Aerobic Exercise to Reduce Insulin Resistance and Hyperandrogenism in Women with Polycystic Ovary Syndrome

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Abstract. Infertility is a condition in which a woman is unable to achieve clinical pregnancy after engaging in unprotected sexual intercourse for more than 12 months. One of the causes is Polycystic Ovary Syndrome (PCOS), a complex endocrine disorder and metabolic syndrome that is most common in reproductive-aged women. These two phenomena create a vicious cycle that leads to hormonal instability, ultimately resulting in infertility. PCOS can be managed through lifestyle changes, including aerobic exercise. **Objective**: The objective of this literature review is to explain the effects of aerobic exercise on metabolic parameters such as hyperandrogenism, insulin resistance, and anthropometric indicators in women with PCOS. **Methods**: This study used the literature review method. Articles were obtained from several online databases, and then screening was performed based on inclusion and exclusion criteria, resulting in the selection of 6 articles for review. **Results**: From the six reviewed articles, it was found that moderate-intensity aerobic exercise for a minimum of 30 minutes per session, at least three days per week, for a duration of 16 weeks, can improve anthropometric indicators, increase insulin sensitivity, and reduce testosterone levels. **Conclusion**: Aerobic exercise can have an impact on improving PCOS symptoms when performed for at least 16 weeks, with a minimum of three days per week and a minimum of 30 minutes per day using moderate-intensity aerobic exercise.

Keywords: *: PCOS, anthropometric, insulin, hyperandrogenism*

1 Introduction

Infertility is a condition in which a woman is unable to achieve clinical pregnancy after engaging in unprotected sexual intercourse for more than 12 months.[1]. One of the causes is Polycystic Ovary Syndrome (PCOS). PCOS is a complex endocrine disorder and metabolic syndrome that is most common in women of reproductive age.[2] This disorder was first described by Stein and Laventhal in 1935, characterized by symptoms such as obesity, amenorrhea, hirsutism, infertility, enlarged ovaries, and the presence of multiple cysts (polycystic).[3] Due to hormonal instability, the ovarian cycle cannot function properly, resulting in difficulty in achieving pregnancy.

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D. V. Ferezagia et al. (eds.), *Proceedings of the International Conference on Vocational Education Applied Science and Technology (ICVEAST 2023)*, Advances in Social Science, Education and Humanities Research 783,
https://doi.org/10.2991/978-2-38476-132-6_20

PCOS has several characteristic symptoms that indicate its diagnosis. There are different opinions regarding the diagnosis, but the most commonly used criteria is the Rotterdam criteria consensus. According to the Rotterdam criteria, a person is diagnosed with PCOS if they meet two out of the following three conditions: 1. Hyperandrogenism (clinical, biochemical, or both), 2. Ovary dysfunction, and 3. Polycystic ovary morphology (PCOM) observed through transvaginal ultrasound examination. [4]

In 2017, there were 1.55 million incidents of PCOS worldwide, and 0.43 million of them were associated with Daily-Adjusted Life Years (DALYs). Epidemiological studies conducted on PCOS have faced challenges in calculating the prevalence due to variations in inclusion criteria used for diagnosing PCOS, sample sizes, ethnicities, study models, and regional areas. However, these incidence rates are likely to increase in parallel with the rising rates of obesity. These numbers may continue to rise considering that 68-75% of individuals with PCOS remain undiagnosed even after seeking healthcare facilities. This indicates that the symptoms of PCOS are often underestimated. [5] Furthermore, symptoms of PCOS can be observed as early as adolescence, starting from around 15 years of age.

PCOS is a multifactorial condition. This collection of factors triggers excessive androgen secretion, insulin resistance, impaired follicle development in the ovaries, and continuous release of inflammatory factors that worsen the metabolic syndrome. The etiological factors can originate from the surrounding environment, diet or nutrition, lifestyle choices, genetics, or even imbalances in the body's microbiota.[2] Environmental pollutants such as endocrine-disrupting chemicals (EDCs) can indeed disrupt the hormonal functioning in the human body. They can manipulate hormonal receptors in the body or block the normal actions of hormones. [6] High calorie consumption and a sedentary lifestyle are likely factors that worsen the symptoms of PCOS. Diets high in sugar content also contribute to PCOS symptoms by potentially altering gut microbiota, exacerbating insulin resistance, increasing inflammatory factors, and promoting androgen production.[7][2] In addition to external factors and lifestyle, several studies have also identified potential genes associated with the expression of PCOS symptoms. These genes, when interacting with each other or with external factors, may contribute to an individual's higher susceptibility to PCOS. [8][2]

The pathophysiology of PCOS is centered around neuroendocrine dysfunction.[9] Broadly speaking, there are two main features of PCOS: hyperandrogenism and insulin resistance, which synergistically interact with each other. Hyperandrogenism leads to ovarian dysfunction, causing excessive production of ovarian hormones such as Anti-Mullerian hormone. This disrupts the hypothalamic pulsatility in producing gonadotropin-releasing hormone (GnRH), resulting in an imbalance in the ratio of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and the formation of ovarian cysts. Hyperandrogenism is further exacerbated by hyperinsulinemia caused by insulin resistance. Insulin resistance leads to adipocyte dysfunction, impeding glucose

metabolism and leading to the accumulation of fat in visceral and subcutaneous areas. [10] Hiperinsulinemia also leads to a decrease in the production of sex hormone-binding globulin (SHBG) in the liver. SHBG plays a crucial role in regulating hormone levels in the bloodstream. When SHBG levels decrease, there is an increase in the availability of free and bioactive forms of hormones such as testosterone. This can contribute to the symptoms of PCOS, including the manifestations of hyperandrogenism such as hirsutism, acne, and male pattern hair loss. The reduction in SHBG levels caused by hiperinsulinemia further exacerbates the hormonal imbalance associated with PCOS. [11] As a result, the circulating levels of androgen hormones increase, exacerbating the condition of hyperandrogenism. The excessive androgens in the bloodstream can further disrupt the normal functioning of the ovaries and contribute to the development of PCOS symptoms such as irregular menstrual cycles, acne, excessive hair growth (hirsutism), and the formation of ovarian cysts. The hormonal imbalance caused by the increased androgen levels can have various effects on the reproductive system and overall health of individuals with PCOS. [12]

PCOS can be managed through lifestyle modifications, and one of the strategies is engaging in aerobic exercise. This is where physiotherapy plays a role by providing exercise therapy to address reproductive function disorders in women. According to the American College of Sports Medicine, aerobic exercise is a form of exercise that involves rhythmic and continuous contractions of large muscles, primarily relying on aerobic metabolism as a source of energy.[13] Examples of aerobic exercises include brisk walking, running, cycling, swimming, and so on..[14] Aerobic exercise encompasses various types, including progressive aerobic exercise training, continuous aerobic training, intermittent aerobic training, high-intensity interval training, and others. Aerobic exercise and its effects on insulin, androgens, and obesity can restore hormonal balance, enabling ovulation to occur and addressing infertility. [15] The reason for choosing this exercise is because it can be easily done at home. This is supported by a study conducted by Harrison et al. in 2011, which stated that regular aerobic exercise performed at a moderate intensity for a short period can improve reproductive function, such as ovulation and menstrual cycle regulation, as well as reduce weight and insulin resistance in overweight women with PCOS.[16]

The purpose of conducting this literature review is to explain the effects of aerobic exercise on metabolic parameters such as hiperandrogenism, insulin resistance, and anthropometric indicators in women with PCOS.

2 Reserach Methode

In this research, the author employed the literature review method by gathering articles from online databases such as Google Scholar, Sage Journal, ProQuest, Scopus, and PubMed. Literature review is a systematic, explicit, and reproducible method used to identify, evaluate, and synthesize research works and thoughts already produced by researchers and practitioners. [17] The articles sought for this literature review have the

following inclusion criteria: they are written in English or Indonesian, published between 2018 and 2023, employ randomized controlled trial, cohort study, or quasi-experimental designs, involve women diagnosed with PCOS based on the Rotterdam criteria aged between 18 and 40 years, focus on aerobic exercise as the intervention, do not include a comparison group, and have outcome measures related to metabolic parameters. The metabolic parameters discussed in this literature review are based on the main symptoms of metabolic syndrome in PCOS, including insulin levels or insulin sensitivity (representing insulin resistance), androgen hormone levels in the body (representing hyperandrogenism), and anthropometric indicators such as waist circumference, hip circumference, waist-hip ratio, and body mass index (representing obesity or abdominal fat). Insulin levels can be measured using the Oral Glucose Tolerance Test (OGTT), HOMA-IR (Homeostatic Model Assessment of Insulin Resistance), fasting glucose, and fasting insulin. Androgen hormone levels can be assessed using the Free Androgen Index (FAI) and testosterone levels. Anthropometric indicators can be measured using waist circumference, hip circumference, waist-hip ratio (WHR), and body mass index (BMI).

The article search was conducted using several keywords combined with Boolean operators (AND, OR, OR NOT, or AND NOT) to specify or expand the desired article search. The keywords used include "Polycystic ovary syndrome" OR "Polycystic ovarian syndrome" OR "PCOS" AND "aerobic exercise" OR "aerobic exercise training" AND "metabolic parameters" OR "metabolic profile" OR "insulin resistance" OR "Body Mass Index" OR "androgen level" OR "testosterone level". This literature review utilized the critical appraisal method to assess the validity, reliability, results, and clinical relevance of the included articles. The JBI Critical Appraisal Tools were used as the critical appraisal instrument, and the appraisal was conducted by two reviewers. The JBI Data Extraction Tool was employed as the instrument for data extraction.

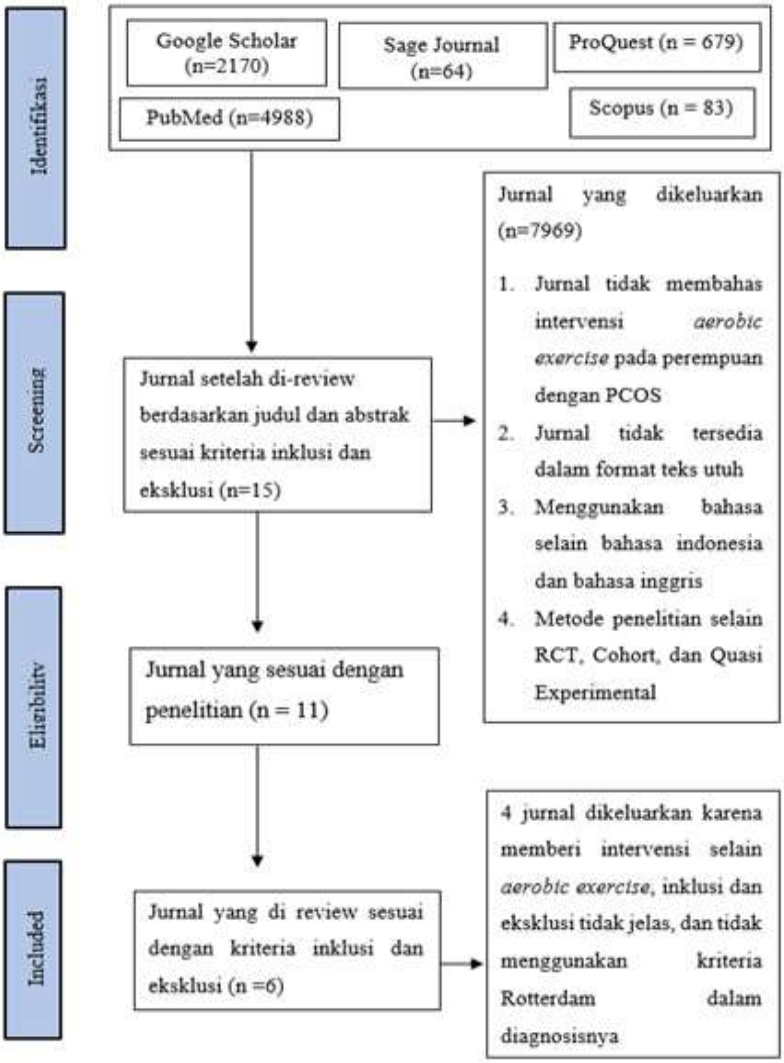

Fig. 1. PRISMA Follow Chart

The simplified approach was used for data synthesis in order to answer the research questions of the literature review. This approach involves organizing and summarizing the findings from the included articles based on the research questions or objectives of the review. The key information, such as study design, population, intervention, outcomes, and results, is extracted from each article and synthesized to provide an overview of the collective findings. The findings are then analyzed and interpreted to draw conclusions and address the research questions or objectives of the literature review.

3 Result

From the initial search using the specified keywords "Polycystic ovary syndrome" OR "Polycystic ovarian syndrome" OR "PCOS" AND "aerobic exercise" OR "aerobic exercise training" AND "metabolic parameters" OR "metabolic profile" OR "insulin resistance" OR "Body Mass Index" OR "androgen level" OR "testosterone level" in the mentioned online databases, a total of 7,984 articles were obtained. Subsequently, these articles were further screened based on their titles and abstracts according to the predetermined inclusion and exclusion criteria, resulting in a total of [number] articles. These articles were then thoroughly analyzed and critically appraised. From this process, a total of 11 articles were identified, and among them, 6 articles met the inclusion criteria, while the rest were excluded.

The six articles all mentioned the effective impact of aerobic exercise on metabolic parameters. All participants had minimal background in physical activity prior to their recruitment. Different intervention techniques were used, including continuous, intermittent, and progressive approaches. Generally, the control groups showed opposite results. Minimal improvements in metabolic indicators were observed within 12 weeks. However, if weight loss or improvement in lipid profile (especially visceral fat) is desired, exercise should be performed for a longer duration, such as 20 weeks or more. [15]

In Costa et al.'s study, all participants were overweight or obese (BMI 25-39.9 kg/m2). The group that underwent aerobic exercise intervention for 16 weeks experienced improvements in cardiorespiratory fitness aspects (VO2 peak, etc.), but there were only minor developments in cardiometabolic profile indicators, which were not statistically significant. Improvement was observed in indicators such as cholesterol and LDL levels, but there were no differences between the exercise group and the control group in terms of fasting blood glucose and insulin levels, OGTT results, and HOMA-IR. Additionally, the instrumentation used was unable to process the irregularity of these variables. The possibility is that most participants did not have clinically diagnosed glycemic dysfunction. However, anthropometric indicators such as BMI and waist circumference showed improvement. [18]

The study by Philbois et al. found that both MICT (Moderate-Intensity Continuous Training) and HIIT (High-Intensity Interval Training) had similar effects on anthropometric, metabolic, and hormonal parameters. Both types of exercise groups showed a decrease in testosterone levels. However, neither exercise group showed an increase in insulin sensitivity, which may be due to the lack of changes in anthropometric parameters during the 16-week intervention period. [19]

In the study by Ribeiro et al., participants who received the CAT (Continuous Aerobic Training) intervention experienced a decrease in waist and hip circumference, as well

as testosterone levels. On the other hand, participants who received the IAT (Intermittent Aerobic Training) intervention experienced a decrease in testosterone levels, waist-to-hip ratio (WHR), and waist circumference. However, both groups did not show a decrease in BMI (Body Mass Index).[20] In the second study by Ribeiro et al., the CAT intervention group experienced a decrease in testosterone levels and a reduction in waist and hip circumference. Meanwhile, the group of participants who received the IAT intervention also experienced a decrease in total testosterone levels, FAI (Free Androgen Index), as well as a reduction in waist circumference and WHR (Waist-to-Hip Ratio).[21]

In the study conducted by Javid et al., it was found that there was a decrease in fasting blood glucose levels and insulin levels compared to baseline measurements. Additionally, there was a reduction in insulin resistance as measured by HOMA-IR, which showed a 42.2% decrease from baseline measurements.[22] In the study conducted by Pandit et al., significant differences were found in all variables, including anthropometric variables (BMI, waist-hip ratio) and insulin resistance (fasting blood glucose levels and fasting insulin levels), with all of them having a p-value < 0.05..[23]

Table 1. Article Screening Result

Study	Sampel	Age	Intervention	Dose	Result
Costa, et al	T : 27 C : 13 I : 14	18 – 34	Aerobic exercise training	F : 3 times a week for 16 weeks I : 60 – 85% HRmax T : progressive aerobic exercise T : 40 minutes	Supervised aerobic exercise training can improve HRQL (Health-Related Quality of Life), cardiorespiratory fitness, and cardiometabolic health in overweight/obese women with PCOS.
Philbois, et al	T : 75 C : 25 I : 50	18 – 39	MICT *aerobic* (n = 25) HIIT *aerobic* (n = 25)	F : 3 times a week for 16 weeks, I : MICT : warm up 50 – 65% HRR, training session 70 – 80% HRR, cool down 40 – 50% HRR HIIT : warm up 50 – 65% HRR, 2	MICT (Moderate-Intensity Continuous Training) and HIIT (High-Intensity Interval Training) have similar effects on anthropometric, metabolic, and hormonal parameters

				menit upper intensity 85 – 90% HRR, 3 menit recovery intensity 65 – 70% HRR, cool down 40 – 50% HRR T : MICT, HIIT T : 60 minutes (5 minutes warm up, 50 minutes training (MICT), 35 – 45 minutes training (HIIT), 5 minutes cool down)	
Ribeiro, et al	T : 87 C : 30 I : 57	18 – 39	CAT (n = 28) IAT (n = 29)	F : 3 times a week for 16 weeks, I : CAT : 65 – 80% HRmax IAT : 2 minutes upper intensity 70 – 90% HRmax, 3 minutes recovery intensity 60 – 70% HRmax T : CAT, IAT T : 30 – 50 minutes	CAT (Continuous Aerobic Training) and IAT (Intermittent Aerobic Training) are equally effective in reducing anthropometric indices and hyperandrogenism, as well as improving quality of life in women with PCOS..
Ribeiro, et al	T : 87 C : 30 I : 57	18 – 39	CAT (n = 28) IAT (n = 29)	F : 3 times a week for 16 weeks I : warm up & cool down 50 – 60% HRmax CAT : 70% HRmax IAT : upper intensity 80% HRmax, recovery intensity 60% HRmax T : CAT, IAT T : 3 0 – 50 minutes	The intervention did not have an impact on telomere length and inflammatory parameters, however, it was able to reduce testosterone levels and anthropometric indicators in PCOS.
Javid, et al	T : 24 C : 12 I : 12	20 – 40	Home-based aerobic exercise	F : Every day at 11 AM for 16 weeks	Aerobic exercise performed at home for 16 weeks can

				I : 22 step per minutes T : aerobic stepping program	reduce insulin resistance and inflammatory factors in patients with PCOS.
Pandit, et al	T : 60 C : 30 I : 30	20 – 40	Home-based aerobic exercise	F : 3 or 5 times a week for 20 weeks I : Heart rate is maintained at ≥120 bpm during physical activity T :aerobic exercise T :30 minutes	Aerobic exercise performed at home for 20 weeks is effective in reducing insulin resistance and inflammatory factors in patients with PCOS.

T: Total samples analyzed; C: Control group; I: Intervention group; MICT: Moderate Intensity Continuous Training; HIIT: High Intensity Intermittent Training; CAT: Continuous Aerobic Training; IAT: Intermittent Aerobic Training; HR: heart rate; HRR: heart rate reserve – calculated by subtracting HRrest from HRmax. [19]

4 Discussion

All research articles utilized in this study employed moderate to vigorous intensity during aerobic exercise. To determine exercise intensity, one approach is to use maximum heart rate (HRmax), as conducted by Costa et al. and Ribeiro et al. HRmax represents the maximum heart rate a person can achieve during physical activity. The conventional method of calculating HRmax (220 - age) is now generally discouraged due to its tendency to provide generalized results (overestimated or underestimated result) .[24] The calculation of HRmax in healthy individuals according to Tanaka et al. is determined by the formula HRmax = 208 - (0.7 x age).[25] Moderate intensity aerobic exercise, according to ACSM, is typically defined as exercising at 50-70% of HRmax, while vigorous intensity is considered to be at 70-85% of HRmax.[24]

4.1 The effect of aerobic training exercise on insulin resistance

Insulin resistance can improve with regular exercise. Recent studies have shown that aerobic exercise at a moderate intensity for 30 minutes, 3 times a week, for a minimum of 8 weeks, can improve insulin sensitivity. This exercise regimen has shown benefits in various groups, including men and women with diabetes, impaired glucose tolerance, obesity, sedentary lifestyle, metabolic syndrome, and type 2 diabetes mellitus.[26] In the study conducted by Costa et al., total cholesterol levels were observed to improve, while glucose and insulin levels did not show significant improvement. This finding is

consistent with the study conducted by Hutchison et al. in 2011. Their research stated that to improve metabolic indicators, a minimum of 12 weeks is required.[27]

Insulin resistance is closely associated with proteins involved in inflammation in the human body, such as IL-6, tumor necrosis factor-alpha (TNF-α), and c-reactive protein (CRP). CRP is a protein produced by the liver in response to inflammation in the body, and its level in the blood can be used as an indicator of inflammation. IL-6, on the other hand, is a protein compound that inhibits glycogenesis, the breakdown of sugar molecules mediated by insulin, and stimulates glucose production by the liver. Higher levels of CRP are associated with increased production of IL-6, which exacerbates insulin resistance.[22]

With aerobic exercise, physiological conditions are adjusted, such as increasing fat tissue reduction and reducing inflammatory markers like hs-CRP, which leads to a decrease in IL-6. This decrease in IL-6 is expected to improve insulin sensitivity.[28] Furthermore, aerobic exercise can enhance glucose clearance by increasing skeletal muscle capillarization, blood flow, and the activity of hexokinase and glycogen synthesis. This results in an increase in muscle mass and the number of glucose transporter proteins, thereby improving insulin sensitivity. [22]

4.2 The effect of aerobic exercise on hyperandrogenism

Hyperandrogenism is closely related to insulin resistance in the body. When insulin sensitivity improves, symptoms of hyperandrogenism typically improve as well. This is characterized by a decrease in total testosterone levels, DHEAS, and androstenedione, all of which are associated with hyperandrogenism in PCOS. Improved insulin sensitivity and glucose regulation can reduce androgen synthesis and hyperandrogenemia in women with PCOS, potentially halting the process of premature ovarian follicle growth and menstrual cycle irregularities. [22]

4.3 Aerobic exercise and anthropometric indicators

One of the most common features of PCOS is the tendency to accumulate fat in the central area of the body, particularly around the abdomen. This accumulation includes both visceral fat and subcutaneous fat beneath the skin. Fat accumulation can be identified through measurements such as BMI and waist-to-hip ratio (WHR). Even individuals with a healthy BMI can experience abdominal obesity due to the accumulation of visceral fat. Visceral fat can contribute to insulin resistance as it produces IL-6. [15] Indeed, reducing visceral fat is likely to lead to an increase in insulin sensitivity. Visceral fat is metabolically active and produces various substances, including inflammatory cytokines, that can interfere with insulin signaling and contribute to insulin resistance. By reducing visceral fat through lifestyle interventions such as aerobic exercise and a healthy diet, insulin sensitivity can be improved, leading to better glucose regulation and overall metabolic health.

4.4 Dose of aerobic exercise program

From the six journals that have been discussed, each of them has its own activity, frequency, dose, and objective. In order to benefit from aerobic exercise, the program should be performed regularly and consistently. To measure the heart rate to enter the aerobic exercise training zone, a smartwatch or other monitoring devices can be used. Costa et al. and Ribeiro et al. used HRmax to calculate the training intensity. It can be calculated using : [25].

$$HRmax = 208 - (0,7 \times age) \quad (1)$$

As for the target heart rate to be achieved during exercise, it can be calculated using : [24]

$$HR\ target = HRmax \times \%\ desired\ intensity \quad (2)$$

So, if someone is 21 years old, their HRmax would be calculated as 208 - (0.7 x 21) = 193 bpm. Then, for the target heart rate during exercise with a desired intensity of 60%, the target HR would be calculated as 193 x 60% = 116 bpm.

Training intensity is divided into three categories: light, moderate, and vigorous/hard. Light intensity falls within the range of 50-64% of HRmax, while moderate intensity falls within the range of 64-77% of HRmax. Vigorous intensity, on the other hand, falls within the range of 77-94% of HRmax.. [21]

Home-based exercise interventions have a significant impact on individual motivation, as individuals are more likely to choose activities they enjoy and can consistently engage in. This can lead to greater consistency and enjoyment in performing the exercises. This is because the feeling of enjoyment or satisfaction also plays a role in the effects of exercise. An alternative to home-based exercise is engaging in activities outdoors with a community, as demonstrated in the study conducted by Costa et al. An enjoyable exercise environment, such as being surrounded by trees or other vegetation, can have an influence on both physiological and psychological responses.[22]

5 Conclusion

From the 6 reviewed articles, aerobic exercise interventions have been shown to reduce clinical manifestations of PCOS, including insulin resistance, hyperandrogenism, and excess weight or fat accumulation as measured by anthropometric indicators. The exercise performed should fall within the training zone to meet the criteria for moderate-intensity aerobic exercise, which is approximately 64-77% of HRmax. Exercise should be performed at least 3 times a week, for a minimum duration of 12-16 weeks. However, for more significant results, aerobic exercise can be consistently

performed for 20 weeks or more. By engaging in aerobic exercise of any type, women with PCOS can still experience the benefits of exercise..

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