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## Literature Review: Effect Moderate Intensity Training on Folliculogenesis Vs Moderate Intensity Continuous Training on Endometrium

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### Abstract

**Background:** An imbalance between incoming calorie intake and expended energy can cause several risks such as obesity, diabetes, reproductive cycle disorders, infertility, endometrial proliferation, and even endometrial cancer. This study aims to analyze the effect of MICT and MIIT on folliculogenesis and MICT on endometrial thickness.

**Subjects and Method:** The method used is to collect and analyze related research articles.

**Results:** Articles from 2013-2022 (10 years) discussing

moderate exercise using Indonesian and English.

**Conclusion:** In folliculogenesis, moderate intensity interval training can result in a decrease in FSH through inhibition of GnRH which can affect the development of follicles that are not appropriate. Meanwhile, moderate intensity continuous training can increase FSH so as to provide proper follicular development. While the effect on the endometrium, moderate intensity continuous training can reduce estrogen secretion so that it affects changes in uterine tissue.

**Keywords:** Moderate Exercise, Folliculogenesis, Endometrium

### Background

Obesity is a world problem that is still increasing, especially in women. Obesity causes morphological changes in a woman's ovaries and a decrease in the number of fertile eggs (Hilal *et al.*, 2020). An imbalance between incoming calorie intake and energy expended causes excessive levels of calories or fat in the body. This can affect the production of the hormone estrogen, thereby triggering endometrial proliferation, endometrial hyperplasia, anovulation, infertility, and miscarriage (Sa'adi *et al.*, 2019)<sup>[9]</sup>. Someone is said to be obese if they have a BMI  $\geq 30$  (WHO, 2019)<sup>[17]</sup>. The prevalence of obesity in women is greater than in men. The prevalence rate of obesity in women in 2018 was 44.40 % (BPS, 2018). Obesity can occur due to lifestyle, unhealthy eating patterns, and lack of physical exercise (Lutfi *et al.*, 2021). Physical exercise is an important point for reducing obesity. One of the physical activities that can be done is moderate intensity exercise. This exercise is physical exercise of moderate duration. Physical exercise can increase blood flow rate and uterine metabolism in women (Samad *et al.*, 2021). Physical exercise results in a significant increase in the 2-OHE1/16 $\alpha$ OHE1 ratio which can affect estrogen metabolism in women (Smith *et al.*, 2013). Low to moderate intensity physical exercise such as brisk walking and swimming can increase the ovulation and pregnancy rates of women with PCOS and improve menstrual cycles, body composition, and metabolism (Benham *et al.*, 2018) Furthermore, physical exercise has an effect on folliculogenesis with reduces the number of follicles that are 6 to 20 mm in size, while increasing the number of follicles that are over 20 mm in size, and lengthens the inter-ovulatory interval in mares (DEKelley *et al.*, 2011). According to research (Rahayu *et al.*, 2021)<sup>[11]</sup> moderate intensity exercise is better for follicular development than high or low intensity physical exercise. This proves that moderate intensity exercise increases follicular maturation, with a positive impact on female fertility. Based on its shape, moderate intensity training consists of two, namely on an ongoing basis and intervals.

According to research conducted by (Konget *et al.*, 2016) Moderate Intensity Continuous Training (MICT) has more significant results in reducing fat levels compared to High Intensity Interval Training (HIIT), although in terms of time MIIT is more economical. The amount of fat content in the body affects the performance of the hypothalamic axis - GnRH secretion - anterior pituitary - FSH and LH. The hormones FSH and LH affect the production of estrogen in the ovaries. So that a decrease in fat levels in the body can prevent the risk of changes or increases in endometrial thickness.

Moderate intensity exercise is an effective method of weight loss. However, its effect on the endometrium and folliculogenesis is unknown. Therefore, it is necessary *literature review* regarding the effect of moderate intensity exercise on the endometrium

and folliculogenesis.

### Subjects and Method

The method used is to collect and analyze related research articles. There are several criteria for this literature review including: 1) Type of Participants: human or animal 2) Type of intervention: Moderate exercise/moderate intensity Interval Training and moderate intensity continuous training), 3) Outcome Type: Follicle and endometrial development. The database used is Garuda and Google Scholar using the keywords moderate exercise, follicular development, MIIT, MICT. All keywords are associated with a Boolean "OR" to get as many quotes as possible.

The articles reviewed are all articles from 2013-2022 (10 years) which discuss moderate exercise using Indonesian and English.

### Results and Discussion

#### Moderate Exercise

*Moderate exercise* consists of several types of exercise, such as running and swimming. Running can be done on a treadmill to control and monitor the pace according to moderate intensity training (Høydal *et al.*, 2007). Exercise in the form of running at a speed of 18 m/minute, with a 5% incline for 30 minutes, with a frequency of 5 times a week (Somboonwong *et al.*, 2015). Exercise in the form of swimming with an additional load of 6% body weight which is carried out continuously or periodically. In research (Mahadani, 2021), experimental animals, namely rats, were given an additional load in the middle position of the rat's tail. The duration of swimming is gradually increased every week, with a frequency of 5 times a week.

#### Folliculogenesis

Folliculogenesis is the process of forming follicles that go through several growths and developments until they either end by producing mature oocytes that turn into corpus luteum (CL) or die into atresia. Folliculogenesis is divided into two phases, namely the preantral or gonadotropin-independent phase and the antral (Graaf) or gonadotropin-dependent phase. Folliculogenesis reaching the ovulation stage requires a long process through two phases. Several growth factors affecting the preantral phase are produced locally via autocrine or paracrine processes. Whereas, *Follicle Stimulating Hormone* (FSH) and *Luteinizing Hormone* (LH) dominates the regulation of the antral phase assisted by several other growth factors that stimulate cell proliferation and contribute to gonadotropin activity (Anwar, 2005; Gershon and Dekel, 2020)<sup>[1,4]</sup>.

#### Endometrium

The endometrium is the epithelial lining that lines the uterine cavity. The surface of the endometrium is composed of a single layer of ciliated columnar cells and tubular glands that extend beneath a thick lamina propa called the endometrial stroma. The functional layer is located superficially which will peel off every month while the basal layer is where the functional layer originates which does not peel off. During the menstrual cycle, the endometrial tissue proliferates, increasing in thickness from about 1 mm after menstruation to 6 mm during secretion (Peckham, 2014)<sup>[10]</sup>. According to Sarwono, (2014)<sup>[13]</sup> changes in endometrial histology are caused by fluctuations in ovarian hormones. Endometrial histological changes consist of; proliferative

phase, secretory phase, and menstrual phase.

#### Effect of Moderate Intensity Interval Training on Folliculogenesis

*Moderate intensity interval training* is kind *moderate exercise* who have rest sessions between training cycles. Treatment *moderate intensity interval training* can lose a significant amount of weight i.e. 2% according to the amount of average weight loss observed in most obesity programs (Reljic D., *et al.*, 2021)<sup>[12]</sup>. Therefore MIIT is effective for weight loss in obese subjects. Weight loss has a positive feedback loop as it increases FSH levels. This is in line with research conducted by (Mahadani, 2021) the group without giving high calories showed an increase in FSH compared to the group that was given high calories. Giving high calories causes an increase in blood sugar or hyperglycemia so that you become overweight. Weight gain causes an increase in insulin hormone resulting in an increase in GnRH. The hormone GnRH stimulates the production of more LH and decreases the secretion of FSH (Uadia *et al.*, 2017)<sup>[16]</sup>.

However, based on research (Mahadani, 2021) the MIIT treatment in rats induced by high calories showed a decrease in FSH levels. This can be caused in addition to sports that use repetition many times and provide a high calorie diet. In general, the reproductive axis is inhibited due to exercise through direct or indirect inhibition of GnRH by corticotropin-releasing hormones, endorphins, and glucocorticoids, thereby reducing the secretion of luteinizing hormone (LH) and FSH, as well as gonadal hormone secretion. and make target tissues of sex steroids resistant to these hormones. In follicular development, FSH plays an important role in the transition of the primary follicle to the preantral follicle.

#### Effect of Moderate Intensity Continuous Training on Folliculogenesis

Moderate intensity continuous training is continuous training without rest which is carried out for moderate duration (Lutfi, 2020)<sup>[7]</sup>. Moderate intensity exercise is determined by 50-70% VO<sub>2</sub> maximum (maximum oxygen uptake) and a loading of 6% body weight (Rahayu *et al.*, 2021)<sup>[11]</sup>.

Influence moderate intensity continuous training in obese rats can increase the number of insulin receptors in adipose tissue, so that it can improve insulin action in correcting obesity (Haryanto *et al.*, 2019)<sup>[5]</sup>. Therefore, Moderate intensity continuous training effective as a method of weight loss. Exercise in weight loss can prevent obesity which is at risk of infertility. This is in line with Kiranmayee's research *et al.* (2017)<sup>[6]</sup> who found that moderate intensity exercise on ovarian reserve markers was associated with high levels of anti-Mullerian hormone and FSH. Thus, during exercise there is a reciprocal relationship between the energy balance and the hypothalamic-pituitary-gonadal axis which triggers proper follicular development. Rahayu's research *et al.* (2021)<sup>[11]</sup> also proved that moderate intensity exercise has a better effect than other intensity exercises, because an increase in ovulation status during moderate exercise can increase the response and sensitivity of follicles to FSH and LH which can affect the number of follicles in follicle growth and development. According to the folliculogenesis phase, an increase in FSH during exercise will affect the gonadotropin-dependent antral phase in the hope that there

will be proper follicular development.

### Effect of Moderate Intensity Continuous Training on the Endometrium

Physical exercise is a structured, systematic and continuous sports activity that aims to improve body fitness. *Moderate Intensity Continuous Training* (MICT) are exercises that are performed for a certain duration and maintain speed without any rest breaks.

*Moderate intensity interval training* is one of moderate intensity exercise that has a rest period each workout.

The study that compared the two physical exercises, namely Keating, *et al* (2014) stated that moderate intensity continuous physical exercise was more significantly able to reduce body fat levels compared to interval physical exercise, even though in terms of MIIT time it was faster.

Several studies have examined that physical exercise can cause a decrease in body fat levels which triggers a decrease in the hormones FSH and LH. This is associated with changes in histological structure or proliferation of the endometrial thickness influenced by the hormone estrogen. At the time of doing sports can inhibit the reproductive axis through GnRH thereby affecting the levels of FSH, progesterone and estradiol Uadia PO, *et al.*(2017) [16]. Chang's research *et al.* (2020) [2] that moderate-intensity continuous physical exercise for 12 weeks was carried out in a group of mice exposed to a high-fat diet, the results were that it could reduce blood glucose levels in mice. Research conducted by Oroh, *et al.* (2021) [8] stated that moderate-intensity continuous physical exercise (MICT) can reduce fat mass and fat presentation in the body. This is associated with the state of fat in the body affecting the production of estrogen levels in the ovaries due to a relationship with the performance of the hypothalamus which functions to stimulate the pituitary in producing FSH and LH (Saadi, *et al.* 2019) [9].

Research conducted by Saadat *et al* (2016) [15] stated that the group of rats that were treated with MICT in the form of swimming had lower levels of estradiol and FSH. Lower FSH production can reduce estrogen secretion so that uterine tissue undergoes dynamic histological structural changes.

### Withclussion

Moderate intensity interval training is more effective in weight loss. However, in folliculogenesis, moderate intensity interval training can result in a decrease in FSH through GnRH inhibition which can affect the development of follicles that are not appropriate. Meanwhile, moderate intensity continuous training can increase FSH so as to provide proper follicular development. While the effect on the endometrium, moderate intensity continuous training can reduce estrogen secretion so that it affects changes in uterine tissue.

### References

1. Anwar R. Ovarian Morphology and Function. Padjadjaran Library, 2005, 1-16. Available at: [http://pustaka.unpad.ac.id/wp-content/uploads/2010/05/morphology\\_dan\\_function\\_ovarium.pdf](http://pustaka.unpad.ac.id/wp-content/uploads/2010/05/morphology_dan_function_ovarium.pdf).
2. Chang G, *et al.* Exercise Affect Blood Glucose Levels and Tissue Chromium Distribution in High-Fat-Diet-Fed C57BL6 Mice, 2020, 1-2.
3. Fisher G, Brown A, Brown M, Alcom A, Noles C, Winwood L, *et al.* High intensity-interval vs moderate intensity-training for improving cardiometabolic health in overweight or obese males: A Randomized controlled trial. PLoS ONE. 2015; 10(10):1-15. <https://pubmed.ncbi.nlm.nih.gov/26489022>.
4. Gershon E, Dekel N. Newly Identified Regulators of Ovarian Folliculogenesis and Ovulation. International Journal of Molecular Sciences. 2020; 21(12):1-18.
5. Haryanto P, Pangkahila A, Safe IGM, Siswanto FM. The Influence of Moderate Intensity Exercise to The Level of Insulin Receptors on Adipose Tissue of Obese Male Rats. 2019; 7(1):23-27.
6. Kiranmayee D, Praveena T, Himabindu Y, Sriharibabu M, Kavya K, Mahalakshmi M. The Effect of Moderate Physical Activity on Ovarian Reserve Markers in Women of Reproductive Age Under and Over 30 Years. Journal of Human Reproductive Sciences. 2017; 10(1):44-48. Available at: <https://pubmed.ncbi.nlm.nih.gov/28479755/>.
7. Lutfi AR. The Effect of Combination of Calorie Restriction and Moderate Continuous Exercise on Serum Free Fatty Acid (FFA) Levels and Visceral Fat Weight in Female Mice that were exposed to a High Caloric Diet. Thesis, 2020, 12-31.
8. Oroh P, Herlina W, Engka J. Physical Exercise in Obese Patients. Biomedical Journal (Jbm). 2021; 13(1):34-43.
9. Pambudi D, Saadi A, Sudjarwo. Analysis of Antimullerian Hormone (AMH) in Serum in Various Body Mass Index Categories. Surya Medika Journal. 2019; 5(1).
10. Peckham M. Histology at a glance. 1st ed. Jakarta: Erlangga, 2014.
11. Rahayu FK, Dwiningsih SR, Saadi A, Herawati L. Effects of Different Intensities of Exercise on Folliculogenesis in Mice: Which is Better? Clinical and Experimental Reproductive Medicine. 2021; 48(1):43-49.
12. Reljic D, Frenk F, Herrmann HJ, Neurath MF, Zopf Y. Effects of very low volume high intensity versus moderate intensity interval training in obese metabolic syndrome patients: A randomized controlled study. Scientific Reports. 2021; 11(1):1-14.
13. Sarwono P. MID SCIENCE. Jakarta: PT Bina Pustaka, 2014.
14. Saadat H, Chaya V, Rai L, *et al.* Factor Influencing Endometrial Thickness In Postmenopausal Women. Annals of medical and health sciences research. 2014; 4(4):608-614. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4160690>.
15. Seyed Saadat SN, Mohammadghasemi F, Ebrahimi H, Rafati Saje, Chatrnour G. Ovarian and Uterine Alterations Following Forced Swimming: An Immunohistochemical Study. Int J Reprod Biomed. 2016; 14:629-36.
16. Uadia PO, Nwokolo CC, Arainru AE, Agwubike EO, Akpata CB. Effect of physical and flexibility exercise on certain hormones and fasting blood sugar of some young Nigerian adults. Too J Pharm Res. 2017; 16:245-50.
17. WHO. Obesity, 2019. Available at: [https://www.who.int/health-topics/obesity#tab=tab\\_1](https://www.who.int/health-topics/obesity#tab=tab_1).