sedentary adults. Diabetes care. 2003;26(3):557-62.
23. Moyer CA, Rounds J, Hannum JW. A meta-analysis of massage therapy research. Psychological bulletin. 2004;130(1):3-18.
24. Aourell M, Skoog M, Carleson J. Effects of Swedish massage on blood pressure. Complementary therapies in clinical practice. 2005;11(4):242-6.
25. Billhult A, Lindholm C, Gunnarsson R, Stener-Victorin E. The effect of massage on immune function and stress in women with breast cancer--a randomized controlled trial. Autonomic neuroscience : basic & clinical. 2009;150(1-2):111-5.
26. Lindgren L, Rundgren S, Winso O, Lehtipalo S, Wiklund U, Karlsson M, et al. Physiological responses to touch massage in healthy volunteers. Autonomic neuroscience : basic & clinical. 2010;158(1-2):105-10.
27. Moyer CA, Seefeldt L, Mann ES, Jackley LM. Does massage therapy reduce cortisol? A comprehensive quantitative review. J Bodyw Mov Ther. 2011;15(1):3-14.
28. Billhult A, Lindholm C, Gunnarsson R, Stener-Victorin E. The effect of massage on cellular immunity, endocrine and psychological factors in women with breast cancer -- a randomized controlled clinical trial. Autonomic neuroscience : basic & clinical. 2008;140(1-2):88-95.
29. Fu TC, Wang CH, Lin PS, Hsu CC, Cherng WJ, Huang SC, et al. Aerobic interval training improves oxygen uptake efficiency by enhancing cerebral and muscular hemodynamics in patients with heart failure. International journal of cardiology. 2013;167(1):41-50.
30. Khost N, Moshtagh Z, Imani E, Alavi- Majd H. Effect of Foot Massage on Physiologic Indicators in Critically Ill Patients Admitted in the I.C.U. The Journal of Shahid Sadoughi University of Medical Sciences. 2006;14(3):69-75.
31. Rahmani Anaraki H, Abdollahi AA, Nasiri H, Vakili MA. Immediate effects of a five minutes back massage on patients' physiological parameters in critical care unit. Journal of Gorgan University of Medical Sciences. 2001;3(2):53-8.
32. Cox C, Hayes J. Physiologic andpsychodynamic responses to the administration of therapeutic touch in critical care. Intensive and Critical Care Nursing. 1999;15(6):363-8.