Pharmacophore

ISSN-2229-5402

Journal home page: http://www.pharmacophorejournal.com

Pharmacophore
an International Journal
ISSN 2229-5402

SYSTEMIC AND VASCULAR INFLAMMATORY RESPONSE TO ACUTE AEROBIC EXERCISE IN PATIENTS WITH CORONARY ARTERY DISEASE AFTER REVASCULARIZATION INTERVENTION

Fatemeh Basati[1], Marefat Siahkoohian[2*], Allahyar Golabchi[3], Mahdi Moshtaghi[4], Fariba Raigan[5]

1. *PhD student, Department of Exercise Physiology, Department Physical Education and Exercise Sciences, Faculty of Education Sciences &Psychology, MohagheghArdebili University,Ardebil, I.R. Iran.*
2. *Professor, Department of Exercise Physiology, Department Physical Education and Exercise Sciences, Faculty of Education Sciences &Psychology, MohagheghArdebiliUniversity,Ardebil, I.R. Iran.*
3. *M.D.Cardiologist, Interventional Electrophysiology, Assistant Professor, Shaheed Beheshti Hospital, Kashan University of Medical Sciences, Kashan, I.R. Iran.*
4. *Student Research Committee, Shaheed Beheshti Hospital, Kashan University of Medical Sciences, Kashan, I.R. Iran.*
5. *M.D. Cardiologist, Assistant Professor, Shaheed Beheshti Hospital, Kashan University of Medical Sciences, Kashan, I.R. Iran.*

ARTICLE INFO

Received:
03thJun 2017
Accepted:
29th Nov2017
Available online:
14thDec2017

Keywords:*Acute aerobic exercise, adhesion molecules, pentraxin, coronary artery disease.*

ABSTRACT

Background: cardiovascular revascularization interventions are frequently performed operations in patients with coronary artery disease (CAD) that induced inflammatory reactions, but systemic and vascular inflammatory response to acute exercise in these patients is controversial. The aim of this study is to investigate effects of one session aerobic exercise on systemic and vascular inflammatory biomarkers in CAD patients after revascularization interventions.

Methods: 65 male with CAD after coronary artery bypass grafting(CABG) and percutaneous coronary intervention (PCI) participated in our study and dedicate in intervention group (IG; n=35, age: 58.31±7.21 years) and control group (CG; n= 30, age: 57.9±7.4 years). Patients in IG performed one session acute aerobic exercise. Plasma levels of pentraxin3 (PTX3), VCAM-1 and C-reactive protein (CRP) measured at baseline and 30 minutes after acute aerobic exercise session include 30 minutes treadmill walking or running at 70% of HRmax in IG and at the same time for CG.

Results: plasma levels of VCAM-1(558±207 vs. 633±138, p=0.049) and CRP (3.32±1.87 vs. 3.88±2.27, p=0.037) increased significantly in IG after acute aerobic exercise session but these changes were not statistically significant in comparison to CG. Plasma levels of VCAM-1 was significantly higher in IG than CG (592.7±151 vs. 534.8±88, p=0.042). There is no significant difference between plasma PTX3 levels before and after acute aerobic exercise in IG and in Compared to CG (p>0.05). Univariate analysis of variance indicate no significant differences in plasma levels of PTX3, VCAM-1 and CRP between PCI and CABG patients in response to acute aerobic exercise.

Conclusion: plasma concentration of VCAM-1 increased in response to acute exercise in CAD patients after revascularization intervention but plasma levels of pentraxin superfamily biomarkers did not change significantly.

ToCite ThisArticle: FatemehBasati, MarefatSiahkoohian, AllahyarGolabchi, Mahdi Moshtaghi, FaribalRaigan, (2017), "Systemic and vascular inflammatory response to acute aerobic exercise in patients with coronary artery disease after revascularization intervention", ***Pharmacophore, 8(6S),****e-1173675.*

Introduction

Coronary artery disease (CAD) is a major cause of morbidity and mortality in the world[1] . Ministry of health and medical education reports that more than one third of Iranian dies of cardiovascular disease, in which CAD accounts for more than 50% of this death[2].

Corresponding Author: MarefatSiahkoohian, Professor, Department of Exercise Physiology, Department Physical Education and Exercise Sciences, Faculty of Education Sciences &Psychology, MohagheghArdebiliUniversi-ty,Ardebil, I.R. Iran, Email:marefat_siahkuhian@yahoo.com

Traditionally atherosclerosis has been considered as a lipid storage disease; nowadays it is also known that atherosclerosis is a dynamic and progressive disease arising from the combination of endothelial dysfunction and inflammation[3]. In facts inflammation is the most important mechanism behind the pathogenesis of atherosclerosis and following cardiac events[4]. Due to the important role of inflammation in the pathology of atherosclerosis, inflammatory biomarkers can be used to identify and predict the risk of cardiovascular disease caused by atherosclerosis[4]. Newly discovered long pentraxin 3 (PTX3), a member of pentraxin super family which include the short pentraxin C-reactive proteins (CRP), identified as an acute-phase reactant and produced by various cells mainly vascular endothelial cell, smooth muscle cells, mononuclear macrophages, fibroblasts and neutrophils specially in cardiovascular tissue in response to stimulants like Lipopolysaccharides, interlukin-1, interleukin-10 and Tumor necrosis factor-α[5, 6]. The type of cells that are capable to producing PTX3 shows that this protein acts as a local (local) protein, whereas CRP is mainly produced in the liver known as systemic protein[7]. CRP is an acute phase protein, produced in the liver and adipose tissue in response to interleukin-6 (IL-6) produced by macrophages, T cells and activates the endothelium and induces vascular adhesion molecules such as VCAM-1 that is vascular inflammatory markers that detected in endothelial cells and atherosclerotic plaques and contribute in development of atherosclerosis[8].

In most studies, CRP has been emphasized as the main factor in predicting cardiovascular disease, but recent studies reported that PTX3 has an important role in the development of atherosclerosis. In addition PTX 3 reaches to high levels after ischemic heart diseases, acute coronary syndrome[9], congestive heart failure[10], heart valvular disease[11]. Studies showed that PTX3 is more important predictor of future cardiovascular events[12]. And it's also a candidate anti-inflammatory mediator in cardiac surgery and revascularization intervention, and recently suggested that PTX3 is more tightly associated with the complexity and severity of CAD than CRP [13, 14].

Research suggests the lifestyle modification and daily physical exercise has anti-inflammatory effects and protected people against cardiovascular and systemic inflammatory disease such as atherosclerosis and decrease inflammatory biomarkers such as CRP, interlukin6, fibrinogen and adhesion molecules in patients with CAD[15], diabetic[16], metabolic syndrome[17] and obesity[18], finding about effects of aerobic exercise on PTX3 levels are limited . Fukada et al(2012) showed that 6 month aerobic exercise can improved plasma levels of PTX3 in patients with cardiovascular disease however plasma concentration of CRP didn't change significantly[14]. In contrast to the anti-inflammatory effects of a long-term exercise programs, acute activities can produce stress hormones and alter the amount and function of immune cells including leukocytes. Such an exercise-induced acute phase response consists of typical changes including leukocytosis and release of cytokines such as IL-6 and IL-1 and acute phase proteins, similar to acute phase responses evoked by other stressors such as trauma and sepsis, so acute exercise can be a good model for inflammatory responses [19-21].

Acute physical challenge includes aerobic or resistance training results in increase inflammation markers like CRP, interlukin-6 and ICAM-1 in healthy subjects as well as in CAD patients [19, 21-28], but we have not observed on response of PTX-3 to acute aerobic exercise in CAD patients after revascularization intervention. It was hypothesized that CRP biomarker of systemic and VCAM-1 and PTX3 markers of vascular inflammation. Therefore, the purpose of our study was to examine the effects of acute aerobic exercise on local and systemic inflammatory markers in CAD patients after revascularization.

Methods

Subjects

This was a randomized, controlled trial to examine effects of one session aerobic exercise on plasma levels of systemic and vascular inflammatory biomarkers in CAD patients after revascularization interventions. 65 male patients with CAD treated with PCI and CABG participated in the present study. After undergoing baseline test, patients allocate to the intervention group (IG; 35 patients, PCI/CABG: 16/19, aging: 58.31±7.21 years) and control group (CG; 30 patients, PCI/CABG: 12/18, aging: 57.9±7.4 years).

Study design

Our patient treated with PCI and CABG.Patients had history of coronary artery disease and had undergone PCI and CABG at ShahidBeheshti Hospital of Kashan University of medical sciences between 2016-17. All patients with PCI enrolled in study between 2-4 weeks after intervention and in CABG patient's duration between surgery and study was 6-8 weeks. Patients were excluded if they have congestive heart failure, immnomodulatory or anti-inflammatory medications other than Aspirin, or known history of immune related disorders, unstable angina, resting systolic blood pressure >200 mmhg or diastolic blood pressure>10mmhg, uncontrolled bradycardia or tachycardia. The experimental protocol was reviewed and approved by ethical committee of Kashan University of medical sciences (Ir .kaums.rec.1395.48) and a written informed consent was obtained from every patient. This study registered in Iranian Registry of Clinical Trials with ID number: IRCT201610085136N3.

At the time of admission, a checklist was completed for patients according to their medical history and physical examination by trained exercise physiologist and nurses. On the first visit patients were familiar with the all instruments in cardiac rehabilitation center (ShahidBeheshti Hospital, Kashan, Iran), and performed symptom limited exercise testwas completed on a motor driven treadmill using the modified Bruce protocol [29], to assess the maximal heart rate (HRmax), also seated blood pressure and anthropometric parameters measured under the supervision of an exercise physiologist, a nurse, and a cardiolo-

gist. After 48 hours subjects performed one supervised aerobic exercise session consists of 30 min of treadmill walking or running at 70% of subject HRmax. Before and 30 minutes after completion of acute aerobic exercise, Seated blood pressure was measured and blood samples obtained for assessment of local and systemic inflammatory biomarkers.

Laboratory analyses

All patients who were included in the study rested for 15 min in the sitting position and then blood pressure was taken using a standardized mercury sphygmomanometer. A trained nurse also took two blood samples from all enrolled patients, before and 30 min after the end of exercise, blood samples were obtained from the antecubital vein. The blood was collected in chilled tube containing EDTA and then centrifuged at 2000×g for 15 min at 4 ºC .The plasma was stored at -20 ºC refrigerator until analyses were performed . All procedures were done in aseptic condition. Plasma PTX3 concentration were determined by commercial enzyme-linked immunosorbent assay kit (Human Pentraxin 3 Elisa Kit 96t - Zellbio Germany) according to the standard recommendation in 96-well high protein binding capacity micro plate. CRP was measured through immunoturbidimetry, by Pars Azmon kits. HDL, LDL, total cholesterol and triglycerides were also obtained from the laboratory analysis.

Statistical analysis

The gathered data were analyzed using SPSS software version 21 for windows. All data expressed as mean ± standard deviation (SD). Assumptions of normality distribution were verified for all data by using Shapiro-Wilk test. If the distribution was non-normal we used the log transformation to make data conform to normality.Paired Student t-test was used to compare significant differences of VCAM-1, PTX3 and CRP differences after one session aerobic exercise in experimental group. Differences between the two groups were assessed using analysis of covariance (ANCOVA). The criterion for statistical significance was $P \leq 0.05$.

Results

Baseline characteristics of the subjects are listed in table 1. There were significant differences between resting heart rate and systolic blood pressure. Plasma concentrations of pentraxin 3, VCAM-1 and CRP before and after acute aerobic exercise show in Figure 1 for IG. Plasma VCAM-1 and CRP levels increased significantly after acute aerobic exercise. Table 2 compares Plasma levels of PTX3, VCAM-1and CRP levels in IG and CG before and after acute aerobic exercise. Plasma concentration of Vcam-1 was higher in IG than CG there is no significant differences between plasma levels of CRP and PTX3 in IG and CG. Differences between PCI and CABG patients in response to acute exercise show in table 3. There is no significant differences between PCI and CABG patients' inflammatory biomarkers response to acute aerobic exercise.

Table 1. Baseline characteristics of participants in intervention and control groups

Characteristics	Intervention group (n=35	Control group (n=30)	P-value
Age (yr)	57.31±7.21	57.9±7.4	NS
Weight (kg)	76/2±11.42	76.4±14.88	NS
Body Mass Index(kg/m^2)	25.93±3.51	26.2±4.6	NS
Resting heart rate(bpm)	82.6±10.36	79.13±7.95	0.02
Systolic blood pressure at rest (mmHg)	118.4±12.24	128±14.4	0.005
Diastolic blood pressure at rest (mmHg)	87.65±14.7	77.2±7.8	NS
Coronary artery bypass graft*	19	18	NS
Percutaneous coronary intervention*	16	12	NS
Risk factors			
Hypertension*	13	11	NS
Smoking*	12	13	NS
Diabetes*	14	15	NS
Positive family history*	12	11	NS
Medications			
Beta blockers*	27	25	NS
Angiotensin converting enzyme inhibitors*	25	22	NS
Statins*	32	28	NS
Anticoagulants*	32	27	NS

* Values are expressed as mean ± SD or numbers

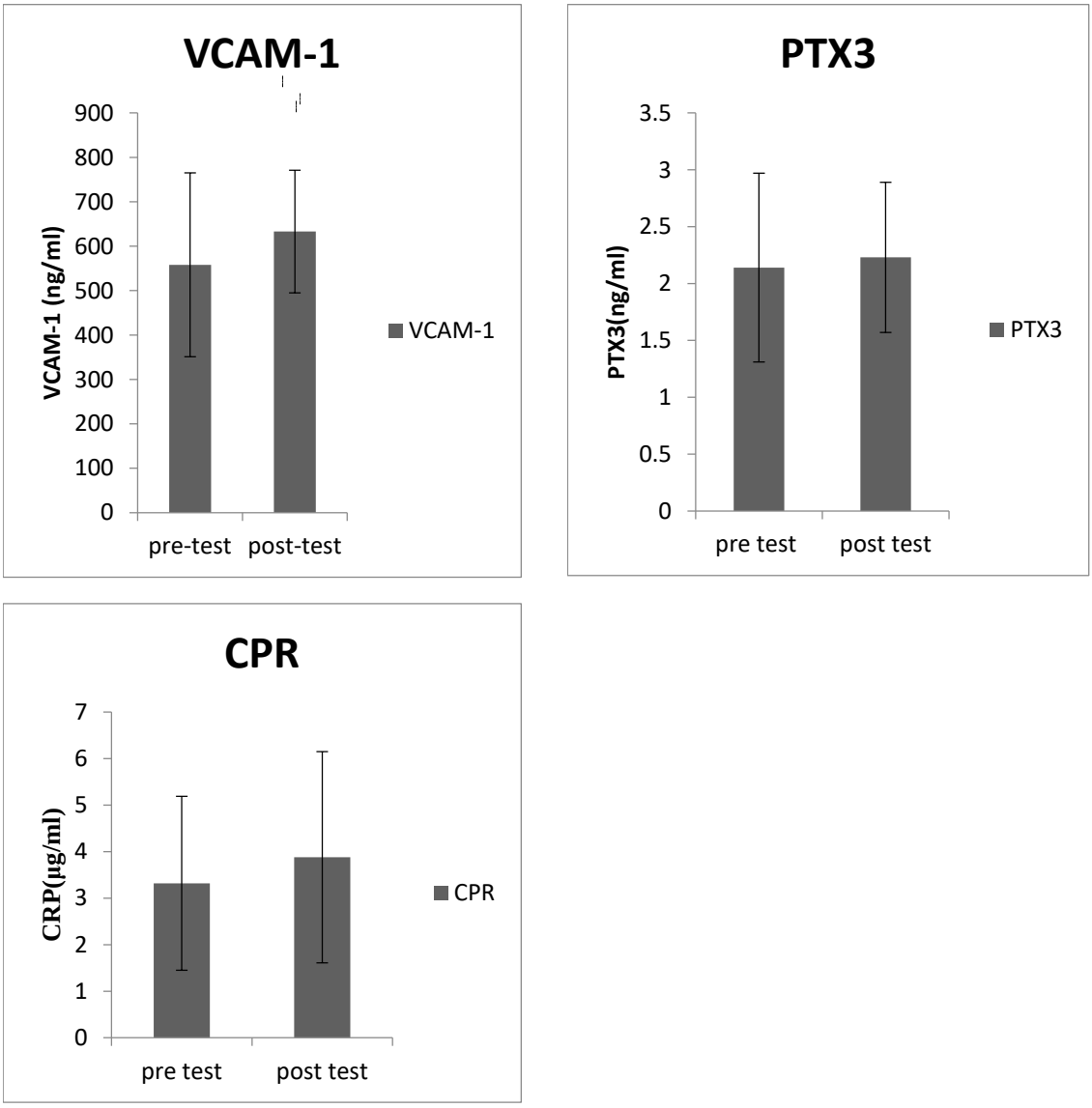

Figure 1. Plasma PTX3, VCAM-1and CRP levels before and after acute aerobic exercise in intervention group

Table 2. Plasma levels of PTX3, VCAM-1and CRP levels in IG and CG before and after acute aerobic exercise

variable	Intervention group		t	p-value	Control group		f	p-value
	Pre-test Mean ±SD	Post-test Mean ±SD			Pre-test Mean ±SD	Post-test Mean±SD		
Vcam-1(ng/ml)	558±207	592.7±151	-2.051	0.049*	572±138	534.8±88	4.13	0.042*
PTX-3(ng/ml)	2.14±0.83	2.2±0.66	-0.52	0.6	2.84±1.9	2.67±0.77	3.63	0.062
CRP(mg/l)	3.32±1.87	3.88±2.27	-2.17	0.037*	3.93±1.7	3.89±1.81	1.22	0.27

VCAM-1, vascular adhesion molecules-1; PTX3, pentraxin 3; CRP, C - reactive protein; *P < 0.05

Table 3. differences between plasma levels of PTX3, VCAM-1and CRP in PCI and CABG patients

variable	CABG	PCI	F	**p-value**	**Partial η^2**
VCAM-1(ng/ml)	640±110	626±166	0.414	0.52	0.14
PTX3(ng/ml)	2.14±0.53	2.34±0.8	0.69	0.413	0.23
CRP(mg/l)	3.72±2.42	4.06±2.17	0.8	0.37	0.25

VCAM-1, vascular adhesion molecules-1; PTX3, pentraxin 3; CRP, c-reactive protein

Discussion

The aim of this study was to investigate the effects of acute aerobic exercise on plasma levels of VCAM-1, PTX3 and CRP in CAD patients after revascularization intervention. After 30 minutes of acute aerobic exercise Plasma levels of VCAM-1 was significantly higher in IG than CG. CRP concentration increased significantly in IG after acute aerobic exercise, but this change was not statistically significant in comparison to CG. Plasma PTX3 concentration enhanced but this enhancement was not statistically significant. Plasma levels of VCAM-1, CRP and PTX3 in PCI patients were higher than CABG patient, but differences were not statistically significant.

In this study Plasma PTX3 did not change significantly in coronary artery patients after acute aerobic exercise in 70% of maximal heart rate intensity. Slusher et al demonstrated that plasma levels of PTX3 was elevated after single boat of continues aerobic exercise[30]. Similar results reported in healthy subjects[26], high cardiorespiratory fitness male[31], obese individuals after acute aerobic exercise[30]. Acute aerobic exercise increases lumen blood flow, and consequently induces pulsatile shear stress in arterial endothelial cell. Lumen shear stress in human aortic endothelial cell elevates nuclear factor κB and activator protein-1 activations, and this transcriptional factor activation leads to the expression of PTX3 gene. Thus, chronic repetition of endothelial cell stimulation mediated by exercise induced shear stress may be necessary to achieve basal high plasma PTX3 level via aerobic exercise training [32-34]. On the other side reduction in PTX3 plasma level reported in obese individuals after acute aerobic exercise in 70% vo2peak intensity [26]. Similar results were not reported in cardiovascular patients. In the all mentioned studies, the increase in plasma level was very small and after acute exercise PTX3 plasma concentration was in the normal range. In healthy subjects and normal vascular conditions PTX3 has anti-inflammatory and protective role in cardiovascular inflammation. , but in chronic diseases, PTX3 identified as pro inflammatory biomarker [35]. The differences between individual (healthy or patients with cardiovascular disease) may affect the 24 response of plasma PTX3 concentrations during exercise training.

In this study plasma levels of CRP increased significantly after acute aerobic exercise in IG, but in comparison to CG this change was not statistically significant. Last studies report that different type of regular exercise such as interval training [25, 36], resistance training [37] and aerobic exercise reduced general inflammatory biomarkers in patients with cardiovascular diseases [14]. previous studies reported that acute exercise in healthy subjects such as marathon runners[38], in untrained healthy subjects after one hour running[39] and in healthy man after exercise training in 70% VO2max intensity[40], plasma levels of CRP increased rapidly, kope et al report similar findings in CAD patients[24], Different results reports in CAD patients after resistant training at low to moderate intensity that CRP decline after one session acute resistance training [18]. The inconsistency between our results and the findings of the studies above may have been caused by differences in characteristics of study subjects, different subjects in control groups. Cytokines are produced by a wide variety of cell types, including skeletal muscle, when exposed to various inflammatory stimuli such as acute high-intensity exercise. CRP is mainly produced in the liver in response to cytokines such as IL-6, also the rapid increase in serum CRP in IG may be caused by release of the preformed protein from the liver. also be due to the response of catecholamine hormones due to exercise activity[41, 42].

One of the important findings of current study is that acute aerobic exercise increased VCAM-1 in IG. The result of our study was similar to other previous studies, Kope et al reported that physical challenge on ergometer increased VCAM-1 in CAD patients and healthy subjects as control group, however VCAM-1 changes was greater in CAD patients[24]. Also acute endurance exercise at moderate intensity [43], and long distance running exercise in trained men and women increased ICAM-1 and VCAM-1[44], similar results was founded in healthy adolescent boys following wrestling exercise[45], but different results reported after resistant training. Thus in various subjects, type, volume and intensity of exercise may affect acute response of adhesion molecules like VCAM-1. One of the possible explanation for an increase in VCAM-1 following exercise may be due to shear force, a direct impact of increased exercise-induced stress on endothelial cell structure. VCAM-1 is mainly expressed in endothelial cells and smooth muscle cells, thus is believed to be a more sensitive marker in response exercise-induced stress[46].

Our results showed that plasma levels of systemic and vascular biomarkers in PCI patients were higher than CABG patients, but this difference was not considerable. Pervious findings showed that in PCI patients rapid changes in PTX3 accrued across the stented vascular bed and in response to stented injury [47].

Revascularization treatments are invasive and cause inflammatory responses. In our study CABG patients after 8 weeks and PCI patients after 4 weeks enrolled in intervention, therefore, it's possible that higher inflammatory biomarkers in PCI patients was due to shorter rest time after surgery.

In addition, in stented vessels in response to injury, leucocytes that are the main source of local PTX3 secretion, aggregate in lesion site, so stenting in coronary artery are associated with PTX3 increasing. Also PCI causes endothelial damage and it followed by inflammatory response and enhancement markers such as CRP and VCAM-1, which all these biomarkers are associated with restenosis after PCI[22].

Conclusion

Our study showed that after acute aerobic exercise plasma levels of CRP and VCAM-1 increased significantly in post revascularization patients, but these changes were not affected by the type of revascularization operation.

Acknowledgments
This study was supported by Kashan University of medical sciences (Kashan, Iran). The authors would like to thank the Cardiac Rehabilitation Center of ShahidBeheshti Hospital (Kashan, Iran) and the patients who devoted their time to participate in this study.

Conflicts of Interest
The authors have not conflicts of interest to declare.

References

1. Fowkes FGR, Rudan D, Rudan I, Aboyans V, Denenberg JO, McDermott MM, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. The Lancet. 2013;382(9901):1329-40.
2. Khosravi A, Taylor R, Naghavi M, Lopez AD. Differential mortality in Iran. Population health metrics. 2007;5(1):7.
3. Taleb S. Inflammation in atherosclerosis. Archives of cardiovascular diseases. 2016;109(12):708-15.
4. Calabro P, Yeh E. Inflammatory vascular markers in atherosclerosis. Current Topics in Atherosclerosis Research. 2005:49-65.
5. Norata GD, Garlanda C, Catapano AL. The long pentraxin PTX3: a modulator of the immunoinflammatory response in atherosclerosis and cardiovascular diseases. Trends in cardiovascular medicine. 2010;20(2):35-40.
6. Shiraki A, Kotooka N, Komoda H, Hirase T, Oyama J-i, Node K. Pentraxin-3 regulates the inflammatory activity of macrophages. Biochemistry and Biophysics Reports. 2016;5:290-5.
7. Alberti L, Gilardini L, Zulian A, Micheletto G, Peri G, Doni A, et al. Expression of long pentraxin PTX3 in human adipose tissue and its relation with cardiovascular risk factors. Atherosclerosis. 2009;202(2):455-60.
8. Slusher AL, Mock JT, Whitehurst M, Maharaj A, Huang C-J. The impact of obesity on pentraxin 3 and inflammatory milieu to acute aerobic exercise. Metabolism. 2015;64(2):323-9.
9. Salio M, Chimenti S, De Angelis N, Molla F, Maina V, Nebuloni M, et al. Cardioprotective function of the long pentraxin PTX3 in acute myocardial infarction. Circulation. 2008;117(8):1055-64.
10. Matsubara J, Sugiyama S, Nozaki T, Sugamura K, Konishi M, Ohba K, et al. Pentraxin 3 is a new inflammatory marker correlated with left ventricular diastolic dysfunction and heart failure with normal ejection fraction. Journal of the American College of Cardiology. 2011;57(7):861-9.
11. Naito Y, Tsujino T, Akahori H, Ohyanagi M, Mitsuno M, Miyamoto Y, et al. Increase in tissue and circulating pentraxin3 levels in patients with aortic valve stenosis. American heart journal. 2010;160(4):685-91.
12. Ferratini M, Ripamonti V, Masson S, Grati P, Racca V, Cuccovillo I, et al. Pentraxin-3 predicts functional recovery and 1-year major adverse cardiovascular events after rehabilitation of cardiac surgery patients. Journal of cardiopulmonary rehabilitation and prevention. 2012;32(1):17-24.
13. Inoue K, Kodama T, Daida H. Pentraxin 3: a novel biomarker for inflammatory cardiovascular disease. International journal of vascular medicine. 2012;2012.
14. Fukuda T, Kurano M, Iida H, Takano H, Tanaka T, Yamamoto Y, et al. Cardiac rehabilitation decreases plasma pentraxin 3 in patients with cardiovascular diseases. European journal of preventive cardiology. 2012;19(6):1393-400.
15. Swardfager W, Herrmann N, Cornish S, Mazereeuw G, Marzolini S, Sham L, et al. Exercise intervention and inflammatory markers in coronary artery disease: a meta-analysis. American heart journal. 2012;163(4):666-76. e3.
16. Brozic AP, Marzolini S, Goodman JM. Effects of an adapted cardiac rehabilitation programme on arterial stiffness in patients with type 2 diabetes without cardiac disease diagnosis. Diabetes and Vascular Disease Research. 2017;14(2):104-12.
17. Balducci S, Zanuso S, Nicolucci A, Fernando F, Cavallo S, Cardelli P, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. Nutrition, Metabolism and Cardiovascular Diseases. 2010;20(8):608-17.
18. Ryan AS, Ge S, Blumenthal JB, Serra MC, Prior SJ, Goldberg AP. Aerobic exercise and weight loss reduce vascular markers of inflammation and improve insulin sensitivity in obese women. Journal of the American Geriatrics Society. 2014;62(4):607-14.
19. Büttner P, Mosig S, Lechtermann A, Funke H, Mooren FC. Exercise affects the gene expression profiles of human white blood cells. Journal of applied physiology. 2007;102(1):26-36.
20. Hoffman-Goetz L, Pedersen BK. Exercise and the immune system: a model of the stress response? Immunology today. 1994;15(8):382-7.

21. Mooren F, Lechtermann A, Fobker M, Brandt B, Sorg C, Völker K, et al. The response of the novel pro-inflammatory molecules S100A8/A9 to exercise. International journal of sports medicine. 2006;27(09):751-8.
22. Almagor M, Keren A, Banai S. Increased C-reactive protein level after coronary stent implantation in patients with stable coronary artery disease. American heart journal. 2003;145(2):248-53.
23. Fehrenbach E, Niess A, Passek F, Sorichter S, Schwirtz A, Berg A, et al. Influence of different types of exercise on the expression of haem oxygenase-1 in leukocytes. Journal of sports sciences. 2003;21(5):383-9.
24. Kop WJ, Weissman NJ, Zhu J, Bonsall RW, Doyle M, Stretch MR, et al. Effects of acute mental stress and exercise on inflammatory markers in patients with coronary artery disease and healthy controls. The American journal of cardiology. 2008;101(6):767-73.
25. Munk PS, Breland UM, Aukrust P, Ueland T, Kvaløy JT, Larsen AI. High intensity interval training reduces systemic inflammation in post-PCI patients. European Journal of Cardiovascular Prevention & Rehabilitation. 2011;18(6):850-7.
26. Nakajima T, Kurano M, Hasegawa T, Takano H, Iida H, Yasuda T, et al. Pentraxin3 and high-sensitive C-reactive protein are independent inflammatory markers released during high-intensity exercise. European journal of applied physiology. 2010;110(5):905-13.
27. Volaklis KA, Smilios I, Spassis AT, Zois CE, Douda HT, Halle M, et al. Acute pro-and anti-inflammatory responses to resistance exercise in patients with coronary artery disease: a pilot study. Journal of sports science & medicine. 2015;14(1):91.
28. Zaldivar F, Wang-Rodriguez J, Nemet D, Schwindt C, Galassetti P, Mills PJ, et al. Constitutive pro-and anti-inflammatory cytokine and growth factor response to exercise in leukocytes. Journal of applied physiology. 2006;100(4):1124-33.
29. Forhan M, Zagorski BM, Marzonlini S, Oh P, Alter DA. Predicting exercise adherence for patients with obesity and diabetes referred to a cardiac rehabilitation and secondary prevention program. Canadian journal of diabetes. 2013;37(3):189-94.
30. Slusher AL, Huang C-J. Association of pentraxin 3 with insulin resistance and glucose response following maximal aerobic exercise in obese and normal-mass individuals. Canadian journal of physiology and pharmacology. 2016;94(7):734-8.
31. Huang C-J, Webb HE, Beasley KN, McAlpine DA, Tangsilsat SE, Acevedo EO. Cardiorespiratory fitness does not alter plasma pentraxin 3 and cortisol reactivity to acute psychological stress and exercise. Applied Physiology, Nutrition, and Metabolism. 2013;39(3):375-80.
32. Basile A, Sica A, d'Aniello E, Breviario F, Garrido G, Castellano M, et al. Characterization of the promoter for the human long pentraxin PTX3 role of NF-κB in tumor necrosis factor-α and interleukin-1β regulation. Journal of Biological Chemistry. 1997;272(13):8172-8.
33. Altmeyer A, Klampfer L, Goodman AR, Vilcek J. Promoter structure and transcriptional activation of the murine TSG-14 gene encoding a tumor necrosis factor/interleukin-1-inducible pentraxin protein. Journal of Biological Chemistry. 1995;270(43):25584-90.
34. Mohan S, Mohan N, Sprague EA. Differential activation of NF-kappa B in human aortic endothelial cells conditioned to specific flow environments. American Journal of Physiology-Cell Physiology. 1997;273(2):C572-C8.
35. Zempo-Miyaki A, Fujie S, Sato K, Hasegawa N, Sanada K, Maeda S, et al. Elevated pentraxin 3 level at the early stage of exercise training is associated with reduction of arterial stiffness in middle-aged and older adults. Journal of human hypertension. 2016;30(9):521-6.
36. Tamburus NY, Paula RF, Kunz VC, César MC, Moreno MA, Silva Ed. Interval training based on ventilatory anaerobic threshold increases cardiac vagal modulation and decreases high-sensitivity c-reative protein: randomized clinical trial in coronary artery disease. Brazilian journal of physical therapy. 2015;19(6):441-50.
37. Theodorou AA, Panayiotou G, Volaklis KA, Douda HT, Paschalis V, Nikolaidis MG, et al. Aerobic, resistance and combined training and detraining on body composition, muscle strength, lipid profile and inflammation in coronary artery disease patients. Research in Sports Medicine. 2016;24(3):171-84.
38. Castell L, Poortmans J, Leclercq R, Brasseur M, Duchateau J, Newsholme E. Some aspects of the acute phase response after a marathon race, and the effects of glutamine supplementation. European journal of applied physiology and occupational physiology. 1996;75(1):47-53.
39. Risøy BA, Raastad T, Hallén J, Lappegård KT, Bæverfjord K, Kravdal A, et al. Delayed leukocytosis after hard strength and endurance exercise: aspects of regulatory mechanisms. BMC physiology. 2003;3(1):14.
40. Li S-P, Goldman ND. Regulation of human C-reactive protein gene expression by two synergistic IL-6 responsive elements. Biochemistry. 1996;35(28):9060-8.
41. Sun H, Koike T, Ichikawa T, Hatakeyama K, Shiomi M, Zhang B, et al. C-reactive protein in atherosclerotic lesions: its origin and pathophysiological significance. The American journal of pathology. 2005;167(4):1139-48.

42. Volanakis JE. Human C-reactive protein: expression, structure, and function. Molecular immunology. 2001;38(2):189-97.
43. Jilma B, Eichler H-G, Stohlawetz P, Dirnberger E, Kapiotis S, Wagner OF, et al. Effects of exercise on circulating vascular adhesion molecules in healthy men. Immunobiology. 1997;197(5):505-12.
44. Nielsen H, Lyberg T. Long-Distance Running Modulates the Expression of Leucocyte and Endothelial Adhesion Molecules. Scandinavian journal of immunology. 2004;60(4):356-62.
45. Nemet D, Mills P, Cooper D. Effect of intense wrestling exercise on leucocytes and adhesion molecules in adolescent boys. British journal of sports medicine. 2004;38(2):154-8.
46. Park JK, Schwarz N, Willoughby D, Koh Y. Acute Changes in Soluble Cell Adhesion Molecules Following Different Intensities of Resistance Exercise. International Journal of Sports Science. 2015;5(6):234-9.
47. Wang J-N, Yan Y-Y, Guo Z-Y, Jiang Y-J, Liu L-L, Liu B. Negative Association of Circulating MicroRNA-126 with High-sensitive C-reactive Protein and Vascular Cell Adhesion Molecule-1 in Patients with Coronary Artery Disease Following Percutaneous Coronary Intervention. Chinese medical journal. 2016;129(23):2786.