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# The protective effect of intermittent fasting and physical exercise on obesity through changes in muscle diameter

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## ABSTRACT

**Introduction:** Obesity is a cause of metabolic syndrome. Intermittent fasting is a method that is quite popular today, and this is an alternative method to lose weight compared to the traditional method of undergoing calorie restriction (20-40% reduction in daily calorie intake) and/or physical activity. However, the effect of intermittent fasting and physical exercise on changes in the muscle remains unclear. This study aimed to determine the changes in muscle histology in intermittent fasting and physical exercise in obese mice.
**Methods:** 8-weeks old mice were given a high-fat diet for two weeks and then grouped into four groups (a control group, group two as a group with a high-fat diet, group three with a high-fat diet which was given physical exercise, and group four was a high-fat diet which was given fasting for 8 hours 5 days a week, for two weeks). Histological analysis was performed to see the changes in the muscles with hematoxylin staining at 40 times magnification.
**Results:** The fasting and physical exercise group were significantly less weight gain. The histological results found that the muscle diameter widened in the physical exercise group compared to the high-fat diet group ($p<0.05$). In comparison, the fasting group was found to have almost the same muscle diameter as the control group without the high-fat diet ($p<0.05$).
**Conclusion:** Both intermittent fasting and exercise were effective in reducing body weight, whereas intermittent fasting is more effective than exercise in maintaining muscle mass by maintaining muscle diameter to prevent obesity.

**Keywords:** obesity, intermittent fasting, exercise.
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## INTRODUCTION

The incidence of obesity is increasing worldwide each year. This phenomenon is caused by obesity-related metabolic disorders such as type 2 diabetes, hypertension, hyperlipidemia, or metabolic syndrome.[1] This disorder can cause damage to multiple organs, including skeletal muscle, which is responsible for 30-40% of human metabolism and 80% is the site of insulin-stimulated glucose uptake.[2] The occurrence of insulin resistance causes impaired glucose metabolism due to increased fat accumulation that develops into type 2 diabetes.[1] Skeletal muscle is where the body uses much fuel, such as burning fatty acids or glucose. It is known that physical exercise and fasting can trigger this higher flexibility, causing changes in metabolism. Another study explained that changes in skeletal muscle during fasting shift fat metabolism through acid-oxidation pathways, oxidative metabolism, and slowing of heavy chain myosin expression activity, which is different from the mechanism produced in physical exercise.[3] Physical exercise can provide mimetic effects of endogenous or non-endogenous origin. Research related to fasting and physical exercise has shown an increase in muscle performance and improvement in NAFLD.[4]

Fasting is different from calorie restriction (CR), which chronically reduces daily calorie intake by 20% to 40%, but the frequency of eating is maintained. Fasting can trigger the process of ketogenesis through metabolic pathways and cellular changes such as lipolysis, stress tolerance, and autophagy.[5] Fasting can prevent and reverse all aspects of multiple sclerosis in the rat. It reduces abdominal fat, inflammation, and blood pressure; beside increases insulin sensitivity. Also, it improves the functional capacity of the nervous, muscular, and cardiovascular systems.[6] However, the difference in muscle changes between physical exercise and fasting is unclear. Based on this background, the researchers wanted to identify differences in muscle histology in exercise and fasting conditions in experimental animals with high-fat diets.

## METHODS

### Study design and animal study

In this study, 16 8-week-old mouse mice were used. A one-week acclimation period was given before the start of the experiment. Mice were assigned to different treatments using random samples. After the adaptation period, four mice were fed a normal diet, and 12 mice continued on a high fat diet (HFD) for two weeks before samples were taken for intervention. Of the 12 mice, they were divided into three groups: high-fat diet (HFD), HFD and exercising three times a week (HFD + ex), and HFD and

**Table 1. Body weight results in each group.**

| | Ctrl | HFD | Exercise | Fasting |
|---|---|---|---|---|
| Body weight pre-intervention (gr) | 28.9±0.91 | 31.17±1.28 | 30.12±0.66 | 29.5±1.29 |
| Body weight two weeks after HFD (gr) | 31.4±1.14 | 36.65±1.92* | 35.87±1.31* | 36.92±1.42* |
| Body weight after intervention (gr) | 33.8±1.30† | 40.5±1.29 | 35.5±1.29† | 32.75±1.70† |

*Values are expressed as mean±SEM (n=4 per group). The experimental groups were Ctrl (normal diet); HFD (high-fat diet); HFD+Ex (high-fat diet with exercise); HFD + fasting (high-fat diet with fasting).*p<0.05 vs. control group;†p<0.05 vs. HFD group.*

fasting five days a week for eight hours (HFD + fasting). The group with a 45% high-fat and 10% regular diet was free to eat and drink water, depending on the characteristics of each group. During the experiment, the light-dark cycle was 12 hours a day, and the room temperature and relative humidity were 24 ± 1 ° C and about 60%, respectively. Two weeks after HFD administration, HFD and the exercise group (HFD + ex) exercised three times a week at a rate of approximately 1518 rpm for two weeks.

### Data mining and statistical analysis

The skeletal muscle was fixed by immersion in 10% buffered formaldehyde overnight, embedded in paraffin, and cut into 5-µm-thick coronal sections. After deparaffinization, muscle sections were stained with hematoxylin and eosin for routine histological evaluation.

All results are expressed as mean ± SEM. Parameter comparisons between the two groups were performed using the unpaired Student's t-test. The dose-response curves were compared by a two-factor repeated ANOVA measurement followed by a Tuckey post-hoc for comparison between groups. The value of p<0.05 was considered important.

## RESULTS

### Body weight

Based on the results of the weight examination, it was found that a high-fat diet increased body weight compared to before HFD administration ($p$<0.05). Meanwhile, animals with HFD who underwent physical exercise had lower body weight compared to the HFD group ($p$<0.05), as well as in the HFD group than underwent fasting, body weight decreased compared to the HFD group ($p$<0.05). However, there was no significant difference between weight loss in the physical exercise group and the fasting group.

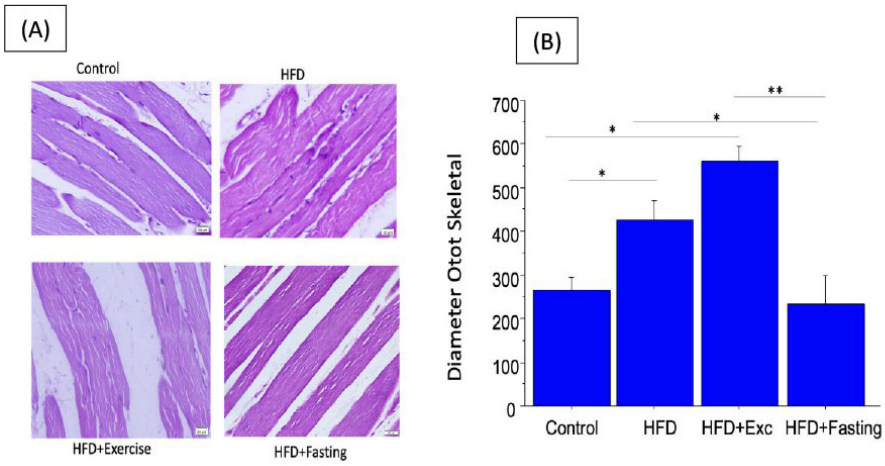


**Figure 1.** Representative histological cross-sections of skeletal muscle. (A) Histological section (B) Measured diameter of muscle based on histology. (n= 4, per group). *; $p$< 0.05, All values are mean ± SEM.

### Effect of exercise and fasting on histology of skeletal muscle

Based on the results of the study, it was found that there were differences in the structure and size of skeletal muscles in the high-fat diet group with regular physical exercise and the high-fat diet with fasting. On HE staining histological examination, it was found that the muscle in the high-fat diet group had a wider diameter ($p$<0.05) than in the control group. In the treatment with physical exercise, the muscle diameter was greater ($p$<0.05) compared to the HFD group. However, the fasting group showed almost the same results as the control group, where the muscle diameter was significantly lower than the physical exercise group ($p$<0.05).

## DISCUSSION

The present study shows that exercise training and intermittent fasting influence the soleus muscles of mice fed a high-fat diet. We demonstrated a positive relationship between muscle diameters in histology after two weeks of fasting. We also found that exercise training positively correlates with weight loss after two weeks.

Physical exercise has been known to increase insulin sensitivity in skeletal muscle and increase fat accumulation in the muscle through increased oxidative capacity. However, a high-fat diet causes an increase in insulin resistance and fat accumulation in the muscles.[7] So, it is necessary to know the appropriate speed and duration to affect obesity conditions positively. Besides physical exercise, fasting can also increase insulin sensitivity in skeletal muscles and lose weight. Based on the results of this study, it was found that there was weight loss after being given physical exercise and fasting for two weeks. Moreover, these results show that fasting loses more weight than physical exercise on a high-fat diet. These results are similar to previous studies; short-term fasting can reduce body weight and fat mass and increase insulin sensitivity.[8] Also,

short-term fasting can reduce 75-100% of incoming calorie intake.[9] However, exercise reduces body weight and overall body fat proportion and increases insulin sensitivity and muscle metabolism.[10] As it is known, a high-fat diet's composition can increase BMI and muscle mass.[11] Previous studies explained that a high-fat diet increases mitochondrial biogenesis and fatty acid oxidative capacities in skeletal muscle, which cause mitochondrial stress. However, physical activity reduces the reliance on carbohydrates, thus increasing the proportion of fatty acids used as an energy source and enhancing muscle fatty acid oxidation, especially during exercise. In the animal model of the present study, the HFD-treated mice exhibited slightly higher skeletal muscle diameters compared to the control group. Linear with these results, histological examination of skeletal muscle showed differences in muscle diameter between exercise and fasting compared to the high-fat diet groups.

## CONCLUSIONS

Our results suggested that intermittent fasting and exercise effectively reduce body weight. In contrast, intermittent fasting is more effective than exercise in maintaining muscle mass by maintaining muscle diameter to prevent obesity. This study needs validation by further research using a more comprehensive design to determine the treatment's continuous effect.

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## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

## AUTHOR CONTRIBUTION

All authors contributed to the thinking from the investigation concepts, information acquisitions, information investigation, factual investigations, and changing the paper until detailing the consider comes about through publication.

## ETHICAL CONSIDERATION

This research was approved by the Health Research Ethics Committee of Universitas Nahdlatul Ulama Surabaya.

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