Original Article

Effects of Aerobic Training on Inflammation marker and CVD in women

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Published online: September 30, 2013

(Accepted for publication September 20, 2013)

DOI:10.7752/jpes.2013.03072;

Abstract:

The purpose of this study was to investigate the effects of 14 weeks of Aerobic training on C-reactive protein (CRP) in postmenopausal women. And if the intensity of 60-75% of the average maximum heart rate is expected recommendation intensity that will leads to lower CRP values. Twenty sedentary females (aged 49.2±2.3 55.2 ±2years ;) volunteered to participate in this study. Subjects were randomly assigned to a training group (n= 10) or control group (n=10). Exercising Subjects will participate in aerobic exercise training. Aerobic training consisted of 60 mints walking and jogging, 3 days a week for 14 weeks at progressive 60-75 % o heart rate reserve. After 14 weeks, the aerobic training group had a significant decrease (p 0.05) in CRP, Body weight, Fat%, and BMI. All reduced compared to the control group. The results showed that: Mean CRP level was significantly reduced after exercise training completed from (1.9mg/l to 1.7mg/l). Fitness level of participates was inversely correlated with CRP level (P< 0.001) maximal oxygen conception (VO₂ max) significantly increased from mean of 20.23 ml/kg/min to 24.52 ml/kg/min. Body weight, Fat%, and BMI were all reduced after training, from mean 92.34.6kg, 38.76 and 35.43 to 87.90 kg, 33.86 and 33.72 respectively.

Conclusions: These finding indicate that increasing maximal oxygen capacity is inversely related to decrease CRP level in postmenopausal women.

Key words: Aerobic exercise, C - reactive protein, cardiovascular disease

Introduction

There is increasing evidence that the development of the atherosclerotic plaque is associated with inflammatory process (Pasceri, 2000, Torzewski, 2000). And that the measurement of this inflammation has predictive value in determining risk for future thrombotic events. A recent meta- analysis revealed that there were statistical significant association between CRP and coronary dieses (Danesh, 2004). Ridker et al. (1997) found that aspirin use decreased risk of myocardial infarction and ischemic stork in apparently healthy men, primarily in those with the highest levels o CRP. This suggests that even a moderate's reduction in inflammation may be protective. There is evidence that physical activity may modify the inflammatory process. Cross-sectional studies of physical activity and physical fitness have shown inverse association with level of CRP (Wannamethee, 2002, Lowe, 2002, Metin, 2006). Intervention studies have demonstrated reduction in CRP (Geffken, 2001, You, 2004) When exercise group are compared with control . Higher level of CRP have also been associated with obesity (Wilmore, 1999 Redker, 2003) The association between excess adipose tissue and elevated CRP concentration, (Cook 2000 & Aronson,2004) has been observed to hold for children, Visser2001,Sites2002, elderly people (Colbert, 2004), And people with metabolic syndrome(Aroson, 2004, Colbert,2004). In fact, obesity may account for a large portion of variation in circulating CRP concentration.

Physical activity is associated with lesser degree of central obesity (Vissor, 1999, Geffken, 2001) and insulin resistance (You, 2004). Taking this finding s together, one could speculate that physical activity may be associated with lower levels of inflammation through its inverse association with central obesity and increasing insulin resistance.

Three levels of C-reactive protein have been proposed in the recommendations by the Center for Disease Control (CDC) and the American Heart Association (AHA): low,< 1mg/l; average, 1.0-3.0 mg/l; and high, >3.0 mg/l. Individuals with elevated levels of CRP have a risk about 2 to 3 times higher than the risk of those with low levels. (Ridker, 1997, King, 2003).

Regular exercise may affect CRP levels. Though there are a number of studies focusing on related topics, there are no published reports on the effect of exercise training and physical fitness combined with specific intensity that my lower CRP levels in postmenopausal women

The aim of this study was to examine CRP concentration in disease-free postmenopausal women and to identify any relationships that might exist with physical activity, aerobic fitness, and if the intensity of 60-75% of

the average maximum heart rate (as recommended by the European guideline on CVD prevention) is expected recommendation intensity that will leads to lower CRP values.

Method

Subjects

In the fall of 2013, Subjects were recruited from the general population of deferent's fitness centers in Amman. Criteria for participation in the studies included the following: CRP level ≥ 1.7 mg/L, nonsmokers, no known heart disease, no lipid modifying medications and aerobically inactive, not having chronic disease or taking medication that prevented their participation in structured exercise training, and any other condition that may interfere with interpretation of the study results. Individuals who participated in the study were volunteers and were not given any kind of remuneration. The subjects were informed about testing procedures, possible risks and discomfort that might ensue, a written informed consent was obtained

20 female subjects (49 ± 5 yrs) met the criteria who had serum CRP level that placed them on the risk of future heart attack (risk ratio ≥ 1.7 mg/L) (Ridker, 1997 & Metin, 2006). Those subjects table (1) were randomly assigned into two groups, group 1 (the exercise group) assigned to supervised exercise program. Group 2 were control untrained group. The control subjects were similar in age, BMI to the exercise group.

Table 1 Mean Physical Characteristics of study subjects

<i>Subjects Characteristics</i>	<i>Exercise group</i>	<i>Control Group</i>
Age (yrs)	49.2	49.7
Weight (kg)	92.34	95.1
Height (m)	1.61	1.626
BMI (kg/m ²)	35.43	35.59
BF (%)	38.76	39.0
Resting heart rate(bpm)	81.00	81.8
VO ₂ max(ml.kg.min)	20.23	21.35

Biochemical Analysis

During one-day prior tests, subjects refrained from training and maintained their normal diet. Laboratory tests were carried out on the same day at the University Of Jordan Hospital in similar conditions for both groups. Room temperature was 23° C and relative humidity was 50%. Pre and post training venous blood sampling were collected in the morning following an overnight fast. These samples were stored in refrigerated (4-8 C). The same medical staff collecting blood samples for both groups and in pre and post training. The primary outcome measure was plasma CRP concentration secondary outcome was, BMI, fat% and Vo₂max. Blood profiles were compared at baseline and after the training program have been completed for the mentioned variables. All variables were assessed at baseline and after the exercise training program by using the same study protocols and methods.

Fitness measurements

At the start and end of the study, the patients' VO₂max was estimated using Cooper test. Subjects exercised until reaching their 90% of their maximal heart rate. body mass index (BMI) was calculated (weight/height² [kg/m²]), and total body fat composition were determined by Skinfold thickness at sites of suprailiac, subscapular, triceps, and abdomen were measured on the right side of the body using a Holtain caliper (Holtain Ltd, Crymych, UK) and for each subjects the average of two measurements was recorded. Percentage of body fat (%BF) was estimated using the Roberge and Ketegian (2003) equation. Body weight and height were measured with standard techniques.

Protocol

Exercising individuals participated in supervised exercise training program about 60 minute sessions 3 times a week for period of 14 week. These sessions consisted of three parts a warm-up period lasts for 5 minutes, the second parts is a supervised exercise session which lasted about 50 minutes and included walking on treadmill. The last part consisted of 5 minutes cool-down and stretching exercises. The women in the exercise group were prescribed walking, jogging as the main methods of aerobic exercise. The training intensity was increased gradually so that by the fourth week participants were training for 50 min at a heart rate of 75% of their maxim heart rate reserve.

Group 2 subjects (sedentary control group) did not participated in any type of activity. The subjects were instructed not to change their lifestyle during the exercise intervention. Maximal oxygen uptake increased by 18% (from 22.23 to 24.52 ml/kg/min) during 14 weeks of exercise indicating the effectiveness of the training program.

Statistical Analysis

All data were analyzed using SPSS statistical package (copy 10), with the level of significant set at $P \leq 0.05$, pre-post training values were analyzed by means were compared using a student's t-test, a nonparametric Wilcoxon's test for statistically significant. Numerical values are expressed as mean $\pm$ Sd. (Mann Whitney U) test was used to compare the two groups in pre and post measurements. Pearson correlation coefficient was used to exam the association between variables.

Results

All subjects, 20 women completed the 12 weeks study. Data are expressed as means $\pm$ SD. Table 2 presented values of CRP and other selected variables. There was a significant difference in mean CRP concentration between pre and post training, ($p \leq 0.05$). CRP level decreased from, 1.9mg/l to 1.7mg/l, $P < 0.001$ after the completion of the aerobic exercise training. The aerobic exercise training induced reduction in plasma CRP levels by 10.5%.

Table 2 mean and stander deviation for the selected variables.

	Before exercise Training		After exercise Training		% change
Vo2 Max (ml/kg/mnt)	20.23 $\pm$	2.83	24.52. $\pm$	2.06	17.5%
CRP mg/L	1.9mg/l $\pm$		1.7mg/l $\pm$		10.5%
%Body Fat	35.43. $\pm$	3.79	33.86 $\pm$	3.41	4.4%
BMI Kg/m2	35.43 $\pm$	3.70	33.72 $\pm$	3.41	4.8%
Body Weight Kg	92.34 $\pm$	12.75	87.9 $\pm$	12.02	4.8%

VO2max: maximum oxygen conception. CRP: C-reactive protein. BMI: body mass indices.

Weight losses

Weight losses of the two groups, the exercising group and the control group differ significantly. Exercising group lost a mean (SD) weight of 4.4kg ($p < 0.000$) by the end of the study. Table 2 the control group increased their weight by a mean (SD) 1.8kg. A 4.8% reduction in body weight was noticed by the end of the exercise training program.

Change in body fat:

At the end of the 12 weeks of exercise training, the exercising group reduced mean body fat by (4.4) %. There body fat decreases significantly from 35.43 at the beginning of the study ($P < 0.005$) to 33.86. At the compilation of the 12 weeks. $P(0.01)$. The control group increased their body fat but was not significant.

Aerobic capacity:

Participant in this group attended a mean average of 96% of exercise sections, there Vo2 max increased significantly by the end of the study by 17.5%, Vo2 max increased from mean of 20.23 ml/kg/m to mean of 24.54 ml/kg/m. ($P < 0.000$) the control group maintained there VO2 max and did not change significantly at the end of the study.

Analysis by Pearson correlation coefficient between CRP levels and variables are shown in table 3. The CRP levels were positively associated with Vo2 max, BMI, body weight and body fat. According to the analysis those variables were found to be independent factors relating to CRP levels.

Table 3: Pearson correlation coefficient examining the association of CRP with Vo2 Max, % body fat, weight and BMI

	VO2 Max(ml/kg/Mnt)	% Body fat	BMI Kg/m2	Body weight Kg
CRP	0.46*	0.52*	0.48*	0.57*
Training group	0.041	0.018	0.032	0.008

*($P \leq 0.05$)

Discussion

The present study investigated the effects of aerobic exercise training on CRP concentration level on healthy postmenopausal women. This is the first study to investigate the relationship between CRP, aerobic fitness, and the intensity level in healthy postmenopausal women

The results of this study show that CRP concentration is markedly lower in the resting state in aerobic s postmenopausal women compared with controls sedentary healthy postmenopausal women. The finding of the study indicated that aerobic exercise was associated with significantly lower CRP level. Previous studies reported similar results that high activity level was associated with lower level of inflammation markers such as

CRP (Tisi, 1997; Smith, 1999; Esposit, 2003; Plaisance, 2006). Our finding also consistent with those reported by Abramson(2002), Pitsavose(2005). A recent review by Plaisance and Grandjean (2006) found that fitness was consistently associated with 6-35% lower CRP level.

Our finding suggest that increasing aerobic fitness is associated with lower CRP level, Although fitness level was assisted by estimations of VO₂ max , It is possible that the direct measurement of VO₂ max might have resulted in more accurate of aerobic fitness and that this might have led to a different relationship with CRP. Nonetheless, Copper test is accepted as a valid and reliable test of aerobic fitness, we presume that the levels achieved were good estimates of maximum aerobic capacity. It has been shown that adults with higher levels of VO₂ max are at a lower risk for all-cause and cardiovascular disease mortality in both men and women. Blair et al (1996) and Kelly, (2006) found that increasing in VO₂ max has been shown to reduce the risk of all –cause mortality by 17% in men and 16% in women. Furthermore, BMI, body weight and body fat were also associated with CRP; after the exercise training program, body weight, BMI, and body fat were significantly reduced. It has been demonstrated that obesity is related to CRP levels and that adipose issue is likely a factor modulating CRP levels. Colbert (2004) Dvorakova (2006). Similar to our finding a recent study by Koren (2006) found that BMI and fitness were consistently associated with lower CRP level. Faurey ,2005; Kelly, 2013; Rawason, 2003; Tchernof 2006; Nissis ,2005 also confirm the same results.

Studies investigating the impact of aerobic fitness on CRP level have yielded mixed results; however, there is evidence of an inverse association between fitness and CRP values. Hamer, 2007; Cook, 2000; Isasi, 2003; Plaisance, 2006; Church, 2007. Tow recent studies failed to confirm an independent inverse relationship between physical activity and CRP, in a longitudinal study by Koren (2006) a 109 healthy men and women BMI, but not physical activity was significantly related to CRP. Similarly, a cross-sectional study, Marcell (2005) found no relationship between physical activity and CRP. On explanation for the absence of an exercise effect in these studies may be the high proportion of sedentary subjects. Also, physical activity remains an important correlated of CRP in multiple studies, Church, 2007; Plaisance 2006; Albert, 2004; Abrmson, 2002; Moran 2005.

Our subjects exercised in intensity of 75% of maximum heart reserve, However, the recent European guidelines on CVD prevention, healthy persons are recommended to choose enjoyable physical activity which fit into their daily routine, preferable 30-45 min, four to five times weekly at 60=75% of the average maximum heart rate. (deBacker,2003) this recommended intensity was effective in reducing CRP level in our study. Our finding suggested that intensity of 75% of maximum heart reserve was effective in reducing CRP and in preventing CVD. Our finding is in consistent with those reported by Hammett (2004). CRP level respond differently to different physical activity intensity, acute heavy physical exercise activity lead to an inflammatory respond with a mark rise in CRP levels. Suggesting muscular damage proportional to the amount of exercise and muscle engaged. However, longer term exercise training (aerobic) produces an opposite effect. (Perk, 2005).

How exercise training reduces inflammation and suppresses CRP level is not well defined. Physical activity is related to several confounders that are independently associated with lower CRP levels. For example, physical activity is inversely related to age, smoking, hypertension, BMI, and waist to hip ratio, total and non high density lipoprotein cholesterol., whereas these factors are directly related to CRP concentrations . Despite the overlap between factors associated with aerobic activity and CRP, higher CRP levels persist in less active subjects in most studies even after adjustment. In summary, it is likely that exercise training reduces CRP both directly by reducing it is production in fat, muscle, and mononuclear cells and indirectly by increasing insulin sensitivity, improving endothelial function, and reducing body weight.

A large number of studies have identified relationship between increasing level of CRP and CVD, Lippy, 2002; Danesh, 2004; Ridker, 2003; Hamer, 2007. Interventions to reduce CRP could contribute to the prevention of atherosclerosis and the reduction of future cardiovascular events. Although the focus of our study was on the independent effects of aerobic exercise on CRP, it may be the exercise in combination with other lifestyle intervention may yield the greatest benefit. For example, in randomized trial conducted by You et al (2004) 6 months of diet plus exercise training, but not diet alone, resulted in statistically significant reductions in CRP among obese postmenopausal women. In another study, Esposito at al (2003) conducted a randomized control trail and found statically significant reductions in CRP after 2 years of increased physical activity and a Mediterranean-style diet in obese women. Furthermore, Milani et al (2004) found statistical significant reductions in CRP as a result of exercise training and diet in both men and women with coronary heart disease. Given these findings, it may be that the greatest redactions in CRP may be derived from a combination of exercise and other lifestyle modifications such as diet.

Conclusions

In the present study, we investigated the effects of aerobic exercise training on CRP concentration level on healthy postmenopausal women. After the training program, all conventional variables of cardiovascular risk in this study were improved, and CRP levels, which are known to have an increased risk of cardiovascular diseases was also significantly lowered. The change in CRP was associated with the reduction of body weight,

BMI, body fat and VO₂max in an intensity of a 75% of maximum heart reserve. Our finding supports the current recommendation to increase moderate intensity physical activity to reduce the risk of cardiovascular disease.

References

- Abramson, J.L., Vaccarino, V. (2002). Relationship between physical activity and inflammation among apparently healthy middle-aged and older U.S. adults. *Arch Intern Med* (162), 1286-1286.
- Albert, M. A., Lynn, R.J., Ridker, P.M. (2004). Effect of physical activity on serum C-reactive protein *Am J Cardiol*, (13), 561-568.
- American Heart Association and Center for disease and prevention. (2004)
- Aronson, D., Sheik-Ahmad M, Avizohar O., et al. (2004). C-reactive protein is inversely related to physical fitness in middle-aged subjects Atherosclerosis, (176),173-170.
- Balady, J.G., Berra, A.K., Golding, A.L., Gordon, F.N., Mahler, A.D., Myers, N.J., et al. (2000). *ACSM's guides for exercise testing and prescription*. In: William Lippincott, Willkins Lippincott, editors. 6th ed.
- Berliner, J.A., Navan, M., Fogelman, A.M., et al. (1995). Atherosclerosis: basic mechanisms. Oxidation, inflammation, and genetics. *Circulation*, (91), 2488-96.
- British Heart Foundation. Coronary Heart disease Statistics. Available at: www.dphpcox.ac.uk/bhfhprg/stats2003.
- Church, T.S., Barlow, C.E., Earnest, C.P., Kampert, J.B., Priest, E.L., Blair, S.N. A. (2002). Associations between cardiorespiratory fitness and C-reactive protein in men. *Arteriosclerosis Thromb Vasc Biol*, (22), 1869-1876.
- Colbert, L.H., Visser, M., Simonsick, E.M., Tracy, et al. (2004). Physical activity exercise and inflammatory markers in older adults, Finding from the health, Aging and Body Composition Study: *J Am Geriatr Soc*, (52), 1098-1104
- Cook, D.G., Mendall, M.A., Whincup, P.H., et al. (2000). C-reactive protein concentration in children : relationship to adiposity and other cardiovascular risk factors. *Atherosclerosis*, (149), 139-150.
- Danesh, J., Collins, R., Appleby, P., et al. (1998). Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. *JAMA*, (279), 1477-82.
- Danesh, J., Wheeler, J.G., Hirschfeld, G.M. et al. (2004). C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. *N Engl J Med*, (350), 1387-1397.
- De Backer, G., Ambrosioni, E., Borch-Johnsen, K., et al. (2003). European guideline on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention in clinical practice. *Eur Heart J*, (24), 1601-1610.
- Dvorakova-Lorenzova, A., P. Suchanek, P.J. Havel, et al. (2006). The decrease in C-reactive protein concentration after diet and physical activity induced weight reduction is associated with changes in plasma lipids, but not interleukin-6 or adiponectin. *Metabolism*, (55), 305-365.
- Esposito, K., Pontillo, A., Di Palo, C., et al. (2003). Effect of weight loss and lifestyle changes on vascular inflammatory marker in obese women: a randomized trial. *JAMA*, (289), 1799-1804
- Fairey, K., Cournoy, C. (2005). Effect of exercise training on C-reactive protein in postmenopausal breast cancer survivors: a Randomized cohort trial. *Brain behave immu*, (34), p.p. 381-388.
- Foreed, E.S. (2002). Does exercise reduce inflammation? Physical activity and C-reactive protein among U.S. adults *Epidemiology*, 13 (5), 561-568.
- Geffken, D.F., Cushman, M., Burke, G.L., Polak, J.F., Sakkinen, P.A., Tracy, R.P. (2001). Association between physical activity and markers of inflammation in a healthy elderly population. *Am J Epidemiol*, (153), 242-250?
- Hak, A.E., Stehouwer, C.D., Bots, M.L., Polderman, K.H., Schalkwijk, C.G., Westendorp, I.C., Hofman, A., Witteman, J.C. (1999). Association of C-reactive protein with measures of obesity, insulin resistance and subclinical atherosclerosis in healthy, middle-aged women. *Arterioscler Thromb Vasc Biol*, (19), 1988-1991.
- Hamer, M. (2007) The relative influence of fitness and fatness on inflammatory factors. Review. *Prev Med*, (44) 3-11.
- Hammatt, C.J., Oxenham, D., Baldi, C. (2004). Effect of six month exercise training on C-reactive protein level in healthy elderly subjects. *J. Am Coll cardio*, (44), p.p. 2411-23.
- Hammatt, C. J., H. C., Oxenham, J. C., Baldi, et al. (2004). Effect of six months' exercise training on C-reactive protein level in healthy elderly subjects. *J. Am Coll. Cardiol*, (44), 2411-2413.
- Isasi, C.R., Deckelbaum, R.J., Tracy, R.P., Starc, T.J., Berglund, L., Shea, S. (2003). Physical fitness and C-reactive protein level in children and young adults the Columbia University BioMarkers Study. *Pediatrics*, (111), 332-338.
- Kelley, G.A., Blair, K.S., Kelley, J. (2006). Effects of aerobic exercise on C-reactive protein, body composition, and maximum oxygen consumption in adults : a meta-analysis of randomized controlled trials. *Metabolism*, (55), 1500-1507.

- King, DE., Carek, P., Mainous III, AG., Pearson, WS. (2003) Inflammatory markers and exercise differences related to exercise type. *Med Sci Sports Exerc*(35) 575-581.
- Koren, Ms., Purnell, JQ ., Breen PA. et al. (2006)Plasma C-reactive protein concentration is not effected by isocaloric dietary fat reduction . *Nutrition* (2006) (22) 444-448.
- Lipp, P., Ridker, P., Maseri, A. (2002). Inflammation and atherosclerosis. *Circulation* (105) 1135-1143.
- Lowe, GD., Rumley, A., Whincup, PH; et al. (2002). Hemostatic and rheological variables and risk of cardiovascular disease. *Semin Vasc Med* (2) 429–39
- Marcell, T. J., K.A., McAuley, T., Traustadottir, and P.D. (2005). Reaven. Exercise training is not associated with improved levels of c-reactive protein or adiponectin. *Metabolism* (54) 533-541.
- Mattuch, F., Dufaux, B., Heine, O., Mertens I, Rost, R (2000). Reduction of the plasma concentration of C-reactive protein following nine months of endurance training. *Int J Sports Med* (21) 21-24.
- Metin, Ergun , Istemihan Tengiz , Ugur Turk, Seckin Senisik, Emin (2006). Alioglu Oguz Yksel Ertugrul Ercan , Cetin Islegen. *Jour Spo Scie Medic* (5) 266-275.
- Milani, RV., Lavie, CJ.,Mehra (2004). Reduction in C-reactive protein through cardiac rehabilitation and exercise training. *J AM Coll Cardiol*, (43), 1056-1061.
- Moran, A., Pankow, JS., Steffen, LM., et al. (2000). Relation of C-reactive protein to insulin resistance and cardiovascular risk factors in youth . *Diab Care* (28) 1240-3.
- Nassis, G. P., Papantakous, K., Skenderi, et al. (2005). Aerobic exercise training improves insulin sensitivity without changes in body weight , body fat, adiponectin, and inflammatory markers in overweight and obese girls. *Metabolism* (54) 1472-1479.
- Pasceri, V., Willerson, JT., Yeh, ET. (2000). Direct proinflammatory effect of C-reactive protein on human endothelial cells. *Circulation* (102), 2165-2168.
- Perk Joep . Exercise training only if needed. *Euro Heart J.* (2005). (26), 1939-1941.
- Pitsavos, C., Chrysohoou, C., Panagiotakos, DB., et al. (2003). Association of leisure-time physical activity on inflammation markers (C-reactive protein, white cell blood count, serum amyloid A, and fibrinogen) in healthy subjects (from the ATTICA study) *Am J Cardiol*, (91), 368-370.
- Plaisance, EP., Grandjean, PW. (2006). Physical activity and high-sensitive C-reactive protein . *Sport Med*, (36), 443-458.
- Rawason, ES., Freedson, PS., Osganninan, SK., Matthews, CE., Reed, G; Ockene IS. (2003). Body mass index, but not physical activity, is associated with C-reactive protein .*Med Sci Sports Exercise* (35), 1160-1166.
- Reuben, DB., L. Judd-Hamilton, T.B., Harris, and T.E. Seeman. (2003). The association between physical activity and inflammatory markers in high-functioning older persons: MaxArthur studies of successful aging. *J. Am.Geriatr. Soc* (51), 1125-1130
- Ridker, PM., Buring, JE., Cook, NR., et al. (2003). C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-years follow-up of 14719 initially healthy American women. *Circulation* (107), 391-397.
- Ridker, P., Cushman, M., Stampfer, M., et al. (1997). Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. *N Engl Med* , 336, 973-9.
- Smith, K.J., Rhesa, Dykes, E., John Guha Krishnaswamy. (1999). Long-tearm exrcise and Atherogenic activity of blood mononuclear cell in persone at risk of developing ischemic heart disease. *JAMA* (28), 1722-1727.
- Tchernof, A., A. Nolan, C.K., Sites, P.A., Ades, and E.T; Poehlman. (2006). Weight loss reduces C-reactive protein levels in obese postmenopausal women. *Circulation*, (105), 564-569.
- Tisi, PV., Hulse, M., Chulakadabba, A., Gosling, P., Shearman, CP. (1997). Exercise training for intermittent claudication: dose it adversary affect biochemical markers of the exercise –induce inflammatory response? *Eur J Vasc Endovasc Surg* , (14), 344-350.
- Torzewski, M., Rist, C., Mortensen ,RF., Zwaka, TP., Bienek, M., Waltenberger, J., Koenig, W, Schmitz (2000). C-reactive- protein in the arterial intima: role of C-reactive protein receptor-dependent monocyte recruitment in atherogenesis. *Arterioscler thromb Vasc Biol*, (20), 2094-2099.
- Visser , M., Bouter, LM., McQuillan, GM., Wener, MH., Harris TB. (1999). Elevated C-reactive protein level in overweight and obese adults. *JAMA*, (282), 2131-2135.
- Wannamethee, SG., Lowe, GD., Whincup, PH., Rumley A, Walker M, Lennon L. (2002). Physical activity and hemostatic and inflammatory variables in elderly men *Circulation*, (105), 1785-1790.
- Wannamethee, SG., Shaper, AG., Walker M. (1998). Changes in physical activity, mortality and incidence of coronary heart disease in older men. *Lance*,. (351), 1603–1608
- Wilmore, J.H., J.P., Despres, P R., Stanforth, et.al. (1999). Alteration in body weight and compositin consequent to 20 wk of endurance training : The HERITAGE family study. *AM. J. Clin. Nutr*, (70), 346-352.
- You , T., Berman, DM., Ryan, AS., Nicklas, BJ. (2004). Effects of hypocaloric diet and exercise training on inflammation and adipocyte lipolysis in obese postmenopausal women. *J Clin Endocrinol M* , (89), 1739-1746.