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Analysis Of Changes In Endothelin-1 (Et-1) And F_2-Isoprostane Levels After The 30 Km Event In The Makassar Bike Community At The "Bike For Health" Event

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ABSTRACT

This study aims to determine changes in ET-1 and F_2-Isoprostane levels after a 30 km cycling event in the Makassar cycling community. This study used a pre-experimental with one group pretest-posttest design on 30 male cyclists aged 30-60 years. The sampling technique used is the purposive sampling method. The pretest was carried out the day before the 30 km cycling event, then the post-test was carried out 2 hours after the cycling event. Blood testing is done with an ELISA Kit. Data were analyzed using the Wilcoxon test to see changes in ET-1 and F_2-Isoprostane levels after cycling events. The correlation of changes in ET-1 and F2-Isoprostane levels was analyzed using the Spearman test. The results of this study found that the 30 km cycling event had no significant effect on changes in levels of ET-1 ($p=0.082$) and F_2-Isoprostane, which means that it has no potential to increase the body's oxidative stress ($p=0.688$). Changes in ET-1 levels did not correlate with changes in F_2-Isoprostane levels which showed no association with impaired cardiovascular function ($p=0.102$).

Keywords: *Cyslists; F2-Isoprostane; Endothelin-1.*

INTRODUCTION

Exercising is a physical activity that is carried out to maintain the health and fitness of the body and restore the freshness of mind which can be done amidst the busy life of today's society. One type of recreational sport that is popular and growing in society is cycling (Götschi et al., 2016). Cycling is used as a healthy lifestyle by some people. They joined in small groups and formed a bicycle community, where the community was formed to share a hobby. Cycling is used as a healthy lifestyle by some people. They joined in small

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groups and formed a bicycle community, where the community was formed to share a hobby.

During the Covid-19 pandemic, the government provided recommendations aimed at cyclists and pedestrians, especially in densely populated urban areas (Barbarossa, 2020). Dari From data collected by The Institute for Transportation and Development Policy (ITDP), during the Covid-19 pandemic, cycling increased by up to 1,000 percent and increased production by up to 30 percent. When social restrictions were enforced for months, cycling was an option for Indonesians to maintain physical fitness and reduce boredom (Budi et al., 2021).

To measure or record sports activities, the application that is usually used is Strava. Strava is an application that is widely used by cyclists. Cyclists use strava to record or view maps and measure distance, time, speed and even the elevation or incline of the track. Strava is an internet service application for tracking and recording sports activities (cycling and running) using GPS data from smartphones (Rupaka et al., 2021).

In carrying out the physical activity it should be following the intensity, duration, frequency and intervals of exercise that have been determined, because if it is too excessive it will increase the incidence of injury or overtraining (Brancaccio et al., 2010). Under certain circumstances, moderate-to-severe intensity physical activity if carried out not following FITT can have a negative effect, namely inhibiting or interfering with physiological processes in the body. Increased use of oxygen, especially by contracting muscles, causes leakage of electrons from mitochondria which will become ROS (Reactive Oxygen Species). Cycling activity has also been shown to have benefits for heart and lung conditions, but when done excessively it can pose a risk of cardiovascular disorders and trigger sudden death due to cardiac arrest or sudden cardiac death (Marijon et al., 2011). SCD or cardiac death is the most common cause of sudden death in athletes, ranging from 1 in 40,000 to 1 in 80,000 athletes per year (Wasfy et al., 2016; Harmon et al., 2014). Reporting of SCD events related to cycling in Europe in 2003-2004 amounted to 7 cases in professional athletes (Santos-Lozano et al., 2016).

Increased oxygen metabolism after acute exertion increases oxidative stress. Even so, short-term training studies and acute activity effects studies conducted in various populations of adults, active young men and children have shown reduced concentrations of markers of oxidative stress after exercise, although other studies have shown no effect (Rudra et al., 2011). F_2-Isoprostane is the most frequently used clinical biomarker to measure in vivo lipid oxidation and oxidative stress (Ma et al., 2017). Besides F2-

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Isoprostane, Endothelin 1 is also a biomarker for tissue damage, especially in blood vessels. An increase in ET-1 levels indicates tissue damage to the blood vessels which can be acute or chronic (Adrianaana et al., 2011).

From the results of observations made on the SLIM cycling community in Makassar, researchers obtained information that the number of members of the SLIM community in Makassar is more than 100 people. Age group ranging from 40 years to 90 years. Where they have undergone an intensive cycling routine for more than 1 year and are included in the category of fun bike cyclists. Cycling activities are carried out every day with a duration of approximately 1 hour, different on weekends, the duration will be increased to approximately 3 hours.

Various studies have shown the positive and negative effects of mileage and average speed on changes in F_2-Isoprostane levels. Right now there is no measure of the intensity of cycling that is right and safe. The existence of these pros and cons makes researchers interested in conducting further studies to support previous research. In addition, few studies have been conducted evaluating changes F_2-Isoprostane levels in cyclists. Based on this background, researchers are interested in conducting this research to assess the level of exercise activity of cyclists in Makassar whether it is classified as safe or overtraining causing disturbances to the physiology of the body, especially cardiovascular conditions.

METHOD

Study Design

This research is a pre-experimental study with one group pretest-posttest design. Ethical clearance was granted by the Research Ethics Committee of the Faculty of Medicine, University of Hasanuddin, Makassar, Indonesia (Approval No: 577/UN4.6.4.5.31/PP36/2022, Protocol No.: UH22080482).

Subject Recruitment

This research was conducted in Makassar City by taking 30 cyclists as subjects. Subjects were drawn from various cyclist communities in Makassar who were willing and met the inclusion criteria in October 2022. The inclusion criteria were men aged 30-60 years who were active in cycling, had cycled for more than one year, had a normal resting EKG, and were willing to have their blood drawn. While the exclusion criteria were having a history of cardiovascular disease, alcohol abuse and obesity. Some basic checks are carried out

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before cycling events such as blood pressure, vo2 max, and Body Mass Index, as well as EKG examinations, carried out at the time of the first blood draw (pretest).

Blood Sample Collection

A total of 3 ml of venous blood samples were taken from the subjects to test F2-Isoprostane and ET-1 levels and then stored in the freezer of the HUM-RC laboratory, at Hasanuddin University Hospital. Serum was separated by centrifuge at 5000 rpm for 5 minutes, then the material was used for examination. Testing blood samples using the ELISA Kit from Elabscience.

Statistic analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 24 (IBM Corporation, Armonk, NY, USA). The Shapiro-Wilk test was carried out to test the normality of the data, with $p < 0.05$ indicating that the data was not normally distributed. To determine the effect of age and speed on changes in F_2-Isoprostane and ET-1 levels, the Wilcoxon test was used. The spearman correlation test was used to determine the correlation of changes in F_2-Isoprostane with ET-1.

RESULTS AND DISCUSSION

Descriptive Analysis Results

Data processing was carried out with the IBM SPSS 24 program using the Wilcoxon test (abnormal distribution) to find out how age and average speed affect changes in ET-1 and F2-Isoprostane levels before and after the 30 km cycling event.

Table 1.
Distribution of General Characteristics of Cycling Subjects

Characteristic	N	%
Age		
30-45 years	15	50
46-60 years	15	50
Categories Exercises		
Trained	13	43,3
Untrained	17	56,7
Smoking History		
Yes	5	16.7
Not	25	83.3
Consumption of Medicines		
Yes	2	6.7
Not	28	93.3

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Table 2.
Distribution of Baseline Examination Results of Cycling Respondents

Baseline Examination Results	N	%
Body Mass Index		
Underweight	0	0
Ideal	16	53.3
Overweight	14	46.7
Energy intake (Food Recall 24 hours)		
< 80 % inadequacy	9	30
80-110 % is enough	14	46.7
> 110 % more	7	23.3
Level VO_2 max		
Excellence	0	0
Good	0	0
Above average	1	3.3
Average	1	3.3
Below average	7	23.3
Poor	8	26.7
Very poor	13	43.3
Category Level VO_2 max		
Median > (Bad)	21	70
Median < (Good)	9	30
Average Speed		
Median > (Fast)	15	50
Median < (Slow)	15	50
ECG		
Usual	30	100
Abnormal	0	0

Analysis of ET-1 levels before and after the 30 km cycling event

To determine the level of ET-1 before and after the 30 km event, the Wilcoxon test was used. The results of the Wilcoxon test in the age group that participated in the 30 km cycling event will be described below.

Table 3.
Analysis of changes in ET-1 levels after a 30 km cycling event

Variables	n	30 km cycling event		p
		Pre-test MeanSD± (µg/l)	Post-test MeanSD± (µg/l)	
ET-1	30	62.62±89.34	86.25 ± 131.81	0.082

Wilcoxon test, meaning when p<0.05

Table 3 shows the ET-1 level before the 30 km cycling activity was 62.62 ± 89.34 µg/l and the ET-1 level after the event was 86.25 ± 131.81 µg/l. The results of statistical test analysis with the Wilcoxon test showed no change in ET-1 levels after cycling 30 km (p>0.005).

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Analysis of Changes in F_2-Isoprostane levels Before and After the 30 km Cycling Event

To determine the F_2-Isoprostane level before and after the 30 km event, the Wilcoxon test was used. The results of the Wilcoxon test in the age group that participated in the 30 km cycling event will be described below.

Table 4.
Analysis of changes in F_2-Isoprostane levels before and after event cycling 30 km

Variables	n	30 km cycling event		p
		Pre-test MeanSD± (pg/ml)	Post-test MeanSD± (pg/ml)	
F2-Isoprostane	30	102.51±50.16	109.22±42.94	0.688

Wilcoxon test, meaning when $p<0.05$

Based on **Table 4**, the F2-Isoprostane level before the 30 km cycling event is 102.51 ± 50.16, while the F_2-Isoprostane level after the 30 km cycling event is 109.22 ± 42.94. The results of the statistical test analysis with the Wilcoxon test obtained p value = 0.688 ($p>0.05$) which means that there was no significant change in F_2-Isoprostane levels after the 30 km cycling event.

Test differences in ET-1 levels before and after cycling events in age, average speed, exercise category, BMI, and smoker category

To determine the difference in changes in ET-1 levels in various categories of groups, the Mann-Whitney test was used. The results of the Mann-Whitney test will be described below.

Table 5.
Analysis of Changes in ET-1 levels in various category groups

ET-1	Pre-test Mean±SD	Post-test Mean± SD	ΔET-1 Mean±SD	p-value
Age				
30-45 Years	59.28 ± 89.07	87.37 ± 139.75	-0.36±2.26	0.101
46-60 Years	5.73 ± 0.57	85.14 ± 128.27	0.58±0.53	
Speed				
Group 1 (Median >)	56.7±84.68	59.67 ± 99.48	0.35±0.57	0.130
Group 2 (Median <)	69.1±96.2	112.36 ± 157.10	-0.14±2.33	
Categories Exercises				
Trained	64.19 ± 93.55	55.11 ± 62.56	-9.08 ± 35.06	0.011
Untrained	60.31 ± 89.48	108.62 ± 165.66	48.31 ± 95.90	
BMI				
Ideal	50.91 ± 46.85	71.77 ± 104.42	20.86 ± 70.86	0.201
Overweight	75.36 ± 122.38	100.52 ± 161.52	28.07 ± 91.73	
Smoking History				
Yes	14.71 ± 11.54	25.64 ± 6.83	10.93 ± 14.80	0.802
Not	72.20 ± 95.12	98.38 ± 141.66	26.18 ± 87.58	

In **Table 5** of the age group of 30-45 years, there was a decrease in the level of ET-1 with a mean SD of -0.368±2.265, while in the age group of 46-60 years, there was an

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increase in the average level of ET-1 with mean±SD 0.581 ± 0.534. The results of the Wilcoxon test showed that there was a very significant influence at the age of 46-60 years on changes in ET-1 levels (p=0.001), while the age group of 30-45 years did not show a significant influence of age. In the > median speed group, there was an increase in ET-1 levels with a mean±SD 0.35±0.57, while in the < median speed group there was a decrease in ET-1. Wilcoxon tests in both speed groups showed an effect of speed on changes in ET-1 levels with significance values in the > median (p=0.027) and < median (p=0.041) groups. In the trained category group there was a decrease in posttest ET-1 levels by -9.08 ± 35.06 and in the untrained category group, there was an increase in ET-1 by 48.31 ± 95.90. The Wilcoxon test showed the untrained group showed a very significant influence on ET-1 (p=0.006), while the trained group showed no significant influence. In the ideal group BMI category, the change in ET-1 levels that occurred after the cycling event increased with a mean of 20.86 ± 70.86. In the overweight group, the juga experienced an increase of 28.07 ± 91.73. Based on Wilcoxon's test results showed no significant changes in the ideal and overweight groups. For the group of smokers and non-smokers, there was an increase in changes in ET-1 levels. The mean±SD mean value of smoking history is 10.93±14.80, while the mean±SD mean value of non-smoking is 26.18±87.58. Based on the table above, there is no effect of smoking or not with changes in ET-1 levels.

Test the Effect of F2-Isoprostane Levels Before and After Cycling Event in Age, Average Speed, Training Category, BMI, VO2max, and Smoker Categories

To determine the influence of the age group (30-45 and 46-60 years) and speed (> median and < median) on changes in F_2-Isoprostane levels before and after the 30 km event, the Wilcoxon test was used. The results of the Wilcoxon test will be described below.

Table 6.
Analysis of the Effect of age and speed on changes in F_2-Isoprostane levels

F2-Isoprostane content	Pre-test Mean±SD	Post-test Mean± SD	Δ F2-Isoprostane Mean±SD	P-value
Age				
30-45 Years	109.240±52.551	95.187± 39.761	-14.052± 41.713	0.065
46-60 Years	95.783±48.519	123.258±42.637	27.474±67.452	
Speed				
(Median >)	112.82±58.54	121.36±41.10	8.54±69.81	0.820
(Median <)	92.19±39.46	97.07±42.60	4.87±48.29	
Category Exercise				
Trained	96.24±51.32	116.27±51.32	20.02±69.83	0.368
Untrained	107.30±50.29	103.83±35.87	-3.47±48.99	
BMI				
Ideal	94.26 ± 55.36	112.58 ± 46.50	18.32 ± 67.73	0.299
Overweight	111.93 ± 43.56	105.37 ± 39 86	-6.55 ± 46.04	

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F2-Isoprostane content	Pre-test Mean±SD	Post-test Mean± SD	Δ F2-Isoprostane Mean±SD	P-value
Smoking History				
Yes	139.54 ± 65.10	137.24 ± 43.04	-2.30 ± 56.82	0.676
Not	95.10 ± 44.62	103.61 ± 41.51	8.51 ± 60.41	

Wilcoxon test, meaning when p<0.05

In **Table 6.** in the age group of 30-45 years, the average difference in F_2-Isoprostane levels before and after the event decreased with a mean±SD of -14,052± 41,713 while in the age group of 46-60 years, there was an increase in the average level of F_2-Isoprostane with a mean±SD of 27,474±67,452. For both velocity groups, there was an increase in F_2-Isoprostane levels with the >median group higher (8.54±69.81) than the < median group (4.87±48.29). In the trained group category, there was an increase in F_2-Isoprostane levels by 20.02±69, while in the untrained group, there was a decrease in F_2-Isoprostane levels by -3.47±48.99. In the BMI category group, there was an increase in F_2-Isoprostane levels in the ideal group by 18.32±67.73 while in the overweight group, there was a decrease in F_2-Isoprostane levels after the cycling event by -6.55±46.04. In the smoking category, the average F_2-Isoprostane pretest value of the smoking group was 139.54±26.57, while in the non-smoking group, it was 95.10±44.62. The difference in changes in F_2-Isoprostane levels after the cycling event in the smoking group was -2.30±23.20, while in the non-smoking group, it was 8.51±60.41.

Wilcoxon test results showed no significant change in F_2-Isoprostane levels (p>0.05) after cycling events in the age group, speed, exercise category, BMI and VO2max categories. However, in the smoking category, Wilcoxon's test results showed significant changes in the smoking group (p=0.006), but not in the non-smoking category group (p=0.638).

Correlation Test of Changes in **ET-1 levels with changes in F_2-Isoprostane levels**

Table 6.
Correlation of changes in F_2-Isoprostane levels with changes in ET-1 levels

Variable	N	R	p-value
Δ F2-Isoprostane <--> ΔET-1	30	**-0,238**	**0.102**

Spearman rank, meaning when p<0.05

Based on **Table 6**, data from the spearman correlation test analysis were obtained which showed that there was no significant relationship between changes in F2-Isoprostane levels and changes in ET-1 levels. (p>0.05) with the strength value of the

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correlation coefficient r=-0.238 indicating that the change in F_2-Isoprostane levels with changes in ET-1 levels has weak correlation strength.

Discussion

Changes in ET-1 levels Before and After the 30 Km Cycling Event

Endothelin-1 (ET-1) is a powerful vasoconstrictor produced by endothelial cells of blood vessels and the human heart Haynes (1993) (in Purnamasari, 2013). Endothelin-1 is derived from the breakdown of prepropeptides containing 203 amino acids. ET-1 is predominantly expressed towards the smooth muscles of the blood vessels. ET-1 induces signals through receptor intermediaries that will activate the G protein.

High metabolic rates, lack of oxygen, and increased procurement of lactic acid during strenuous physical exercise will stimulate the production of free radicals affiliated with ROS (reactive oxygen species). (Shahrastani et al., 2019). Free radicals can form as a result of physical exercise when muscles contract and in tissues ischemic reperfusion occurs when their amount exceeds the antioxidant defence system will initiate lipid peroxidation, thereby increasing ET-1 and F_2-Isoprostane which marks an increase in free radicals in the body (Syahrastani et al., 2019). With age, the endothelial function will further decrease.

The results showed that there was a significant influence of age on changes in ET-1 levels, especially in the older age group (46-60 years) while the age group of 30-45 did not show a significant influence on changes in ET-1 levels. When viewed from the average value of changes in ET-1 levels after cycling, the age group of 30-45 years experienced a decrease in ET-1 levels while the age group of 46-60 years experienced an increase in ET-1 levels. These results suggest that the increase in ET-1 levels occurs in older age groups. This is in line with Maeda's research that high concentrations in healthy elderly women have doubled due to intravenous exogenous infusion significantly increasing systemic blood vessels whose secretion is known to be carried out by polarized endothelial cells into blood vessels (Maeda et al., 2017). The increase in levels in older age groups is also in line with research conducted by Miyauchi which showed significantly higher concentrations in old age than in young age. (Miyauchi et al.,2003) This study shows that the age category of 40 years and older is prone to sudden cardiac death. Meanwhile, the speed group showed greater improvement in cyclists with the median > speed group. These results were in line with research in the group of mice that exercised with an intensity of 45 minutes at a speed of 25 m / min where there was a greater increase in ET1 than in mice in the control group (Maeda et al., 2003).

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Changes in F_2-Isoprostane levels Before and After the 30 Km Cycling Event

Isoprostan products in the human body were first discovered in the form of prostaglandin-like compounds, which were eventually given the name F_2-Isoprostane. F_2-IsoPs are metabolites produced by the peroxidation of arachidonic acid-free radicals through the free radical catalyzing mechanism, regardless of the action of cyclooxygenase. Some researchers believe that F_2-IsoPs have a stable chemical structure, are formed at the site of attack of free radicals, then leave the plasma membrane, circulate in the blood, and are excreted in the urine. (Montuschi et al., 2004; Cracowski, 2004; Janicka et al., 2010) .

In the blood, F_2-IsoP exists in 2 forms, free and bound to phospholipids or lipoproteins. F_2-IsoP bound to phospholipids is released as a free form in plasma by phospholipase activity. And this form of Free F_2-IsoPs will be excreted through the urine. One study found that changes in free F_2-IsoPs levels in the blood could be caused by increased lipid peroxidation, increased phospholipase activity, or decreased renal clearance. (Dalle-Donne et al,2006) Researchers say that the measurement of total levels of F_2-IsoPs (free and bound to phospholipids) better describes the actual state of oxidative stress compared to using only free F_2-IsoPs. (Barden et al., 2010; Hung, 2006).

The results showed that there was no significant influence of age group and speed on changes in F_2-Isopostane levels before and after participating in cycling events at a distance of 30 km (Table 2). However, when viewed from the average value of the difference from changes in F_2-Isoprostane levels before and after cycling, then subjects with a younger age group category (30-45 years) there was a decrease in F_2-Isoprostane levels and an older age group (46-60 years) F_2-Isoprostane levels increased, which means an increase in oxidative stress levels was found. The results of this study are following research from Ma et al (2017) as the level of F_2 isoprostane levels increases can experience a significant increase in fish. (Adrianna 2011) In old age, especially 46-60 years if there is an increase in F_2-Isoprostane levels, it can be a marker of an increased risk of cardiovascular disorders in line with research that shows that as they get older, normal IsoP levels in rats and humans will increase.

Changes in ET-1 levels after the 30 km Cycling Event in the Age, Speed, Training Category, BMI and Smoking History Categories

As the endothelial function ages it decreases, in this study, shows that there is a significant influence of age on changes in ET-1 levels, especially in the older age group

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(46-60 years). When viewed from the average value of changes in ET-1 levels after the event, the age group of 30-45 years experienced a decrease in ET-1 levels while the age group of 46-60 years experienced an increase in ET-1 levels.

These results suggest that the increase in ET-1 levels occurs in older age groups. This is in line with Maeda's research that high concentrations in healthy elderly women have doubled in those caused by intravenous exogenous infusion that significantly increases systemic blood vessels, where it is known that their secretion is carried out by polarized endothelial cells into blood vessels (Maeda et al.,2001; Sarah P, 2016). The increase in levels in older age groups is also in line with research conducted by Miyauchi which showed that concentrations are significantly higher in old age than in young age (Tanabe et al., 2003). This study shows that the age category of 40 years and older is prone to sudden cardiac death. While at the young age of 30-45 years experienced a decrease in ET-1 levels This is following research conducted by Maeda which shows that chronic exercise causes an increase in no production and a decrease in the production of ET-1 in humans, which can produce beneficial effects (that is, vasodilative and antiatherosclerotic) on the cardiovascular system (Maeda et al., 2001). By practising regular physical exercise, the level of endothelin-1 in the circulation decreases (Maeda et al., 2002). A decrease in endothelin-1 levels can be caused by an increase in the clearance of the substance. While the speed group showed a greater increase in cyclists with a median > speed group. These results were in line with research in the group of mice that exercised with an intensity of 45 minutes at a speed of 25 m/min where there was a greater increase in ET1 than in mice in the control group (Kobayashi et al., 1998).

Table 5 also shows a very significant change in ET-1 levels after the 30 km event in the untrained cycling group, where there was an increase. These results are in line with the research that the effects of aerobic exercise have the opposite result on plasma ET.where the trained group decreases while in the untrained group, it increases (Antonios, 2004). This change occurs due to neurohumoral factors (catecholamines and angiotensin II) as well as factors from hemodynamic shear stress that can trigger release from ET-1 (Takamura et al., 2013). Whereas in the trained group research showed that by doing regular physical exercise, endothelin-1 levels in circulation decreased (Maeda et al., 2002). A decrease in endothelin-1 levels can be caused by an increase in the clearance of the substance. Endothelin-1 clearance is related to the work of endothelin-B receptors in the endothelium. The large amount of endothelin-1 that binds to the endothelin-B receptor will cause a decrease in endothelin-1 levels in circulation.

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In the Body Mass Index (BMI) category group, the results of this study showed no significant changes to ET-1. In the ideal and overweight category groups, it showed an increase in ET-1 levels after the 30 km cycling event. In the overweight group, the pretest values were found to have higher values, where this occurred due to an imbalance between NO and ET-1 production, this was further proven in the Cardillo study where obesity and overweight showed insulin-induced vasoconstriction and an increase in ET-1-dependent vasoconstrictor tone as well as a decrease in No-dependent vasodilators (Schinzari et al., 2015; Cardillo et al., 2004).

In the above study in the smoking category, there was no significant change between smokers and those who did not. Where it is necessary to know that nicotine consumption through cigarettes can induce health problems in passive smokers with an increase in endothelin-1 plasma (ET-1). This increase in endothelin plasma occurs after the occurrence of an increase in plasma vasopressin (a hormone that functions to reduce the urinary formation and increase blood pressure). An increase in endothelin-1 plasma can lead to the occurrence of the pathogenesis of some disorders in the cardiovascular. This can occur in connection with the plasma properties of endothelin-1 which is a peptide that is a vasoconstrictor (blood vessel constricting element) that is strong and has an effect on the growth of smooth muscles and muscle cells from the heart (Lula, 2018).

Effect of F_2-Isoprostane Levels after a 30 Km Cycling Event on Age Group, Speed, Training Category, BMI, VO2max, And Smoking History Category

When a person is in a family, the need for oxygen metabolism will increase. As a result, the production of ROS (Reactive Oxygen Species) that occurs, especially during overtraining, can defeat the body's antioxidant defence mechanisms. This can trigger an increase in systemic oxidative stress where F_2-isoprostane is the biomarker most often used to measure oxidative stress levels and free radicals (Ma et al., 2017) (Arikawa et al., 2013) (Van 't Erve et al., 2017).

Current results showed that there was no significant effect on age group and speed on changes in F_2- Isoprostane levels before and after participating in a 30 km cycling event. However, when viewed from the average value of the difference in changes in F_2-Isoprostane levels before and after the cycling event, in the younger age group (30-45 years) there was a decrease in F_2-Isoprostane levels, while in the older age group (46-60 years) there was an increase in levels F_2-Isoprostane after cycling event which means higher there is an increase in free radicals and oxidative stress. As we age, the heart's response will

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decrease to exercise. The results of this study are in line with the results of the study of Ma et al (2017) which obtained the results of the level of F_2-Isoprostane urine found to increase progressively with age (Ma et al., 2017). The results of other studies also showed an increase in F_2-Isoprostane levels in healthy parents with age (Savage et al., 2022). In another study, it proved that there was no significant correlation between F2-Isoprostane and the patient's age even though the value of F_2-Isoprostane rose slightly without reaching significant levels (Volpe et al., 2006).

In this study in the speed group, there was an increase in F_2-Isoprostane levels in both speed groups although it did not reach significant levels, where the >median speed group there was a higher average increase than the <median group. That is, the higher the speed, the higher the increase in F_2-Isoprostane levels which also shows an increase in oxidative stress levels. Higher speed versus low speed can be one of the categories of training intensity (whether it includes light, moderate, or heavy-level training).

In the training category group, there was an increase in the endurance of cyclists. This is following research that showed an increase in F_2-Isoprostane in the short-term low-intensity exercise group when compared to the control group. Although the increase did not reach significant figures, Baraas et al concluded that exercise did not change the production of Reactive Oxygen Species (ROS) indicated by the F_2-Isoprostane biomarker.

This study showed no change in F_2-Isoprostane levels in the trained and untrained group of cyclists. However, when viewed from the average value of F_2-Isoprostan levels, trained or trained cyclists experienced an increase while untrained experienced a decrease, according to research conducted by Baraas which showed that the group in the trained category showed an increase in F_2-Isoprostane, although this study did not achieve a significant increase.

For the BMI category in this study, the F_2-Isoprostan change was not significant after the 30 km cycling event, but when viewed from the baseline data value or at the time of the pretest, the overweight group value was higher than the cyclist group in the ideal category. F_2-Isoprostane changes also decreased after cycling events. These results are in line with research that shows that oxidative stress can be reduced by exercising, especially in overweight and obese subjects, where obesity can cause oxidative stress states due to an imbalance between free radicals and antioxidants in the body (Niki, 2018).

There was a significant change in F_2-Isoprostane levels in the smoking group, and not in the non-smoking group. The average value of pretest F_2- isoprostane in the smoking

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group was higher compared to the non-smoking group. In line with the theory that smoking can form lipid peroxidation where this process changes the components of the cell membrane and forms toxic compounds. Oxidative damage can have worse impacts on health (Lopes et al.,2013). However, after the cycling event, there was a decrease in F_2-Isoprostane levels in the smoking group. These results illustrate the positive effects of exercise that reduce oxidative stress levels in line with the study (Arikawa et al., 2013). These results are also supported by the theory that smoking triggers various cardiovascular disorders, but the positive effects of physical activity and exercise can prevent the development of the risk of such cardiovascular diseases (Dobrosielski, 2021).

Correlation Test of Changes in ET-1 levels with Isoprostane F_2 Levels

The results of the spearmen correlation test in this study showed that there was no correlation between changes in CKMB levels and F_2-Isoprostane levels. This means that the hypothesis is not accepted. In contrast to the theory of studies on the effects of increased production of ET-1 mediated through ETA receptors in vascular walls localized to smooth muscle cells, it provides an ET-1 vasoconstrictor effect under physiological conditions. This leads to an increase in vasoconstrictors, increased inflammatory activity and increased oxidative stress.

CONCLUSIONS AND SUGGESTIONS

Conclusions

Based on the results of the research and discussion that the authors have explained, the authors of this study can conclude that there is a significant effect of age on changes in ET-1 levels, especially in the older age group (46-60 years) while the 30-45 age group shows no effect significant effect on changes in ET-1 levels. When viewed from the average value of changes in ET-1 levels after the event, the age group 30-45 years actually experienced a decrease in ET-1 levels while the age group 46-60 years experienced an increase in ET-1 levels. These results indicate that the increase in ET-1 levels occurs in the older age group.

The results of the study related to changes in F2-Isoprostane levels before and after a 30 km cycling event showed no significant effect in the age group and speed on changes in F2-Isopostane levels. However, from the average value of the difference between changes in F2-Isoprostane levels before and after cycling events in younger age subjects (30-45 years) there was a decrease in F2-Isoprostane levels, and in the older age group (46-60

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years) isoprostane F2 levels increased, which means an increased level of oxidative stress was found.

The results of the correlation between changes in F2-Isoprostane levels and changes in ET-1 before and after the 30 km cycling event showed no correlation, where changes in F2-Isoprostane levels with changes in ET-1 levels had a moderate correlation strength.

Suggestions

The author's suggestion for the future is to carry out a test on the third post blood sampling 24 hours after cycling to find out whether tissue damage is only temporary and can return to basal values after exercise.

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