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THE EFFECT OF EXERCISE ON C-REACTIVE PROTEIN (CRP) LEVEL AMONG OBESE POST-MENOPAUSAL WOMEN

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ABSTRACT

Menopausal transition is associated with increased fat and inflammation. Obesity is a major health problem in the world that increase the risk of cardiovascular disease, complications and even death. C-reactive protein (CRP) is the most accessible acute phase protein sensitive biomarker for systemic inflammation. Exercise is an effective approach recommended to prevent the risk and improve quality of life. This article aims to assess the effect of exercise on inflammatory biomarkers CRP as a predictor of cardiovascular disease in postmenopausal women with obesity, then further explore the potential role of CRP in this association. Data were collected from literature with keywords of menopause, obesity, exercise and CRP. The articles were clinical trial, observational trial dan review study from 2013-2023 and 5 reviews were included.Aerobic and resistance exercise, moderate to high intensity, 3-5 days a week, 40-90 minutes duration for 2-6 months is proven to reduce CRP levels. Exercise can prevent cardiovascular disease and aging process. Such results can be accomplished as single intervention or combination with other physical and dietary activities. Exercise must be done continuosly in reducing CRP levels to boost cardiovascular health and quality of life. Increase the intensity and duration of the exercise is associated with the decrease in CRP in post-menopausal obesity women. To reduce CRP level, aerobic and resistance exercise are advised. These results should be taken carefully, considering the lack of randomized controlled trials and no meta-analysis data associations exercise and CRP level among post-menopausal obesity women.

Keywords: exercise, obesity, menopause, CRP

INTRODUCTION

Menopause is a natural process in the life of every woman with physiological and psychological changes associated with health conditions such as obesity, overweight, cardiovascular disease, and inflammation [1]. Menopause is known as the cessation of menstrual periods for at least 12 consecutive months due to failure of ovarian function and not due to physiological (lactation) or other pathological causes [2]. Menopause begins at the average age of 50, but can also occur normally in women who are over or under 50 years old [3]. Women often worry approaching menopause that they will become unhealthy, unfit, and not beautiful as before [4]. Most menopausal women experience menopausal symptoms which can affect their daily activities and reduce their quality of life [5].

Based on data from the 2017 Indonesian Demographic Health Survey (IDHS), the proportion of women aged 30-49 in Indonesia experiencing menopause has increased, with a total of 28.767 women. The percentage of menopause by age group 30-34 years is 9.7%, age 35-39 years is 11%, age 40-41 years is 12.7%, age 42-43 years is 14.2%, age 44-45 years of 17.1%, and ages 46-47 years of 26.7%, and ages of 48-49 years of 43.1% [6]. Based on statistical data from the Ministry of Health (2023) Indonesia's population is 275,7 million and 136,3 million of them are women, including million women aged 50 years and over. In 2022 the number of women aged 50 years and over in menopause has reached 30,6 million people, which is included in the age of menopause [7]. This needs to get attention because it will arise various kinds of health complaints.

Quality of life in postmenopausal women is impaired as a result of vasomotor symptoms (hot flashes

and night sweats), depression, anxiety, insomnia, difficulty concentrating, decreased libido, vaginal dryness, pain during sexual intercourse (dyspareunia), and urinary incontinence [14]. There are also public health demands, especially for postmenopausal women, to experience a healthy aging process and better quality of life [8]. Hormone replacement therapy is indicated to reduce menopausal symptoms, but there is debate regarding the risks and benefits in postmenopausal women [9].

Menopause is linked to an increased risk of cardiovascular disease and exercise can reduce risk factors for cardiovascular disorders, prevent cancer and metabolic syndrome, increase the immune system and anti-oxidant activity [2, 10]. The world's leading cause of death, disability, and complications is a *cardiovascular* disease [10]. Women who are postmenopausal and have a body mass index (BMI) of more than 30 kg/m^2 have lower physical, energy, and quality of life than women who are at their ideal weight [9]. Overweight and obesity are currently a major public health problem in the world. Obesity can cause serious health problems such as cardiovascular disease (heart disease and stroke), type 2 diabetes mellitus, musculoskeletal disease (osteoarthritis), and cancer (endometrium, breast, intestine) which can cause premature death and disability [11]. Worldwide, at least 2.8 million people die every year as a result of being overweight or obese [12]. Obesity frequently reported can affect several aspects of life, including quality of life, social functioning, vitality, body aches, mobility issues, depression and low self-esteem,and general health issues [9, 13].

The causes of obesity should be prevented and avoided, including an imbalance consumption of calories from foods that are high in fat and sugar compared to the calories expended. There is also a decrease in physical activity due to changes in the type of work, transportation, and increasing urbanization [11].

An alternative treatment for mood disorders, anxiety, slow cognitive decline, and improved quality of sleep that is also cost-effective is exercise [9, 13]. However, previous studies involving the impact of exercise on biomarkers of systemic inflammation in postmenopausal women with obesity were limited.

CRP is one of the plasma protein that produced in the liver, and its increase is a response to infectious disease, tissue damage, or inflammation [14]. CRP is vascular inflammatory markers for endothelial dysfunction associated with risk of diabetes mellitus and coronary heart disease. A sensitive biomarker and a protein of the acute phase, CRP is the most accessible for identifying individuals with systemic inflammation. IL-6, IL-1, and TNF alpha boost hepatic CRP production [15]. CRP is the important key in innate immune response where chronic low-grade inflammation is associated with the pathological process of obesity and insulin resistance. CRP is a biomarker of inflammation that suggests a possible biological mechanism [16]. CRP activates the endothelium and induce vascular adhesion molecules that associated with insulin resistance in subjects with type 2 diabetes mellitus. Increased CRP is associated with the development of hypertension, stroke, peripheral arterial disease, transient ischemic attack, and sudden coronary heart death [17].

Based on existing studies, it is reported that CRP is positively related to an increased risk of cardiovascular events like myocardial infarction and stroke as well as obesity [17]. In addition, Shafiee (2017), conducted a study that was semi-experimental research and correlation on 36 overweight or obese women, over 8 weeks period. Their results demonstrated significant decrease of CRP in aerobic, resistance, and concurrent exercise program [18]. These indicate the role of exercise in modulating inflammatory processes that are related to increasing the risk of chronic disease among postmenopausal women with obesity.

Only a few previous literature reviews have examined the relationship between exercise and CRP in postmenopausal obesity women populations. That ideal and proper exercise can control the increase in inflammatory cytokines in postmenopausal obese women and expected that the quality of life will also increase is still inconclusive. This study aims to evaluate the effect of exercise on inflammatory cytokine CRP in postmenopausal women with obesity. However, with inconsistent evidence from observational studies and interventional trials, the role of exercise in reducing chronic inflammation remains unclear. Therefore, we provided this literature review to confirm the finding of the role of exercise that is ideal and correct in the relationship with proinflammatory cytokine CRP among postmenopausal obese women and illustrated the potential mechanism that is required.

METHODS

a. Methodology

The method used is a systemic literature review using secondary data. The databases of the articles used are Google Scholar, Proquest, PubMed with a range of years taken from 2013 - 2023, with a combination of categories of exercise (exercise, aerobic, resistance exercise), cytokine inflammation (CRP, C-reactive protein, hs-CRP, high sensitivity CRP), obesity, menopause (postmenopausal).

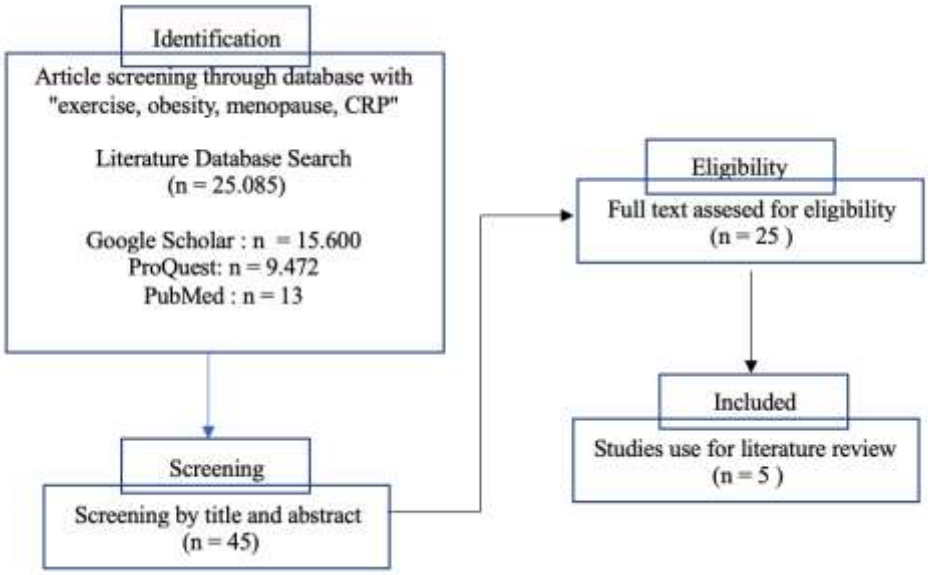

Figure 1. Literature Review Methodology

b. Material and procedure

The reviewed articles are those that can be accessed in their entirety in English. The criteria for the articles taken were those with research subjects aged 50 years and over, women, who had experienced menopause, and were obese with a BMI of 30 kg / m^2. Participants did not have a history of certain serious diseases such as heart disease, stroke, arthritis, musculoskeletal disorders (arthritis), kidney disorders, liver, diabetes, chest disease, no history of taking drugs such as drugs for heart disease, estrogen replacement therapy, no complaints of pain chest, shortness of breath, arrhythmia during exercise. The articles used are those that use exercise interventions and examine inflammatory biomarkers (CRP). Articles were excluded based on the following criteria: no CRP measurement, no exercise intervention, not menopausal yet, not obese, or duplication.

RESULTS

Table 1. Study intervention description and results

Author	Purpose and Population	Protocol Test	Outcomes
(El-Kader SA, Al-Jiffri OH, 2019) [9]	The aim was to compare the effects of aerobic versus resistance training on inflammatory biomarkers and quality of life in obese postmenopausal women in Saudi Arabia. Postmenopausal women with obesity in Saudi Arabia, age 50-	Participants were randomly divided into 2 groups: 3 months of Aerobic Training treadmill or RT (3x/week), for 30 min, HR target: 60-70% HR max, with 5 min warming up and stretching and 5 min cooling down.	CRP was measured before and after 3 months of study. Blood samples were taken from the antecubital vein after 12 hours of fasting, method by ELISA. CRP decreased ($p < 0.05$) in the aerobic

	58 yo, BMI 30 - 35 kg/m^2 (n =100) Pre-and post-trial design.		exercise group and RT group, with CRP reduction levels more significant in the aerobic exercise group.
(Shabani A *et al.*, 2019) [10]	Assessing the effects of Endurance and Resistance exercise on cardiorespiratory capacity and cardiovascular risk factors in overweight or obese postmenopausal women. Healthy postmenopausal women with obesity, 50 - 60 yo. (n=24) Randomized controlled trial.	The participants were split into 2 groups: - CG (control group) maintain their regular daily activity, 30 mins, 5 days/week -Endurance and Resistance (ER) exercise group, 8 weeks, 3x/week, 90min/session. Include Strength Training for upper and lower limbs, 35 mins, with weights 50%-75% of 1RM, using Brzycki equation; and Endurance Training (treadmill running, bicycle pedalling), 40min, 50-80% target HR calculated using Karvonen equation. Include 5-10mins warming up using light weights and cooling down 5-10mins.	High sensitivity- CRP significantly decrease in the exercise group ($p = 0.001$). In the control group, there was no significant decrease in hs-CRP Hs-CRP checked by turbidimetric method with autoanalyzer. Blood samples were taken after 12 hours of fasting before exercise and at week 8.
(Ketabipoor SM, Jahromi MK, 2015) [19]	Evaluate the impact of Anaerobic Exercise in water on C-reactive protein, serum estrogen,and BMI in obese and normal-weight postmenopausal women. Non-athletic women (age 57.04 ± 4.68 yo) with obesity (BMI = 30.21 ± 3.89 kg/m^2) and normal weight (BMI = 22.43 ± 2.45 kg/m^2) (n = 29) Quasi-experimental design.	Both groups did aquatic exercise training for 8 weeks, 3x/week, with the progressive intensity of 50 -70% HR max, 45 mins, at 10-11 am. Includes: 10 min warm up, 25 mins synchronized aerobic exercise by all the muscles of the upper and lower body, 10 mins cool down.	No significant decrease in the obese group after participating in exercise aquatic training ($p = 0.084$). Decrease in CRP in the normal weight group after participating in aquatic exercise training ($p = 0.005$). Blood tests were taken previously and 2 days after exercise through the left brachial vein, with the ELISA method.
(Yoon *et al.*, 2018) [2]	Analyze the relationship between aerobic exercise and indicators of metabolic syndrome, immune function, antioxidant function, physical health, estrogen resistance, and tumor markers, in obese postmenopausal women. Obese postmenopausal women with 30% body fat. (n=30) Randomly divided into 3 groups: Aerobic exercise group (age 53.70 ± 3.37 yo), Resistance exercise group (age	Participants were randomly divided into 3 groups, 12 weeks of exercise: -Aerobic exercise group, walk on the treadmill at different speeds, with 60-80% target HR calculated using the Karvonen equation. -Resistance exercise group, with 60% intensity of 1 RM, 3 sets, 1 min rest time between exercises, 8-12 repetitions. -Control group. Include: 10 mins walking and stretching warm-up, 40 mins exercise, 10 mins stretching.	No significant decrease in CRP ($p = 0.0628$) Taken from venous blood samples after 10 hours of fasting, with the turbidometry method.

	52.20 ± 2.15 yo), Control group (age 52.50 ± 2.68 yo)		
(Ryan, *et al* 2014) [20]	To examine the effect of aerobic exercise training (AEX) plus weight loss (WL) and weight loss alone with vascular marker inflammation and insulin sensitivity in obese women. Overweight and obese sedentary post menopausal women, BMI ≥ 25 kg/m^2 , 50 - 76 yo, menopause at least 1 year. (n=77) Prospective controlled study Randomly divided into 2 groups : AEX + WL (n = 88), WL (n = 86)	Participants were randomly divided into 2 groups : 1. Grup AEX + WL : 6 months, 3 days/week, treadmill, Include: 5-10 mins warming-up and stretching warm-up, and 5 - 10 mins cool-down. HR target : 50-60% HRR increase gradually in intensity and duration until 85% HRR for 45 min. 2. Group WL : Therapeutic Lifestyle Change (TLC) instructions: low-fat, high-fiber, low-sodium diet: once a week for 6 - 8 weeks, attended weekly weight loss classes for 6 months monitored by 7-day diet record.	AEX + WL decreased CRP by 29% ($p < 0.01$) WL decreased CRP by 21% ($p = 0.02$) Taken from venous blood samples after 12 hours of fasting, with electrochemiluminescence using a multispot microplate.

*Statistically Significant ($p < 0.05$), RT: Resistance Training; yo: years old, ER: Endurance and Resistance, 1RM: one repetition maximum, BMI: Body Mass Index, CRP: C-reactive protein, AEX : aerobic exercise training, WL: Weight Loss, HRR: Heart Rate Reverse

First study by El-Kader and Al-Jiffri (2019) analized a group of postmenopausal obese women who did aerobic exercise and a comparison group that did resistance training. The decrease of CRP was more significant in the group that did aerobic exercise compared to resistance training. Aerobic exercises were done 3 times a week, 30 minutes for 3 months, with heart rate target 60-70% of maximal heart rate. The exercise include 5 minutes warming up and 5 minutes cooling down [9].

Second study by Shabani A *et al.* (2019) enrolled a control group of postmenopausal obese women who did combination of endurance and resistance exercise and a comparison group that did regular daily activity. The decrease of hs-CRP significantly decrease in endurance and resistance exercise group. Endurance and resistance exercise was done 3 times a week, 90 minutes, for 8 weeks. The resistance exercise include strength training for upper and lower limb for 35 minutes and the endurance exercise was treadmill running or bicycle pedalling for 40 minutes, with heart rate target. Warming up using light weights for 10 minutes and cooling down for 10 minutes [10].

Third study by Ketabipoor and Jahromi (2015) investigated obese and normal-weight postmenopausal obese women who did aquatic exercise. The result shown that there were no significant decrease in the obese group with aquatic exercise, but there were significant decrease of CRP level in the normal weight group after aquatic aerobic exercise. The aquatic aerobic exercise were done 3 times a week, for 45 minutes. Warming up done for 10 minutes and cooling down done for 10 minutes. The aquatic aerobic exercise done for 25 minutes by synchronized aerobic movement of all the upper and lower body muscles [19].

Fourth study by Yoon *et al* (2018) conducted three groups of postmenopausal obese women who did aerobic exercise, resistance exercise and control group. The result shown no significant decreased of CRP. Aerobic exercise group did treadmill at different speed with 60 to 80% target heart rate. The resistance exercise group did 3 sets of 8-12 repetitions. The exercise include 10 minutes warm-up, 40 minutes exercise and 10 minutes cooling down [2].

Fifth study by Ryan *et al* (2014) assigned a group of postmenopausal obese women who did aerobic exercise plus weight loss group, and weight loss only group. The decrease of CRP was more significant in the group that did aerobic exercise together with weight loss program. The exercise done for 60 minutes, include 10 minutes warm-up, 45 minutes aerobic exercise and 10 minutes stretching or cooling down. The aerobic exercise was treadmill, 3 times a week, for 6 months. Weight loss program was did lifestyle changes such as eat low-fat, high-fiber, low-sodium diet for 6 months. The participants attended weekly weight loss class for 8 weeks, once a week and monitored by 7 day diet record [20].

Based on the description of the research results above, shows that exercise, both at high and low intensity, 3-5 days a week, with duration 40-90 minutes, continuously for 2-6 months, is proven to reduce CRP levels. Such results can be accomplished as single intervention or combination with other physical and dietary activities.

DISCUSSION

In a study conducted by El-Kader and Al-Jiffri (2019) by comparing a group of postmenopausal obese women who did aerobic exercise and a comparison group that did resistance training for 3 months, the quality of life score increased, with an average serum proinflammatory cytokines CRP, TNF, IL-2, IL-4, and IL-6 significantly decreased in both groups [9]. The decrease was more significant in the group that did aerobic exercise compared to resistance training. This shows that postmenopausal women with obesity who do aerobic exercise modulate levels of inflammatory cytokines more than resistance training [9].

It is not entirely clear how exercise reduces inflammation precisely. Some data point that repeated muscle contractions in exercise result in an improvement in inflammatory status, due to modulation of intracellular signaling pathways and cellular functions mediated by Nitric Oxide (NO) and Reactive Oxygen Species (ROS). The anti-inflammatory effect of exercise also occurs due to a decrease in the percentage of body fat and accumulation of macrophages in adipose tissue, as well as muscles that release IL-6 inhibitors of TNF-α and cholinergic anti-inflammatory pathways [9]. Aerobic and resistance training improves the quality of life in obese postmenopausal women, related to the state of health, physical function, body pain, general body health, vitality, social functioning, emotion, and mental health. Regular exercise can improve strength, endurance, flexibility, and balance in postmenopausal women[9] . Exercise is an effective therapy for dealing with hot flushes in postmenopausal women[21]. The effects of exercise on mental health are suspected due to physiological and psychological mechanisms including increasing a sense of self-worth, controlling self-perception, and reducing emotional tension. Exercise can stimulate neurogenesis, increase synaptic plasticity and brain vascularization. Social contact that occurs during regular exercise is also an important mechanism, where they get a positive response from others so that self-esteem increases[9].

Then Shabani *et al*. conducted a study, randomized control trial on 24 obese postmenopausal women with the endurance and resistance exercise group compared to the control group who carried out regular to moderate activities for 8 weeks. The results showed that the group that continuously performed endurance and resistance exercises reduced cardiovascular disease risk markers with decreased body mass index (BMI), heart rate (HR), systolic and diastolic blood pressure, and triglyceride, high sensitivity C-reactive protein (hs CRP). significant. Followed by an improvement in plasma lipid profiles which is an increase in high-density lipoprotein (HDL) and cardiorespiratory capacity (VO_{2max}) [10].

Simultaneous endurance and resistance (ER) training can be a good exercise program because it can reduce body weight by 6-7%, thereby reducing body fat composition, improving plasma lipid profiles, reducing high-sensitivity CRP, and increasing cardiorespiratory capacity (VO_{2max}) in postmenopausal women. Weight loss of 3-5% can result in clinical changes that are good for health [10]. An increase in visceral fat tissue appears 3-4 years before menopause, correlating with a decrease in circulating estradiol (E2) and an increase in serum FSH (follicle-stimulating hormone). Estrogen plays a role in regulating appetite and activating lipoprotein lipase and increasing lipolysis [8]. Menopause and obesity lead to an, imbalance in autonomic nervous control of the cardiovascular system where there is sympathetic vagal hyperactivity and lower sympathetic activity in the group of postmenopausal women. Postmenopausal women have lower cardiorespiratory capacity and risk of cardiovascular disease, especially coronary heart disease. A decrease in hs-CRP indicates an antiatherogenic state that can reduce the risk of cardiovascular disease, especially coronary heart disease. Exercise such as endurance and resistance training, is an important component of lifestyle modification in postmenopausal obese women by taking into account the type, duration, and intensity of physical exercise so that it can provide optimal results for the body [10].

Ketabipoor dan Jahromi, assessed serum estrogen, CRP and body mass index following 8 weeks of aerobic exercise in water in 29 healthy post-menopausal obesity women in the obese and normal weight group. They concluded that 8 weeks program of the anaerobic exercise was not enough to reduce significantly of CRP in post-menopausal women in the obese weight group, but however CRP decreased significantly when compared pre exercise and after eight weeks post exercise in normal weight group [19].

Exercise can affect the inflammatory process through adipocyte function. CRP decreased significantly in the normal weight group, perhaps because the normal weight group was more effective at reducing inflammatory factors, resulting in a decrease in CRP. Exercise can result in increased energy use, increased fat oxidation due to exercise metabolism, and also decreased appetite after exercise resulting in weight loss in individuals with obesity. It ultimately then lead to a decrease in the factors that cause inflammation and a decrease in the risk of atherosclerotic disease. Weight loss is an effective method for lowering CRP [19].

Exercise may also lower CRP through a direct effect on the inflammatory process. Exercise reduces the expression and blood levels of leukocyte adhesion molecules, inhibits the interaction between endothelial cells and monocytes, reduces the production of pro-inflammatory cytokines, increases the production of anti-inflammatory cytokines by mononuclear cells, and maintains the balance of anti-inflammatory and pro-inflammatory cytokine production in skeletal muscle. Long-term exercise results in stimulation of the vagus nerve which is associated with an increase in pro-inflammatory and anti-inflammatory cytokines which are not reflected in CRP levels. This supports the results of CRP reduction which was not significant in the obese group. Besides that, it can also be influenced by various factors such as age, gender, diet and lifestyle, smoking, stress, duration, and intensity of physical exercise [19].

Exercise affects sexual hormones in postmenopausal women where estrogen levels increase significantly after exercise in groups of women with normal weight and obesity. The increase in serum estrogen after exercise is related to the purification and metabolism of estrogen, this is due to decreased hepatic blood flow. Physical exercise causes a significant decrease in estradiol and testosterone levels wherein the decrease in estrogen and the decrease in androgen aromatization occurs due to reduced adipocyte tissue, especially from decreased abdominal fat and weight loss. Although there is a reduction in fat tissue as a source of estrogen secretion, there is an ovary as a source of estrogen secretion which is also affected by exercise. The mechanism that influences estrogen metabolism is through the regulation of the cytochrome p450 enzymes responsible for estrogen hydroxylation and estrogen methylation of catecholamine. Aquatic aerobic exercise can reduce BMI and increase estrogen, thereby reducing cardiovascular risk factors [19].

Also, Yoon *et al.* assessed estrogen, tumor markers, immune function, and antioxidant function changes following 12 weeks of aerobic and resistance exercise in 30 postmenopausal women with a body percentage of more than 30%. The results of the study found a decrease in body weight, body fat percentage, waist circumference, and an increase in HDL showed a reduced risk of metabolic syndrome. The hormone estrogen increases after aerobic and resistance training. This study revealed that aerobic exercise and resistance increase estrogen levels. Postmenopausal women experience a decrease in estrogen, which functions as a cardioprotective, thereby increasing the risk of cardiovascular disease. Estrogen deficiency associated with menopause accelerates the accumulation of visceral fat, thus increasing the risk of metabolic syndrome, which causes abdominal obesity and insulin resistance. Estrogen is important for lymphocyte activation, menopause results in decreased efficiency of antibody-mediated and cell-mediated responses due to thymic atrophy [2].

Menopause results in decreased skeletal muscle, so resistance training is important to improve myocardial function and prevent chronic disease. Aerobic exercise is recommended for postmenopausal women because it is effective for preventing cancer, metabolic syndrome, boosting the immune system and antioxidant activity. Menopause is related to the cessation of menstruation due to failure of ovarian function. Postmenopausal women with obesity are at high risk of developing cancer. Aerobic exercise in postmenopausal women for 16 weeks can prevent breast cancer by increasing estrogen metabolite 2-hydroxytesytosterone and decreasing 16α-hydroxyestrone [22].

The results of a study by Yoon *et al*, stated that aerobic and resistance training did not cause significant changes in CRP inflammatory markers. This could be influenced by confounding factors such as physical activity, smoking, drinking, eating habits, and stress levels which were not considered as confounding factors that could influence the results of research measurements. In addition, it was found that aerobic and resistance training resulted in an increase in the tumor marker AFP, a tumor marker for liver cancer. This may be related to liver diseases such as hepatitis, liver cirrhosis, and liver tumors in the participants. Future research needs to assess from several perspectives that need to be controlled for the participants [2].

Ryan, *et al* (2014) assessed that there was reduction in plasma CRP expresion when aerobic exercise was combined with weight loss in obese postmenopausal women. The reduction of CRP in aerobic exercise with weight loss is greater than weight loss only group without exercise. Weight loss indicating as an important factor in reducing CRP levels. Reducing CRP levels independently predicts a decreased risk of

atherosclerosis progression and coronary disease in postmenopausal women. This study provides evidence that, in obese postmenopausal women, there were markers of vascular inflammation and systemic inflammation which is CRP, that associated with obesity and insulin resistance. CRP levels decreased with combination of weight loss and aerobic exercise. Variety approaches may be needed to improve vascular inflammation and clinical outcomes in older obese women. The CRP level correlated directly with early central obesity regardless of glucose tolerance status. Greater waist circumference, or waist:hip ratio, is directly related to higher CRP levels. Aerobic exercise and weight loss can decrease percentage of fat, fat mass, visceral fat and subcutaneous abdominal fat, blood pressure, improve fasting triglycerides, fasting plasma glucose and insulin [23].

Nie *et al.*, ivestigated in 4867 postmenopausal men and women participants reported that serum progesterone significantly increased the risk of obesity, where the relationship between progesterone and obesity was mediated by hsCRP. Based on this mechanism it is reasonable that high progesterone levels lead to systemic inflammation which results in obesity [16]. Decreased estrogen due to menopause results in a decrease in nitric oxide which triggers endothelial cell instability where endothelial activation and vascular damage occurs, followed by molecular adhesion and endothelial dysfunction in the form of increased vascular resistance and impaired tissue perfusion. In the final stage, the function of immune cells decreases, triggering inflammation and increasing the risk of cardiovascular disease. Changes in intima-media thickness are associated with proinflammatory molecules and endothelial dysfunction so they can be used as an initial diagnostic tool for endothelial damage in menopause [24].

CURRENT DATA LIMITATIONS AND FUTURE RESEARCH OPPORTUNITIES

The study population was limited to obese, post-menopausal women with obese at moderate risk of CVD, the result can be vary in women in other ages or men. Further research sample including both gender with larger sample and controlling type of diet and daily activities of the participants is needed to give a firm recommendation. More extensive studies involving cohort studies are needed to confirm this finding. In addition, to elaborate on how exercise affects the inflammatory process in more detail, further research is needed.

CONCLUSION

There is a relationship between exercise and CRP plasma level as inflammatory markers. Exercise has a positive effect on serum CRP levels which can lead to a decrease in CRP. Exercise must be carried out routinely continuously to maintain the effect on CRP. Lifestyle modifications such as exercise, limitation of alcohol consumption, optimal blood pressure control, stopping smoking, and weight control are also important to lower CRP levels for the development of diabetes mellitus, cardiovascular disease, and metabolic syndrome [2]. Exercise combine with weight loss program such as doing healty diet eat low-fat, high-fiber, low-sodium diet for long term at least 6 months duration can result significant decrease of CRP plasma level[20].

Exercise training is an essential lifestyle change for obese post-menopausal women. Simultaneous aerobic and resistance exercise continuously can decrease serum proinflammatory cytokines CRP level. By doing exercise regularly, it will result decrease in the percentage of body fat and will induce anti inflammatory effect [10].

Aerobic and resistance exercise can improves the quality of life in obese postmenopausal women, related to thestate of health, physical function, body pain, general body health, vitality, social functioning, emotion, and mental health [9]. Regular exercise can improve strength, endurance, flexibility, and balance in postmenopausal women. Exercise also important for mental health, reducing emotional tension and reduce hot flush in post menopausal women [9,21].

Both aerobic and resistance exercise has many advantages for post menopausal obese women. Exercise can reduce cardiovascular disease risk markers CRP significant, followed with decreased BMI, body fat percentage, heart rate, systolic and diastolic blood pressure, and lipid profile such as triglyceride, increase HDL and cardiorespiratory capacity (VO_{2max}). By doing exercise regularly also have anti oxidant activity that can boost the immune system and prevent cancer [10].

Aerobic exercise that is suggested include treadmill, bicycle pedalling or aquatic aerobic exercise that can reduce BMI and increase estrogen level. Aerobic exercise should be done for at least 8 weeks to 6 months or more, with medium to high intensity, duration 40 to 60 minutes include warm-up and cooling down to reduce muscle injury, with optimum heart rate reach which is 60-80% of heart rate maximum [2,9 10]

[19, 23] . Long term exercise is suggested to maintain lower level of CRP. Resistance exercise or strength training should be done for upper and lower limb.Resistance exercise could be done 3 times a week, 3 sets of 8 - 12 repetition, and gradually increase in intensity, include warm-up and cooling down to reduce side effect [2,9 2,10].

Menopause and obesity lead to an increase risk of cardiovascular disease [10]. Exercise correlating with anti- inflammatory effect that can lower the risk of cardiovascular disease, resulting in decrease in CRP that indicates an antiatherogenic effect and can reduce the risk of cardiovascular disease, especially coronary heart disease, metabolic syndrome and improve insulin resistance [2]. In other hand, exercise can increase energy and metabolism, then can increased fat oxidation and decreased appetite resulting in weight loss in obesity individual [19] . Weight loss is an effective method for lowering CRP[23]. Exercise is an important component of lifestyle modification in postmenopausal obese women by taking into account the type, duration, and intensity of exercise so that it can provide optimal results for the body.

CONFLICT OF INTEREST

The authors declare no conflict on interest.

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