2024, Retos, 51, 726-731

Aerobic Exercise Increases Release of Growth Hormone in the Blood Circulation in Obese Women
El ejercicio aeróbico aumenta la liberación de la hormona del crecimiento en la circulación sanguínea en mujeres obesas

*Adi Pranoto, *Purwo Sri Rejeki, *Muhammad Miftahussurur, **Ghana Firsta Yosika, *Mufarrihul Ihsan, *Lilik Herawati, *Ilham Rahmanto, ***Shariff Halim
*Universitas Airlangga (Indonesia), **Universitas Tanjungpura (Indonesia), *** University Technology MARA (UiTM) Pulau Pinang (Malaysia)

Abstract. Physical exercise is one of the modulators in increasing the release of growth hormone (GH) levels in blood circulation, but the effective exercise model for obese subjects is still being debated. Therefore, this study aims to prove the effect of aerobic exercise on increasing the release of GH levels in the blood circulation in obese women. A total of 20 obese adult women, aged 21.00 ± 1.08 years were selected to be subjects in the study and were given one aerobic exercise intervention by running on a treadmill at moderate-intensity (60-70% HR_{max}) for 40 minutes. The ELISA method was used to measure the release of GH levels in all samples (pre- and post-exercise). Statistical analysis in this study used an independent sample t-test with a significant level of 5%. The results showed that the release of GH levels in the blood circulation was found to be higher in post-exercise compared to pre-exercise after one session of aerobic exercise (484.92±128.29 vs 892.63±273.54 pg/mL; p=0.001) and has a large effect size with a Cohen's d value of 1.909. GH levels in the post-exercise blood circulation in the aerobic exercise group (Exr) were also found to be higher than the GH levels in the control group (Ctr) (892.63±273.54 vs 542.97±140.01 pg/mL; p=0.003) and has a large effect size with a Cohen's d value of 1.609. This study proves that one session of aerobic exercise with moderate intensity increases the release of circulating GH levels in obese women. Therefore, aerobic exercise with moderate intensity can be used as an alternative therapy option to increase the release of circulating GH levels in individuals with obesity.
Keywords: aerobic exercise, growth hormone, metabolism, obesity.

Resumen. El ejercicio físico es uno de los moduladores del aumento de la liberación de los niveles de la hormona del crecimiento (GH) en la circulación sanguínea, pero aún se está debatiendo cuál es el modelo de ejercicio eficaz para sujetos obesos. Por tanto, este estudio tiene como objetivo demostrar el efecto del ejercicio aeróbico sobre el aumento de la liberación de niveles de GH en la circulación sanguínea en mujeres obesas. Un total de 20 mujeres adultas obesas, con edades de 21,00 ± 1,08 años, fueron seleccionadas para participar en el estudio y se les realizó una intervención de ejercicio aeróbico corriendo en una cinta rodante a intensidad moderada (60-70% FCmáx) durante 40 minutos. Se utilizó el método ELISA para medir la liberación de niveles de GH en todas las muestras (antes y después del ejercicio). El análisis estadístico en este estudio utilizó una prueba t de muestra independiente con un nivel significativo del 5%. Los resultados mostraron que la liberación de niveles de GH en la circulación sanguínea fue mayor en el post-ejercicio en comparación con el pre-ejercicio después de una sesión de ejercicio aeróbico (484,92±128,29 vs 892,63±273,54 pg/mL; p=0,001) y tiene un tamaño de efecto grande con un valor d de Cohen de 1,909. También se encontró que los niveles de GH en la circulación sanguínea post-ejercicio en el grupo de ejercicio aeróbico (Exr) eran más altos que los niveles de GH en el grupo de control (Ctr) (892,63 ± 273,54 vs 542,97 ± 140,01 pg/mL; p = 0,003). y tiene un tamaño de efecto grande con un valor d de Cohen de 1,609. Este estudio demuestra que una sesión de ejercicio aeróbico de intensidad moderada aumenta la liberación de niveles circulantes de GH en mujeres obesas. Por lo tanto, el ejercicio aeróbico de intensidad moderada se puede utilizar como una opción de terapia alternativa para aumentar la liberación de niveles circulantes de GH en personas con obesidad.
Palabras clave: ejercicio aeróbico, hormona del crecimiento, metabolismo, obesidad.

Fecha recepción: 21-05-23. Fecha de aceptación: 05-10-23
Purwo Sri Rejeki
purwo-s-r@fk.unair.ac.id

Introduction

The prevalence of obesity in the world continues to increase due to high food intake followed by low physical activity (Alvarez et al., 2020) and is dominated by women compared to men (Blüher, 2019). Physiologically, obesity has become a risk factor that may affect the release or regulation of growth hormones (Høgild et al., 2019). Hejla, Dror, Pantanowitz, Nemet, & Eliakim (2022) reported that GH secretion was lower in overweight and obese individuals than in normal weight individuals. The association of obese individuals with low growth hormone levels was also reported by Savastano, Di Somma, Barrea, & Colao (2014) Obesity causes a decrease in GH secretion, resulting in increased fat mass, decreased lipolysis, and decreased insulin sensitivity, leading to metabolic disorders (Høgild et al., 2019). Obesity stands as a primary risk factor for mortality (Hruby & Hu, 2015). Therefore, decreased GH secretion in obese individuals may lead to an increase in serious health problems (Misra et al., 2008). Obesity is generally caused by a long-term imbalance between calories consumed and calories expended (Camacho & Ruppel, 2017; Solis-Urra et al., 2019). Promoting a less sedentary lifestyle and incorporating regular physical activity are key factors in preventing the development of obesity (Romieu et al., 2017; Dávila Grisalez, Mazuera Quiceno, Carreño Herrera, & Henao Corrales, 2021).

Exercise is promoted as an appropriate and effective approach to increase GH-mediated energy expenditure to prevent the development of obesity (Rejeki et al., 2023; Strasser, 2013). Exercise can also improve metabolic health by increasing physical performance, lipid and glucose metabolism (lipolysis and insulin sensitivity), and weight maintenance (Wang et al., 2020; Dávila Grisalez, Mazuera

Quiceno, Carreño Herrera, & Henao Corrales, 2021), so it can improve metabolic health (Dourida et al., 2019). Exercise is also known to prevent deficiency of GH secretion in overweight and obese individuals (Al-Samerria & Radovick, 2021). This finding was supported by research conducted by Sugiharto, Merawati, Pranoto, & Susanto (2022), which demonstrated that a single session of endurance training at an intensity of 60-70% HR_{max} performed for 30-35 minutes on a treadmill increased GH secretion in obese women. Research conducted by Berry, Hubal, & Wideman (2018) also reported that treadmill exercise in moderate intensity performed for 60 minutes increased the release of GH levels in healthy and pre-diabetic subjects with obesity (BMI = 32.1±4.0 kg/m^2). However, research by Sasaki et al. (2014) found no change in GH response after 4 weeks (3 days/week, 12 sessions total) of high-intensity interval training (10 sets of 1 min pedaling at 85% VO_2max with a 30 s rest between sets) in sedentary men. In another case, research conducted by Hejla, Dror, Pantanowitz, Nemet, & Eliakim (2022) a single session of the Wingate anaerobic test (WAnT) with 10 bouts of 15-second cycling separated by 1 minute of rest significantly reduced GH levels in children with overweight and obesity compared with those with normal weight. Meanwhile, a study by Deemer et al. (2018) used a crossover design in five young women to compare the effects of high-intensity interval exercise (HIE) (four 30-s "all-out" sprints with 4.5 min of active recovery) and 30-min continuous cycling with moderate-intensity continuous exercise (MOD) on GH secretion. The results showed that a single bout of HIE increases 12.5 h GH secretion compared to the sedentary control condition and was not different from MOD exercise.

Based on these findings, it is still debatable which exercise model is effective in increasing the release of GH levels in obese subjects. Therefore, the primary objective of this study is to demonstrate the effect of aerobic exercise at moderate intensity on increasing the release of GH levels in the blood circulation, especially in obese women since the prevalence of obesity is higher in this population than in men. The results of this study can strengthen the existing research that is still being discussed and used as a potential non-pharmacological treatment option to enhance the release of GH levels in the blood circulation of individuals with obesity, thereby improving their metabolic health.

Materials and methods

This research adopts a true experimental design with a pre-test and post-test control group. A total of 20 obese adult women, age 21.00 ± 1.08 years, with body mass index (BMI) 29.59 ± 1.24 kg/m^2 (according to Asia-Pacific guidelines), percentage of body fat (PBF) 45.17±2.90 %, blood pressure (systolic: 113.80 ± 3.65 mmHg; diastolic: 75.25 ± 3.96 mmHg), resting heart rate (RHR) 72.15 ± 6.08 bpm, oxygen saturation (SpO_2) 97.60 ± 1.14 %, maximum oxygen volume (VO_{2max}) 27.43 ± 2.56 mL/kg/min, and fasting of blood glucose (FBG) 90.50±5.29 mg/dL were selected to be subjects in this research. The selected subjects had no history of chronic diseases, smoking, or alcohol consumption. It was also confirmed that all subjects were not active in sports activities and were not enrolled in any weight loss program that involved the use of medication or dietary modifications. Before the study was conducted, all selected subjects were given a detailed description of the research objectives and methods which was clearly and consciously communicated verbally or in writing, and then all subjects completed and signed an informed consent form. The day before the test, all subjects were instructed to get enough sleep (7-8 hours/night) and fast overnight for 10-12 hours. During the research, water intake was monitored to maintain hydration. The test was carried out in the morning on the 5-7^{th} day of the menstrual cycle, to control hormonal status.

The subjects with matching BMI were randomly assigned to participate in experimental: the control group (Ctr; n = 10), and the aerobic exercise group (Exr; n = 10). The calculation of the sample size using the Higgins & Kleinbaum formula (1985) with reference values from previous similar studies so that a minimum sample size was obtained and 20 subjects were taken (Sugiharto, Merawati, Pranoto, & Susanto, 2022). All procedures performed in this research were approved by the Health Research Ethics Committee, Faculty of Medicine, Airlangga University (No. 283/EC/KEPK/FKUA/2021).

The aerobic exercise intervention program was implemented and supervised by professional staff from Pusat Pelayanan Kesehatan Olahraga (PPKO) in Malang City, East Java, Indonesia, to minimize the occurrence of incorrect use of the treadmill and the risk of injury. Aerobic exercise was performed on a treadmill in a single session at an intensity of 60-70% of HR_{max}, following the research by Pranoto et al. (2023), but with a duration of 40 minutes. Warm-up and cool-down were performed by brisk walking on the treadmill at an intensity of 50% HR_{max} for 5 minutes each (Rejeki et al., 2023). HR_{max} was determined using the following formula: HR_{max} – age in years (220 - age in the year) (Santos et al., 2019; Susanto, Sugiharto, Taufiq, Pranoto, & Purnomo, 2023). Heart rate was monitored during aerobic exercise using the Polar H10 heart rate sensor (Pranoto et al., 2023). The intervention would be stopped if abnormal physical signs were detected, such as shortness of breath, rapid increase in heart rate, dizziness, nausea, pale face, and muscle cramps. The environment used for the research site has a room temperature of 26 ± 1°C with a humidity level of 50 – 70% (Rejeki et al., 2023). During the intervention, the subjects did not experience any problems or difficulties that interfered with the completion of the aerobic exercise session. Details of the aerobic exercise intervention program and the blood sampling procedure are shown in Figure 1.

2024, Retos, 51, 726-731

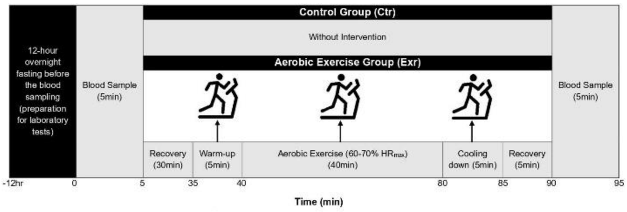

Figure 1. Exercise protocol and blood sampling

Growth hormone (GH) levels were measured 30 minutes before (pre-exercise) and 10 minutes after exercise (post-exercise) using the Human GH ELISA Kit (Cat. No. E-EL-H0177; Elabscience, Inc., USA) with detection range: 78.13-5000 pg /mL and sensitivity: 46.88 pg/mL.

The normality and homogeneity test was performed using the Shapiro-Wilk and Levene's tests. The paired sample t-test was used to determine differences in GH levels before and after exercise in each group, while the independent sample t-test was used to determine differences in GH levels between the control group and the aerobic exercise group. Statistical analyses were performed at a 5% significance level, and all values are presented as the mean ± standard deviation (SD). The Statistical Package for The Social Sciences (SPSS) software was used for all statistical analyses.

Results

Table 1 presents the basic data on the characteristics of the subjects in the control group (Ctr) and the aerobic exercise group (Exr) and the result was no significant difference between the groups. The results of growth hormone (GH) level analysis in both groups are shown in Figure 2-3.

Table 1.
The characteristics of obese subjects

Parameters	unit	n	Ctr	Exr	p-Value
Age	yrs	10	20.90±1.19	21.10±0.99	0.689
Weight	kg	10	76.31±5.86	73.31±6.61	0.297
Height	m	10	1.59±0.05	1.58±0.04	0.699
BMI	kg/m²	10	30.04±1.30	29.14±1.05	0.108
PBF	%	10	46.23±3.04	44.10±2.46	0.102
SBP	mmHg	10	114.40±4.01	113.20±3.36	0.478
DBP	mmHg	10	75.20±4.13	75.30±4.00	0.957
RHR	bpm	10	71.40±7.32	72.90±4.82	0.596
SpO_2	%	10	97.50±1.27	97.70±1.06	0.707
VO_{2max}	mL/kg/min	10	26.79±2.07	28.06±2.93	0.278
FBG	mg/dL	10	92.30±4.57	88.70±5.56	0.132

Description: BMI: Body mass index; DBP: Diastolic blood pressure; FBG: Fasting of blood glucose; PBF: Percentage of body fat; RHR: Resting heart rate; SBP: Systolic blood pressure; SpO_2: oxygen saturation; VO_{2max}: maximum oxygen volume. Ctr: Control group; Aerobic exercise group. Values are expressed as mean ± SD. Independent sample t-test was used to determine the p-Value.

Figure 2 shows the mean of GH levels between pre-exercise vs. post-exercise on Ctr (533.98±137.49 vs. 542.97±140.00 pg/mL; p=0.714), and Exr (484.92±128.29 vs. 892.63±273.54 pg/mL; p=0.001) has a large effect size with a Cohen's d value of 1.909. Meanwhile, Figure 3 shows the difference in GH levels between Ctr vs. Exr at pre-exercise (533.98±137.49 vs. 484.92±128.29 pg/mL; p=0.420), at post-exercise (542.97±140.00 vs. 892.63±273.54 pg/mL; p=0.003) has a large effect size with a Cohen's d value of 1.609, delta (8.99±75.10 vs. 407.71±279.93 pg/mL; p=0.001) has a large effect size with a Cohen's d value of 1.946, and change in GH from pre (3.55±20.31 vs. 94.48±85.91 %; p=0.009) has a large effect size with a Cohen's d value of 1.457

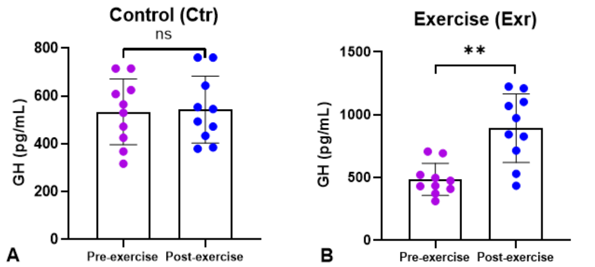

Figure 2. GH levels (pg/mL) pre-exercise and post-exercise in both groups (Ctr, Exr). Description: (A) Ctr: Control group; (B) Aerobic exercise group. (ns) Not significant ($p \geq 0.05$). (**) Significant at pre-exercise ($p \leq 0.001$). Values of GH are expressed as mean ± SD. Paired sample t-test was used to determine the p-Value.

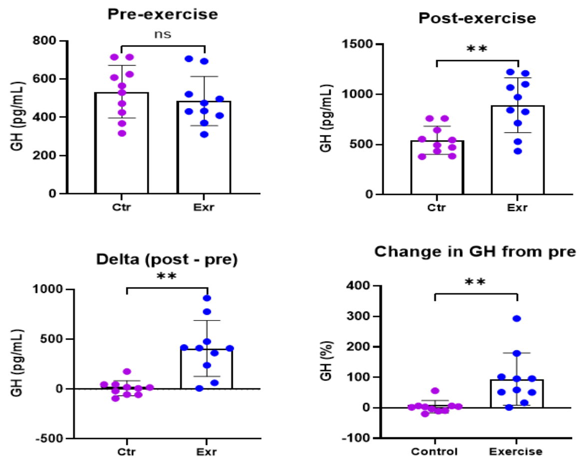

Figure 3. GH levels (pg/mL) between Ctr vs. Exr. Description: (ns) Not significant ($p \geq 0.05$). (**) Significant at the control group (Ctr) ($p \leq 0.001$). Values of GH are expressed as mean ± SD. Independent sample t-test was used to determine the p-Value.

Discussion

Growth hormone (GH) is a polypeptide consisting of 191 single-chain amino acids and the human GH gene is located on chromosome 17q22 and GH synthesis occurs in somatotropic cells in the anterior pituitary gland (Olarescu et al., 2019; Kraemer, Ratamess, & Nindl, 2017; Guyton & Hall, 2014; Greenstein & Wood, 2011). One of the factors that inhibit GH synthesis is obesity (Dichtel et al., 2014). In the presence of obesity, various metabolic disorders such as increased insulin levels (hyperinsulinemia), decreased adiponectin levels (hypoadiponectinemia), increased leptin levels (hyperleptinemia), decreased ghrelin hormone production, and increased free fatty acids (FFA) levels manifest and lead to the suppression of GH secretion from the pituitary gland (Savastano, Di Somma, Barrea, & Colao, 2014). Previous research conducted by Stanley & Grinspoon (2015) found significant differences in the release of circulating GH levels in overweight and obese individuals as opposed to normal-weight individuals. Normal-weight individuals have higher post-exercise GH levels than overweight and obese individuals. The results of this study confirm that overweight and obesity are factors that inhibit the release of GH levels in the blood circulation, so GH levels are lower in overweight and obese individuals than in normal-weight individuals (Sabag, Chang, & Johnson, 2021). Exercise is considered a non-pharmacological approach that can be used to increase the release of GH levels into the blood circulation (Oliver et al., 2010). The study conducted by Gough, Castell, Gatti, & Godfrey (2016) showed that aerobic exercise in the form of running on a treadmill for 40 minutes at a pace 5% below the lactate threshold speed significantly increased serum GH levels. Our results demonstrated that aerobic exercise performed for 40 minutes at an intensity of 60-70% HRmax significantly increases the release of GH levels in blood circulation. This increase is consistent with the research of Sauro & Kanaley (2003) who reported that GH levels were significantly increased in young women after 10 minutes of treadmill and cycling exercise at an intensity of 75% VO_2peak.

The results of this study, shown in Figure 3, demonstrate a significant increase in circulating GH levels after aerobic exercise compared to the control group (no exercise intervention). These findings are consistent with a study by Mannerkorpi et al. (2017), which showed that a 15-minute session of acute moderate-intensity exercise using an ergo cycle significantly increased GH levels in women with a BMI 28.2 ± 5.3 kg/m^2. The increase in GH levels is predicted to be caused by the intervening factor of aerobic exercise which increases energy demand and metabolism. During exercise, the body requires glucose as the main source of energy, which is derived from carbohydrates and fats that are converted into energy (adenosine triphosphate) (Guyton & Hall, 2014). This condition will cause a decrease in blood glucose levels (hypoglycemia) as a result of ingestion and use in the body's cells. The decrease in blood glucose levels causes stimulation of the central nervous system (CNS) to activate the hypothalamus which stimulates GhRH and somatostatin to increase GH secretion in blood circulation (Wood, Clow, Hucklebridge, Law, & Smyth, 2018).

The release of GH secretion into the blood circulation is predicted to remain high for 24 hours after exercise and will gradually decline to baseline conditions in obese women (Sugiharto, Merawati, Pranoto, & Susanto, 2022). This state is very beneficial because it can increase basal metabolism, thus increasing energy expenditure (Al-Samerria & Radovick, 2021), and has implications for reducing fat mass (Dinas, Markati, & Carrillo, 2014). The results of this study indicate a significant role for aerobic exercise as a breakthrough non-pharmacological obesity therapy in reducing the prevalence of obesity (Gar et al., 2020). Our research strengthens previous studies regarding the positive effects of aerobic exercise on GH levels in obese women. However, there are several other factors that increase the release of GH secretion in blood circulation, including gender, age, puberty, exercise, diet, fasting, sleep, and body composition. This study still has some limitations, so further research is recommended to consider these factors, using a larger sample as well as involving male subjects is necessary to obtain best results. It is also advisable for future research to contrast different methods and mediums because can influence the hormonal response of the population. In addition, do not lose sight of the covariate variables because that can affect the dependently.

Conclusion

This study proves that a single 40-minute session of aerobic exercise, performed at an intensity of 60-70% HR_{max}, can increase the release of growth hormone levels in the blood circulation in obese women. Therefore, aerobic exercise can be recommended as a modulator in increasing the release of growth hormone levels in the blood circulation to maintain the balance of glucose metabolism, increase lipolysis, and improve insulin resistance in obesity.

Acknowledgements

We thank you for the support given by the Faculty of Medicine, Airlangga University in this study. We also do not forget to thank all the subjects who participated in this study.

References

Al-Samerria, S., & Radovick, S. (2021). The Role of Insulin-like Growth Factor-1 (IGF-1) in the Control of Neuroendocrine Regulation of Growth. *Cells, 10*(10), 2664. https://doi.org/10.3390/cells10102664.

Alvarez, C. E., Herrera Monge, M. F., Herrera González, E., Villalobos Víquez, G., & Araya Vargas, G. (2020). Sobrepeso, obesidad, niveles de actividad física y autoestima de la niñez centroamericana: un análisis comparativo entre países (Overweight, obesity, physical activity levels, and self-esteem in Central American children: comparative analysis between cou. *Retos, 37*, 238–246. https://doi.org/10.47197/retos.v37i37.71680.

Berry, N. T., Hubal, M., & Wideman, L. (2018). The effects of an acute exercise bout on GH and IGF-1 in prediabetic and healthy African Americans: A pilot study investigating gene expression. *PloS one, 13*(1), e0191331. https://doi.org/10.1371/journal.pone.0191331.

Blüher, M. (2019). Obesity: global epidemiology and pathogenesis. *Nature reviews. Endocrinology*, 15(5), 288–298. https://doi.org/10.1038/s41574-019-0176-8.

Camacho, S., & Ruppel, A. (2017). Is the calorie concept a real solution to the obesity epidemic?. *Global health action, 10*(1), 1289650.

https://doi.org/10.1080/16549716.2017.1289650.

Dávila Grisalez, A. A., Mazuera Quiceno, C. A., Carreño Herrera, A. L., & Henao Corrales, J. L. (2021). Effect of a high intensity aerobic interval training program on an overweight or obese female school population. Retos, 39, 453–458. https://doi.org/10.47197/retos.v0i39.78200.

Deemer, S. E., Castleberry, T. J., Irvine, C., Newmire, D. E., Oldham, M., King, G. A., Ben-Ezra, V., Irving, B. A., & Biggerstaff, K. D. (2018). Pilot study: an acute bout of high intensity interval exercise increases 12.5 h GH secretion. *Physiological reports, 6*(2), e13563. https://doi.org/10.14814/phy2.13563.

Dichtel, L. E., Yuen, K. C., Bredella, M. A., Gerweck, A. V., Russell, B. M., Riccio, A. D., Gurel, M. H., Sluss, P. M., Biller, B. M., & Miller, K. K. (2014). Overweight/Obese adults with pituitary disorders require lower peak growth hormone cutoff values on glucagon stimulation testing to avoid overdiagnosis of growth hormone deficiency. *The Journal of clinical endocrinology and metabolism, 99*(12), 4712–4719. https://doi.org/10.1210/jc.2014-2830.

Dinas, P. C., Markati, A. S., & Carrillo, A. E. (2014). Exercise-Induced Biological and Psychological Changes in Overweight and Obese Individuals: A Review of Recent Evidence. *International Scholarly Research Notices, 2014*, Article ID 964627, 11 pages. https://doi.org/10.1155/2014/964627.

Dourida, M., Tzanela, M., Asimakopoulou, A., Botoula, E., Koutsilieris, M., & Philippou, A. (2019). Endocrine responses after a single bout of moderate aerobic exercise in healthy adult humans. *Journal of applied biomedicine, 17*(1), 46. https://doi.org/10.32725/jab.2018.004.

Gar, C., Rottenkolber, M., Haenelt, M., Potzel, A. L., Kern-Matschilles, S., Then, C., Seissler, J., Bidlingmaier, M., & Lechner, A. (2020). Altered metabolic and hormonal responses to moderate exercise in overweight/obesity. *Metabolism: clinical and experimental, 107*, 154219. https://doi.org/10.1016/j.metabol.2020.154219.

Greenstein, B., & Wood, D. F., (2011). *The Endocrine System at a Glance 3rd Edition, Kindle Edition*. Hoboken, New Jersey: Wiley-Blackwell.

Gough, L., Castell, L. M., Gatti, R., & Godfrey, R. J. (2016). Growth Hormone Concentrations in Different Body Fluids Before and After Moderate Exercise. *Sports medicine - open, 2*(1), 30. https://doi.org/10.1186/s40798-016-0054-z.

Guyton, A. C., & Hall, J. E. (2014). *Medical Physiology 12th Edition*. Jakarta: EGC Medical Book.

Hejla, D., Dror, N., Pantanowitz, M., Nemet, D., & Eliakim, A. (2022). Reduced Growth Hormone Response to Anaerobic Exercise Among Children With Overweight and Obesity. *Journal of strength and conditioning research, 36*(8), 2194–2197. https://doi.org/10.1519/JSC.0000000000003798.

Higgins, J.K., & Kleimbaun, A.P. (1985). Design Methodology for Randomized Clinical Trials; Family Health International: Arlington, VA, USA. pp. 24–25.

Høgild, M. L., Gudiksen, A., Pilegaard, H., Stødkilde-Jørgensen, H., Pedersen, S. B., Møller, N., Jørgensen, J. O. L., & Jessen, N. (2019). Redundancy in regulation of lipid accumulation in skeletal muscle during prolonged fasting in obese men. *Physiological reports, 7*(21), e14285. https://doi.org/10.14814/phy2.14285.

Hruby, A., & Hu, F. B. (2015). The Epidemiology of Obesity: A Big Picture. *PharmacoEconomics, 33*(7), 673–689. https://doi.org/10.1007/s40273-014-0243-x.

Kraemer, W. J., Ratamess, N. A., & Nindl, B. C. (2017). Recovery responses of testosterone, growth hormone, and IGF-1 after resistance exercise. *Journal of applied physiology (Bethesda, Md. : 1985), 122*(3), 549–558. https://doi.org/10.1152/japplphysiol.00599.2016.

Mannerkorpi, K., Landin-Wilhelmsen, K., Larsson, A., Cider, Å., Arodell, O., & Bjersing, J. L. (2017). Acute effects of physical exercise on the serum insulin-like growth factor system in women with fibromyalgia. *BMC musculoskeletal disorders, 18*(1), 37. https://doi.org/10.1186/s12891-017-1402-y.

Misra, M., Bredella, M. A., Tsai, P., Mendes, N., Miller, K. K., & Klibanski, A. (2008). Lower growth hormone and higher cortisol are associated with greater visceral adiposity, intramyocellular lipids, and insulin resistance in overweight girls. American journal of physiology. *Endocrinology and metabolism, 295*(2), E385–E392. https://doi.org/10.1152/ajpendo.00052.2008.

Olarescu, N. C., Gunawardane, K., Hansen, T. K., Møller, N., & Jørgensen, J. O. L. (2019). *Normal Physiology of Growth Hormone in Adults. In K. R. Feingold (Eds.)* et. al., Endotext. MDText.com, Inc.

Oliver, S. R., Rosa, J. S., Minh, T. D., Pontello, A. M., Flores, R. L., Barnett, M., & Galassetti, P. R. (2010). Dose-dependent relationship between severity of pediatric obesity and blunting of the growth hormone response to exercise. *Journal of applied physiology (Bethesda, Md. : 1985), 108*(1), 21–27. https://doi.org/10.1152/japplphysiol.00589.2009.

Pranoto, A., Cahyono, M. B. A., Yakobus, R., Izzatunnisa, N., Ramadhan, R. N., Rejeki, P. S., Miftahussurur, M., Effendi, W. I., Wungu, C. D. K., & Yamaoka, Y. (2023). Long-Term Resistance-Endurance Combined Training Reduces Pro-Inflammatory Cytokines in Young Adult Females with Obesity. *Sports (Basel, Switzerland), 11*(3), 54. https://doi.org/10.3390/sports11030054.

Pranoto, A., Rejeki, P., Miftahussurur, M., Setiawan, H., Yosika, G., Munir, M., Maesaroh, S., Purwoto, S., Waritsu, C. & Yamaoka, Y. (2023). Single 30 min treadmill exercise session suppresses the production of pro-inflammatory cytokines and oxidative stress in obese female adolescents. *Journal of Basic and Clinical Physiology and Pharmacology, 34*(2), 235-242.

https://doi.org/10.1515/jbcpp-2022-0196.

Rejeki, P. S., Pranoto, A., Rahmanto, I., Izzatunnisa, N., Yosika, G. F., Hernaningsih, Y., Wungu, C. D. K., & Halim, S. (2023). The Positive Effect of Four-Week Combined Aerobic-Resistance Training on Body Composition and Adipokine Levels in Obese Females. *Sports (Basel, Switzerland), 11*(4), 90. https://doi.org/10.3390/sports11040090.

Romieu, I., Dossus, L., Barquera, S., Blottière, H. M., Franks, P. W., Gunter, M., Hwalla, N., Hursting, S. D., Leitzmann, M., Margetts, B., Nishida, C., Potischman, N., Seidell, J., Stepien, M., Wang, Y., Westerterp, K., Winichagoon, P., Wiseman, M., Willett, W. C., & IARC working group on Energy Balance and Obesity (2017). Energy balance and obesity: what are the main drivers?. *Cancer causes & control : CCC, 28*(3), 247–258. https://doi.org/10.1007/s10552-017-0869-z.

Sabag, A., Chang, D., & Johnson, N. A. (2021). Growth Hormone as a Potential Mediator of Aerobic Exercise-Induced Reductions in Visceral Adipose Tissue. *Frontiers in physiology, 12*, 623570. https://doi.org/10.3389/fphys.2021.623570.

Santos, V. O. A., Browne, R. A. V., Souza, D. C., Matos, V. A. F., Macêdo, G. A. D., Farias-Junior, L. F., Farias-Júnior, J. C., Costa, E. C., & Fayh, A. P. T. (2019). Effects of High-Intensity Interval and Moderate-Intensity Continuous Exercise on Physical Activity and Sedentary Behavior Levels in Inactive Obese Males: A Crossover Trial. *Journal of sports science & medicine, 18*(3), 390–398.

Sasaki, H., Morishima, T., Hasegawa, Y., Mori, A., Ijichi, T., Kurihara, T., & Goto, K. (2014). 4 weeks of high-intensity interval training does not alter the exercise-induced growth hormone response in sedentary men. *SpringerPlus, 3*, 336. https://doi.org/10.1186/2193-
34(1), 61–67. https://doi.org/10.1515/jbcpp-2022-0060.

Susanto, H., Sugiharto, Taufiq, A., Pranoto, A., & Purnomo, J. D. T. (2023). Dynamic alteration of plasma levels of betatrophin in younger female onset obesity post acute moderate-intensity exercise training. *Saudi journal of biological sciences, 30*(2), 103546. https://doi.org/10.1016/j.sjbs.2022.103546.

Wang, X., Wang, S., Wu, H., Jiang, M., Xue, H., Zhu, Y., Wang, C., Zha, X., & Wen, Y. (2020). Human

.

1801-3-336.

Sauro, L. M., & Kanaley, J. A. (2003). The effect of exercise duration and mode on the growth hormone responses in young women on oral contraceptives. *European journal of applied physiology, 90*(1-2), 69–75. https://doi.org/10.1007/s00421-003-0863-x.

Savastano, S., Di Somma, C., Barrea, L., & Colao, A. (2014). The complex relationship between obesity and the somatropic axis: the long and winding road. *Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF Research Society, 24*(6), 221–226. https://doi.org/10.1016/j.ghir.2014.09.002.

Solis-Urra, P., Fernández-Cueto, N., Nanjarí, R., Huber-Pérez, T., Cid-Arnes, M. P., Zurita-Corvalán, N., Rodriguez-Rodriguez, F., & Cristi-Montero, C. (2019). A mejor condición física mejores resultados de una ley contra la obesidad (Better fitness, better results of a law against obesity). *Retos, 36*, 17–21. https://doi.org/10.47197/retos.v36i36.66782.

Stanley, T. L., & Grinspoon, S. K. (2015). Effects of growth hormone-releasing hormone on visceral fat, metabolic, and cardiovascular indices in human studies. *Growth hormone & IGF research : official journal of the Growth Hormone Research Society and the International IGF Research Society, 25*(2), 59–65. https://doi.org/10.1016/j.ghir.2014.12.005.

Strasser B. (2013). Physical activity in obesity and metabolic syndrome. *Annals of the New York Academy of Sciences, 1281*(1), 141–159. https://doi.org/10.1111/j.1749-6632.2012.06785.x.

Sugiharto, Merawati, D., Pranoto, A., & Susanto, H. (2022). Physiological response of endurance exercise as a growth hormone mediator in adolescent women's. *Journal of basic and clinical physiology and pharmacology,*
growth hormone level decreased in women aged <60 years but increased in men aged >50 years. *Medicine, 99*(2), e18440. https://doi.org/10.1097/MD.0000000000018440.

Wood, C. J., Clow, A., Hucklebridge, F., Law, R., & Smyth, N. (2018). Physical fitness and prior physical activity are both associated with less cortisol secretion during psychosocial stress. *Anxiety, stress, and coping, 31*(2), 135–145. https://doi.org/10.1080/10615806.2017.1390083