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High-intensity interval training was more effective than moderate-intensity interval training in lowering creatine kinase and interleukin 6 levels among sports students

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ABSTRACT

Background: This study aimed to prove that high-intensity interval training (HIIT) is superior to medium-intensity continuous training (MICT) in reducing creatine kinase and interleukin 6 (IL-6) levels in sports students after 4 weeks of exercise.
Methods: The study examined the effects of two different training methods—MICT and HIIT. This study included 30 students aged 19-22 years, using a pretest-posttest control group design. Participants were randomly assigned to MICT, HIIT, or control groups (no training) and trained three times a week for four weeks. Creatine and IL-6 levels were analyzed by blood sampling. Data analysis included descriptive statistics, normality tests, and ANOVA tests to evaluate group differences.
Results: HIIT was found to be more effective than MICT and the control group in reducing CK and IL-6 levels in sports students after 4 weeks of training ($p < 0.001$).
Conclusion: The HIIT and MICT reduced creatine kinase and IL-6 levels compared to the control group, but HIIT was more effective in reducing creatine kinase and IL-6 levels than MICT in sports students after 4 weeks of exercise.

Keywords: creatine kinase, high intensity interval training, IL-6, sports student, interleukin 6, moderate intensity continous training.
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INTRODUCTION

University students are a productive age group that often faces high academic demands. Lecture activities include attendance in class, completion of assignments, exams, and involvement in other campus organizations or activities.[1] All of these things can lead to a great deal of busyness, which impacts students' lifestyles, including their physical activity levels.[2] The density of their activities makes it difficult for students to get time to practice, especially for sports students. Sports students are required to maintain fitness and performance as sports students.[3] Therefore, it is very important for them to choose a suitable exercise program and provide the best time efficiency.[4] The selected exercise must be able to improve their performance or maintain their fitness but must also produce maximum benefits by minimizing the risk of muscle injury so that the recovery process after training can take place quickly and they can return to activities with optimal performance in a short time.[5]

Exercise interventions have a significant impact on creatine kinase (CK) and interleukin-6 (IL-6) levels in the body, especially since they both serve as biochemical indicators that respond to physical stress and the recovery process after activity.[6] CK is an enzyme that indicates the extent to which muscle damage occurs, especially after performing strenuous or unusual physical activity.[7] Meanwhile, IL-6 is a cytokine produced by skeletal muscles during physical activity, also known as myokine.[8] Exercise interventions can temporarily increase CK and IL-6 levels, which are both physiological and adaptive responses.[9] An increase in CK indicates stress on the muscles due to exercise, while IL-6 plays a role in tissue repair and energy recovery. With regular and planned exercise, the body will adapt better, produce a more regular CK and IL-6 response, and improve overall health.[10] Therefore, it is important for students to choose a type of exercise that not only provides a maximum performance improvement, but is also accompanied by a decrease in CK and IL-6 levels as an indication that muscle damage from the exercise is minimal, while still providing significant benefits.[11]

High-Intensity Interval Training (HIIT) and Moderate-Intensity Continuous Training (MICT) are two

types of exercise methods that are often evaluated for their effectiveness in relation to several physiological indicators, such as CK and IL-6 levels.[12] HIIT, which consists of high-intensity exercise in short intervals followed by rest periods, has several advantages compared to MICT, which is performed at moderate intensity on a sustained basis for a longer duration. MICT training involves activities that are performed at a consistent pace or intensity over a long period of time, such as running or cycling at a moderate pace.[13] Previous research has shown that MICT exercises are effective in providing long-term fitness benefits. However, MICT exercises take longer to provide benefits.[14] This becomes a challenge for individuals with busy schedules, as these exercises take longer to achieve the same results. In addition, the body can quickly adapt to the constant intensity of moderate exercise, so the benefits of sustained moderate-intensity exercise in improving fitness can diminish over time.[15] Once the body gets used to it, the benefits may diminish unless the duration or intensity of the exercise is increased, which requires additional time and effort.[16]

Meanwhile, HIIT is a form of high-intensity training with a short duration. HIIT is a form of high-intensity, short-duration activity training and is performed near maximum, or super maximum, interspersed with passive or active recovery for short periods of time.[7] HIIT is a popular workout and provides efficient time. HIIT is often used in sports to induce cardiorespiratory and metabolic adaptations that can improve athletes' fitness and endurance performance.[18] HIIT is the right training method to improve the physiological ability of athletes to move towards physiological adaptability at a higher level. HIIT is considered one of the most effective forms of exercise to improve athletes' physical performance.[19]

The novelty of this study is to show that the HIIT intervention was more effective than MICT in influencing CK and IL-6 levels. A biochemical approach in exercise, with an emphasis on CK (a marker of muscle damage) and IL-6 (a marker of inflammation and metabolism), can help us deeply understand how the body functions physiologically in response to two different types of exercise. HIIT can offer the same or even greater benefits than MICT in a shorter period of time, making it the perfect choice for those with limited time. This study aims to prove that HIIT is superior to MICT in reducing CK and IL6 levels after 4 weeks of exercise. This research contributes to various aspects of fitness and health that are of great importance to the global community, especially in efforts to promote healthy lifestyles, time efficiency, fitness-enhancing exercises with minimal muscle breakdown effects, and long-term health management. The finding that HIIT is more successful than MICT in lowering CK and IL-6 levels can be explained through various physiological mechanisms and the body's adaptation to exercise.

HIIT is more effective than MICT in lowering CK and IL-6 levels because this type of exercise triggers faster physiological adaptation, efficiency in recovery, and management of the body's inflammation.[20] With high intensity, the body responds faster to physical stress, repairs tissues better, and manages inflammatory processes effectively, which ultimately results in lower levels of CK and IL-6. This discovery confirms the advantages of HIIT as a powerful exercise method to improve overall health and fitness.[21] This decrease is due to the nature of HIIT that allows the body to adapt more quickly and efficiently to the physical stress that arises during exercise. In addition, the study not only provides solutions to public health problems, but also presents valuable information for individuals looking for more efficient and more time-saving ways to exercise.[22]

METHODS

This research involved a total of 30 young students who were participants. The inclusion criteria were individuals aged 19-22 years, body mass index (BMI) 15-25 kg/m2, normal systolic and diastolic blood pressure 120-110/90-80 mmHg, resting heart rate (RHR) 70-90 bpm, oxygen saturation 97-100%, and body temperature 36.5-37.2°C. Subjects were verified to have no history of smoking, non-alcoholic consumption, non-hypertension, and non-diabetes. In addition, the participants did not have any diseases with personalized therapy through specific medical interventions.

The study involved two independent variables: MICT and HIIT, as well as two dependent variables: CK and IL6. After informed consent, subjects underwent a health examination and pretest for CK and IL6 examination and were then randomly divided into three groups: the MICT group, the HIIT group, and the control group without training. The training program is carried out for 4 weeks with a frequency of 3x/week (Table 1). In this study, researchers conducted compliance control of research subjects by recording the attendance of research subjects and conducting direct monitoring in the field during the training session.

The research process was carried out through the following steps: First, the research subject is asked to fill out an approval form. After giving consent to participate, all participants underwent a health check-up that included pulse rate and blood pressure measurements, as well as pretests to measure CK and IL-6 levels. The subjects were then randomly divided into three groups: A, B, and C. Group A took part in MICT, group B did HIIT, while group C did no training at all. This sports program is carried out for 4 weeks with a frequency of 3 times a week. After the intervention period was completed, a posttest was performed to remeasure the levels of CK and IL-6 in the subjects. Data analysis included descriptive statistics, normality tests, and ANOVA tests to evaluate group differences.

RESULTS

Figure 1 shows the differences in CK levels before and after exercise in the HIIT, MICT, and control groups. Figure 1 indicates that HIIT training results in a greater reduction in creatine kinase levels compared to the MICT and control groups, with the control group showing the smallest decrease. Figure 2 illustrates the differences in IL6 levels before and after exercise in the HIIT, MICT, and control groups. Figure 2 shows that HIIT training leads to a more significant reduction in IL6 levels compared to the MICT and control groups, with the control group exhibiting the least reduction.

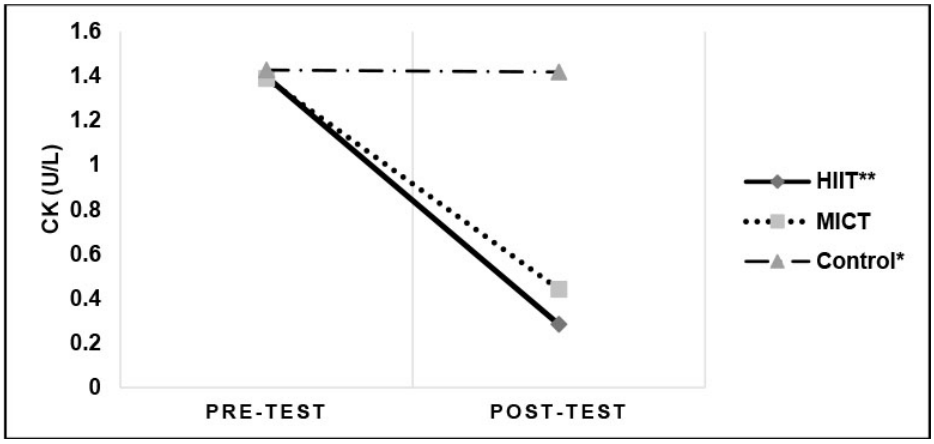

Figure 1. Comparison of creatine kinase between the high intensity interval training (HIIT), medium intensity continuous training (MICT), and control groups
*, the change was not significant; **, received highest change score compared to other interventions.

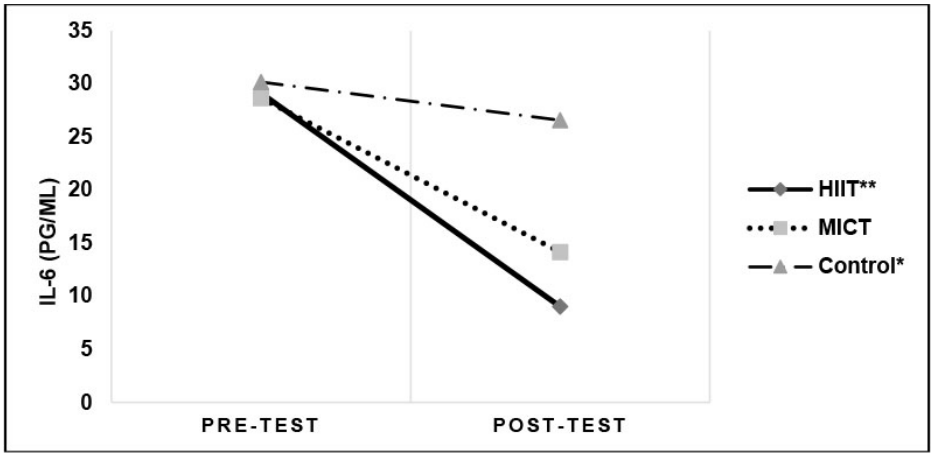

Figure 2. Comparison of interleukin 6 (IL6) between the high intensity interval training (HIIT), medium intensity continuous training (MICT), and control groups
*, the change was not significant; **, received highest change score compared to other interventions.

Table 2 presents the characteristics of the subjects in this study. The characteristics of the 30 participants, divided equally into the MICT, HIIT, and control groups, showed comparable baseline values across all measured variables. Resting heart rate averaged between 68 and 70 bpm, while oxygen saturation was consistent at 97–98%. Both systolic and diastolic blood pressure were within normal ranges and similar among groups, as were fasting blood glucose (around 92–93 mg/dL) and hemoglobin levels (13.8–14.4 g/dL). Body temperature averaged 36.4–36.5°C, with body weight ranging from 59.9 to 62.8 kg and height around 1.6–1.7 m, resulting in a mean BMI of approximately 21.6–21.7 kg/m^2. The mean age of participants was about 19–20 years. These results indicate that the three groups had no significant differences in baseline characteristics, ensuring comparability before the intervention.

Table 3 shows the results of pre-tests and post-tests on creatine kinase and interleukin 6 with control, MICT, and HIIT groups. The data show that creatine kinase values remained relatively stable in the control group (1.4 to 1.4), while a reduction was observed in both the MICT group (1.4 to 0.4) and the HIIT group (1.4 to 0.3). For interleukin-6, the control group showed only a slight decrease (30.2 to 26.6), whereas a more pronounced reduction occurred in the MICT group (28.7 to 14.2) and the HIIT group (29.1 to 9.0). These findings indicate that both MICT and HIIT training contributed to lowering muscle damage markers (CK) and inflammatory response (IL-6), with HIIT showing the greatest effect.

Table 4 shows the results of the ANOVA test to identify significant differences in the means of the MICT, HIIT, and control groups. The CK measurement at the pre-test obtained no significant mean difference among the three groups (p-value = 0.985), while the post-test measurement obtained a significant mean difference (p-value < 0.001). In the IL-6 measurement, no significant mean difference was obtained among groups at the pre-test (p-value = 0.903), but a significant mean difference was found after the groups' interventions (p < 0.001).

DISCUSSION

HIIT and MICT are two training methods that are widely chosen to improve fitness and performance.[23] While both have been shown to be effective, it's important to determine which one provides the greater benefit with minimal impact on muscle damage after a specific period of exercise. This study showed that HIIT was much more effective than MICT in lowering CK and IL-6 levels after 4 weeks of exercise.[24] HIIT and MICT offer benefits for skeletal muscle, exercise adaptation, and athletic performance. Recent research shows that sustained MICT is effective in improving aerobic fitness rapidly.[25] MICT is an option for improving overall fitness. However, to get these benefits, MICT must be done over a long period of time, which can require quite a high amount of time and cost. Many people find it difficult to undergo MICT training because of the long duration and monotonous rhythm.[26]

In recent times, HIIT has become increasingly popular because it has a short workout duration, high intensity, and short intervals, which are able to effectively improve fitness and health. HIIT has become known as an important fitness trend in recent years thanks to its efficient nature in utilizing time.[27] Previous research has explored whether HIIT is a superior exercise method compared to MICT.[28] In high-intensity workouts that use HIIT interventions, the body undergoes more strenuous activity compared to MICT workouts.[29] This is especially important for students who

Table 1. Training programs among the medium intensity continuous training (MICT), high intensity interval training (HIIT), and control groups

Time	MICT group	HIIT group	Control group
First week	70% MAS 40 Min	15 s @100% MAS : 15 s 70% MAS X 10 Reps (3 Min Rest BS) X 4 Set	No intervention
Second week	70% MAS 50 Min	15 s @107% MAS : 15 s 70% MAS X 10 Reps (3 Min Rest BS) X 4 Set	No intervention
Third week	70% MAS 50 Min	16 s @114% MAS : 15 s 70% MAS X 10 Reps (3 Min Rest BS) X 4 Set	No intervention
Forth week	70% MAS 60 Min	17 s @120% MAS : 15 s 70% MAS X 10 Reps (3 Min Rest BS) X 4 Set	No intervention

BS, between set; MAS, maximum aerobic speed.

Table 2. Characteristics of the 30 participants of the study

Characteristic	MICT (N=10) (Mean ± SD)	HIIT (N = 10) (Mean ± SD)	Control (N=10) (Mean ± SD)
Resting heart rate (bpm)	68.5 ± 7.9	70.20 ± 4.70	68.7 ± 3.5
Oxygen saturation (%)	97.1 ± 1.4	97.5 ± 1.08	97.9 ± 0.9
Systolic blood pressure (mmHg)	118.1 ± 3.8	117.70 ± 5.10	117.5 ± 3.4
Diastolic blood pressure (mmHg)	76.2 ± 2.7	73.90 ± 5.80	74.4 ± 4.9
Fasting blood glucose (mg/dL)	93 ± 12.2	92.60 ± 5.10	92.7 ± 4.1
Hemoglobin (g/dL)	13.8 ± 1.5	14.40 ± 0.60	14 1,2 ± 0.2
Body temperature (°C)	36.5 ± 0.3	36.4 ± 0.21	36.4 ± 0.2
Weight (kg)	62.8 ± 6.9	59.9 ± 6.20	61.5 ± 6.2
Height (cm)	1.7 ± 0.05	1.60 ± 0.06	1.6 ± 0.02
Body mass index (kg/m^2)	21.7 ± 2.9	21.60 ± 2.70	21.6 ± 1.09
Age (years)	19.5 ± 1.08	19.60 ± 1.30	19.6 ± 2.3

°C, degree celcius; Bpm, beat per minute; cm, centimeter; g/dl, gram per deciliter; HIIT, high intensity interval training; kg, kilogram; m^2, meter square; mg/dL, milligram per deciliter; MICT, medium intensity continuous training; mmHg, millimeter mercury.

Table 3. Results of pre-test and post-test on creatine kinase and interleukin 6 of the control, medium intensity continuous training (MICT), and high intensity interval training (HIIT) groups

Number of subject	Creatine kinase						Interleukin 6					
	Control		MICT		HIIT		Control		MICT		HIIT	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	1.4	1.2	1.4	1.0	1.1	0.7	37.7	14.6	24.5	10.7	31.0	7.2
2	0.0	1.3	0.1	0.3	1.1	0.1	18.0	35.0	18.2	14.1	27.5	6.2
3	1.2	1.2	1.5	0.1	1.5	0.1	36.1	15.4	40.9	19.3	31.8	6.9
4	1.7	1.3	1.5	0.3	2.0	0.1	37.1	18.7	37.8	13.3	25.9	10.0
5	1.9	1.5	1.5	0.1	1.8	0.1	35.3	48.0	19.3	13.3	23.7	13.0
6	1.5	1.7	1.4	1.3	1.3	0.1	31.0	25.9	47.5	16.9	29.0	7.7
7	1.7	1.5	1.1	0.1	1.1	0.5	19.3	36.6	20.8	11.3	34.2	8.5
8	2.3	2.2	2.3	0.7	1.2	0.1	35.1	43.0	33.2	13.8	29.8	10.0
9	1.0	0.9	1.7	0.1	1.5	1.0	26.6	11.8	18.3	16.4	27.7	14.1
10	1.5	1.4	1.3	0.3	1.4	0.1	25.8	16.9	26.2	12.5	30.9	6.7
Mean	1.4	1.4	1.4	0.4	1.4	0.3	30.2	26.6	28.7	14.2	29.1	9.0

have limited time, as they need an effective and efficient form of exercise to improve their fitness and performance.[30]

Compared to MICT, HIIT shows similar or even better effects. Participants who participated in HIIT programs had higher levels of adherence and satisfaction than those who underwent MICT, thanks to variations in their exercise designs.[31] Individuals with tight schedules often face common challenges in performing physical activity, especially related to the lack of available time. In the last decade, many studies have focused on busy teens or adults to evaluate the impact of HIIT interventions.[32] HIIT is recognized as a powerful and widely accepted exercise method due to its ability to significantly improve cardiovascular endurance and strengthen overall muscles.[33]

HIIT activates fast muscle fibers that play a role in producing high strength. This activation supports muscle adaptation and strength gain.[34] In addition, HIIT

Table 4. Results of one-way analysis of variance (ANOVA) test of creatine kinase and interleukin 6 between the medium-intensity continuous training (MICT), high-intensity interval training (HIIT), and control groups

Creatine kinase		Mean±SD	P-value	Interleukin 6		Mean±SD	*P*-value
Pre	MICT	1.4 ±0.6	0.985	Pre	MICT	28.7±10.5	0.903
	HIIT	1.4±0.3			HIIT	29.1±3.1	
	Control	1.4±0.6			Control	30.2±7.4	
Post	MICT	0.4±0.4	0.000	Post	MICT	14.2±2.7	0.000
	HIIT	0.3±0.3			HIIT	9.0±2.7	
	Control	1.4±0.3			Control	26.6±13.1	

stimulates the production of anabolic hormones such as testosterone and growth hormone, which are essential for muscle protein synthesis as well as muscle growth and hypertrophy.[35] HIIT also causes metabolic stress and micro-tears in muscle fibers, which trigger physiological responses that amplify anabolic signaling and growth factors, thereby increasing muscle strength and hypertrophy. Thus, HIIT can improve physical condition and performance.[36]

Physical activity has a strong relationship with levels of CK and IL-6.[37] Researchers have tested HIIT and MICT workouts, which generally lead to increased levels of CK and IL-6 after intense exercise. Both serve as indicators of muscle damage and inflammation, so it's important to find the type of exercise that is not only beneficial for fitness and performance but also minimizes muscle damage from repetitive exercise. By doing exercises consistently and regularly, it is hoped that the body can adapt, thereby reducing muscle damage that occurs.[38]

High-intensity physical exercise done in a short period of time can negatively impact inflammatory mediators.[39] However, on the other hand, physical exercise done in the long term can improve physical condition and performance and reduce inflammation. The intensity of the exercise greatly affects the positive or negative effects of the training session. Some studies show a significant improvement in performance after 3.5 to 7 weeks of HIIT.[40] Recently, there has been a study examining the sports immunology literature that shows an increase in the number of cells after exercise, such as leukocytosis, neutrophils (NE), monocytosis (MO), and lymphocytosis (LY).[41]

Previous research has shown that white blood cells experience significant increases during maximal activity with high intensity. Interestingly, there is also evidence that leukocytosis due to intensive exercise can be caused by increased muscle damage in general.[42] In fact, the immune status tends to improve in reaction to increased physical activity. However, after adapting to high-intensity exercise, the immune status decreases. In addition, various studies have shown a slight decrease in immune parameters in response to high-intensity training or long-term training programs in athletes due to the adaptation process.[43]

It has been shown that physical activity causes a temporary increase in biochemical markers of muscle damage, such as CK.[44] Previous research noted a significant increase in CK. In previous studies, it was observed that CK levels remained stable and even decreased after an off-season rest period.[45] In addition, the study also showed a significant decrease in CK concentration during rest time after undergoing high-intensity aerobic exercise for 4 weeks.[46]

Research shows that long-term exercise can affect a variety of indicators of muscle damage. Therefore, it is important to determine the right intensity and duration during HIIT in order to improve performance while minimizing muscle damage and the risk of injury.[47] In addition, the intensity of exercise plays a significant role in causing damage to the sarcolemma, which allows enzymes from damaged muscles to enter the bloodstream. In recent years, coaches and athletes have been exploring modern training methods that can improve performance and support optimal adaptation.[48] In fact, the stiffness and pain after the training session decreased when the exercise was repeated a week later thanks to the adaptation that occurred in the muscles.[49]

Based on the available literature, it is proposed that increased exercise intensity may improve muscle adaptation to reduce signs of muscle damage after exercise and that HIIT training will provide more significant results than the control group.[26] Previous research has shown that after participating in a HIIT program, CK levels are significantly lower than before the training program.[29] These results are in line with the findings of Baird et al, which suggest that serum CK levels reflect complex interactions related to energy status and muscle breakdown levels. In addition, Brewster et al also showed that more intense physical activity can increase cellular energy and improve muscle contractions, leading to decreased muscle damage.[16]

HIIT does not show a significant difference in the level of markers of muscle damage in the long term. The inflammatory response during exercise is related to muscle metabolism and the rate at which muscle injury develops.[15] The process of muscle adaptation includes an increase in the number of sarcomeres in muscle fibers after a certain training program. Thus, after undergoing the HIIT program, the decrease in markers of muscle damage seen in both groups in this study could be attributed to muscle adaptation.[6]

Increased exercise intensity can improve performance and reduce markers of muscle damage after a short period of intense exercise, and each HIIT can result in a larger change than the control group.[27] In a training program, the two main goals are to improve performance and prevent injuries. To achieve this goal, a HIIT program is recommended because it does not cause any additional muscle damage.[44] However, contrast analysis suggests that participation in the HIIT protocol described in this study can result in significant muscle gains. HIIT performed for 8 weeks with a short and

intense duration can reduce biomarker damage in physically active young men.[50]

The four-week HIIT intervention was more effective in lowering muscle damage markers (CK), reducing pain scores, and increasing muscle strength after cycling, compared to the placebo group.[46] IL-6 concentrations peaked after exercise, while the lowest changes in CK and myoglobin were found in trained individuals.[47] The increase in post-HIIT CK was less significant in trained athletes compared to individuals who were less trained or not trained at all. This suggests that individuals who are trained or trained regularly experience less muscle damage than those who rarely exercise or exercise at low intensity.[20]

Exercise-induced increases in IL-6 and its association with exercise intensity and duration have been noted before.[3] In one study, IL-6 response showed a decrease after six weeks of HIIT. This is due to the high intensity of HIIT training, which causes the muscles to adapt, resulting in less muscle damage.[4] When the same exercise was repeated to assess the effect of a particular exercise program on IL-6 response, the release of IL-6 in plasma decreased.[11]

All of these effects can be seen as examples of increased adaptation to exercise, which is associated with higher fitness levels.[46] The only difference between the groups observed after the training period lies in the progression of CK level changes, where trained individuals show a lower decline compared to moderately trained and untrained individuals, who tend to be stable.[46] Given all this information, sports-related muscle damage, judged based on changes in post-workout CK, turned out to be the lowest in well-trained athletes; this was in line with expectations, most likely thanks to their improved adaptation to training.[51] The findings also relate to higher post-workout IL-6 concentrations and fewer changes in biochemical markers of muscle damage in individuals with good training.[26]

In another study, it was found that the highest concentration of IL-6 was caused by decreased levels of adipose tissue, which resulted in reduced levels of inflammation in the body. This finding is in line with the results of research conducted by the author.[20] In this study, CK and IL-6 levels in all groups were initially high, but after being remeasured after 4 weeks of exercise with 12 training sessions, there was a decrease in blood samples in each group.[22] The HIIT group showed the most significant reductions in CK and IL-6 compared to the other groups.[16]

Meanwhile, the control group showed little or no change. This may be due to the body's adjustment to the sport, resulting in minimal muscle damage. This research also has limitations. These limitations include the influence of overall diet and lifestyle that can affect outcomes. Without monitoring of calorie intake, sleep quality, stress levels, and increased activity beyond the researchers' observations, the effects of HIIT or MICT may not fully reflect the impact of exercise itself. The study focused on students who were already physically active before the intervention. Previous studies have shown that HIIT training for up to 8 weeks can reduce biomarker damage in physically active young men and reduce IL-6 levels. Further research is needed to determine the effects of HIIT for more than 8 weeks, whether it remains a superior exercise or carries the risk of causing higher fatigue.

CONCLUSION

The conclusions of this study showed that the group that participated in the HIIT intervention was more effective in lowering CK and IL-6 levels compared to MICT performed continuously after 12 sessions over a period of 4 weeks. These findings are relevant for various health and fitness programs, especially for individuals who are looking for exercise that is effective, efficient, and provides great benefits to the body with minimal impact on muscle damage after the adaptation process. Practically, the results of this research can be used to design a more efficient, accessible, and flexible fitness program for people with limited time. With the right adjustments, these results have the potential to have a positive impact on public health.

ETHICAL CONSIDERATION

The Ethics Committee of Universitas Negeri Surabaya with registration number B/87396/UN38.6.3/TD.00/2024. Informed agreement from the respondents to the survey was also provided, which approved the use of sampling.

CONFLICT OF INTEREST

The authors stated that they have no conflict of interest.

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AUTHOR CONTRIBUTIONS

RN conceptualized the study design and prepared the manuscript; AR and YT conceptualized the study design; AS and FES collected the data; MAS and RI prepared the manuscript; BL and ADC owned the funding; and AP, IDMAWK, and LMA analyzed the data.

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