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Influence of ACE Gene Polymorphism on Heart Rate Dynamics During Submaximal Exercise Following a 3-Month Fartlek Training Program in Male Adolescents

Fatoni Fatoni [1], Muhammad Kamal [2], Hasbi Asyhari [3], Juhanis Juhanis [3],

[1] Department of Physical Education, Health and Recreation Universitas Negeri Makassar, Indonesia.
fatoni@unm.ac.id
[2] Department of Physical Education Health and Recreation, Universitas Negeri Makassar, Indonesia.
kamal212@unm.ac.id
[3] Department of Physical Education Health and Recreation, Universitas Negeri Makassar, Indonesia.
hasbi.asyhari@unm.ac.id
[4] Department of Physical Education Health and Recreation, Universitas Negeri Makassar, Indonesia.
juhanis@unm.ac.id

ABSTRACT

Objective: This study aims to analyze the effect of angiotensin-converting enzyme (ACE) gene polymorphism on heart rate dynamics during submaximal exercise in male adolescents after participating in a fartlek exercise program for 3 months.

Methods: This quantitative experimental study involved 59 healthy male adolescents aged 13–15 years who participated in a structured fartlek training program for 12 weeks. ACE genotypes were determined using polymerase chain reaction (PCR) and classified into ACE II and non-II (ID/DD) groups. Heart rate was measured every minute during 6 minutes of submaximal stationary cycling exercise before and after the intervention. Statistical analyses were performed using paired t-tests and independent t-tests at a significance level of $p < 0.05$.

Results: After the intervention, there was a significant decrease in heart rate across all minutes of exercise in both genotype groups ($p < 0.001$). The group with the ACE II genotype showed a greater decrease in heart rate than the non-II group, indicating more efficient cardiovascular adaptation to endurance-based exercise.

Conclusion: ACE gene polymorphisms influence heart rate dynamics during submaximal exercise in adolescent boys after fartlek training. ACE II genotype is associated with higher cardiovascular efficiency, confirming the role of genetic variation as a biological modulator of adaptive responses to exercise.

Keywords: ACE gene polymorphism; heart rate dynamics; submaximal exercise; endurance-based training; adolescents

Corresponding Author:
(Fatoni Fatoni)

- Department of Physical Education, Health and Recreation Universitas Negeri Makassar, Indonesia.
- Email: fatoni@unm.ac.id

1. INTRODUCTION:

Cardiovascular system efficiency is a key determinant of physical fitness, health, and sports performance. Cardiovascular adaptability reflects the body's physiological regulatory capacity to maintain performance during prolonged physical activity (Brandt et al., 2025; López & Santos-García, 2025). Endurance training is known to increase cardiac output, oxygen utilization efficiency, and autonomic nervous system control, thus supporting more stable submaximal performance (Kodli, 2023; Taylor et al., 2021).

Although adaptive responses to training are often assumed to be homogeneous, evidence suggests substantial interindividual variation, even when given a uniform training stimulus. This variability is influenced by age, initial fitness level, and biological characteristics, including genetics (Lopes et al., 2022; Sandroff et al., 2018). In this context, genetic factors are increasingly recognized as important contributors to differences in cardiovascular adaptation and endurance (Bedrač et al., 2024; Bossi et al., 2023).

The angiotensin-converting enzyme (ACE) gene, specifically the insertion/deletion (I/D) polymorphism, is one of the most extensively studied genetic markers in exercise physiology. This variation results in three genotypes (II, ID, DD) associated with differences in ACE activity, vascular regulation, and cardiovascular response to exercise (Hadi & Rosyanti, 2019; Ouali et al., 2025). The I allele is consistently associated with better aerobic performance and endurance adaptations, while the D allele is more frequently associated with strength characteristics and higher cardiovascular responses during exercise (Dai et al., 2019; Grover et al., 2025; Neto et al., 2024).

Although the relationship between ACE polymorphisms and endurance performance has been extensively studied in adults and athletes, evidence regarding their influence on heart rate dynamics during submaximal exercise in adolescents is limited (Rolim et al., 2018; Soares et al., 2023; Valdivieso et al.,

2017). Given that growth and maturation can influence cardiovascular regulation, studies in this age group are scientifically relevant.
Therefore, this study aimed to evaluate the effect of ACE gene polymorphism on minute-by-minute heart rate dynamics during submaximal exercise after a 3-month fartlek training program in male adolescents.

2. Methods

2.1 Study Design and Participants

This study used a quantitative experimental design with pre- and post-intervention measurements. The study subjects were 59 male adolescents aged 13–15 years recruited from a junior high school in South Sulawesi Province. All subjects met the inclusion criteria, had no history of cardiovascular or metabolic disease, and had never participated in a structured endurance training program before the study was conducted. Written informed consent was obtained from all participants and their parents/guardians, and all study procedures were approved by the Research Ethics Committee (Approval Number: 557/H4.8.4.5.31/PP36-KOMETIK)

2.2 Training Intervention

Participants participated in a structured 12-week fartlek training program, consisting of 36 training sessions. Each session consisted of continuous running at varying intensities, aimed at providing moderate to high aerobic activity. This training protocol focused on developing cardiovascular endurance through varying running tempos, a common characteristic of fartlek training in endurance training programs for adolescents

2.3 Genotyping

Venous blood samples were taken from each participant for genetic analysis. Insertion/deletion (I/D) polymorphisms in the angiotensin-converting enzyme (ACE) gene were identified using conventional polymerase chain reaction (PCR) techniques, followed by analysis using agarose gel electrophoresis. Based on these results, ACE genotypes were classified into II, ID, and DD, and further grouped into ACE II and non-II (ID/DD) categories for statistical analysis.

2.4 Cardiovascular Measurements

Heart rate dynamics were the primary variable in this study and were defined as minute-by-minute changes in heart rate observed during physical activity. Resting heart rate was measured after participants rested in a supine position for 15 minutes under controlled conditions. Furthermore, the heart rate response during activity was assessed through 6 minutes of submaximal exercise on a stationary bicycle, performed before and after the exercise intervention. Heart rate was recorded at one-minute intervals throughout the exercise phase.

To obtain a more comprehensive picture of the participants' cardiovascular condition, several supporting measurements were also performed. Cardiovascular endurance was evaluated using a 12-minute running test used to estimate maximal oxygen consumption capacity (VO_2max). Additionally, blood pressure was measured using a calibrated digital sphygmomanometer, while plasma angiotensin-converting enzyme (ACE) levels were analyzed using an enzyme-linked immunosorbent assay (ELISA).

2.5 Statistical Analysis

Data analysis was performed using SPSS version 24. A normality test was performed as a prerequisite before inferential analysis. Comparisons before and after the intervention within one group were analyzed using the paired t-test, while differences between groups were analyzed using the independent t-test and the general linear model. A p-value <0.05 was used as the limit of statistical significance.

3. Results

Heart rate analysis results during a 6-minute stationary bicycle exercise load test showed a consistent decrease in heart rate after a 3-month fartlek training program. This pattern of decrease was observed in the genotype II group, the non-II group, and the overall sample. The decrease in heart rate occurred at all measurement points during the exercise (HR-CE 1 to HR-CE 6) and was statistically significant

In the ACE II genotype group, the mean pre-intervention heart rate showed a gradual increase with increasing exercise duration, from 122.0±10.9 beats/min^{-1} in the first minute to 150.0±16.2 beats/min^{-1} in the sixth minute. Following the exercise intervention, heart rate values decreased across all minutes of measurement, ranging from 109.1±14.5 beats·min^{-1} at HR-CE 1 to 141.7±15.5 beats·min^{-1} at HR-CE 6. The largest decrease occurred in the initial minutes of exercise, specifically at HR-CE 1, at 12.9±3.6 beats·min^{-1}, and tended to decrease gradually until HR-CE 6, at 8.3±0.7 beats·min^{-1}. All these differences demonstrated strong statistical significance ($p < 0.001$)

A similar response pattern was also found in the non-II genotype group. Before intervention, the mean heart rate increased from 124.0±12.8 beats·minute^{-1} at HR-CE 1 to 155.5±11.8 beats·minute^{-1} at HR-CE 6. After following the fartlek training program, there was a consistent decrease in heart rate at every minute of exercise, with values ranging from 112.4±13.7 beats·minute^{-1} at HR-CE 1 to 147.3±10.1 beats·minute^{-1} on HR-CE 6. The magnitude of the decrease in heart rate ranged from 11.6±0.9 beats·minute^{-1} in the first minute and decreased to 8.2±1.7 beats·minute^{-1} in the sixth minute, with all changes being statistically significant ($p < 0.001$)

When viewed across the entire sample, mean pre-intervention heart rate increased progressively from 123.1±12.0 beats·min^{-1} at HR-CE 1 to 153.0±14.1 beats·min^{-1} at HR-CE 6. After the intervention, heart rate showed a consistent decrease across all measurement points, with values ranging from 110.9±14.0 beats·min^{-1} at HR-CE 1 to 144.9±12.8 beats·min^{-1} at HR-CE 6. The largest decrease was found in the first minute of exercise at 12.2±2.0 beats·min^{-1}, which then decreased gradually until the sixth minute at 8.1±1.3 beats·min^{-1}. All changes were statistically significant ($p < 0.001$)

Comparatively, the group with the ACE II genotype showed a greater decrease in heart rate per minute of exercise than the non-ACE II group. The difference was most pronounced in the initial minutes of exercise, particularly the first to second minutes, indicating faster and more efficient cardiovascular adaptation in the ACE II genotype group.

4. Discussion

The results of this study indicate that the heart rate response during submaximal exercise significantly decreased after participants participated in a fartlek training program. This decrease was more pronounced in individuals with the ACE II genotype. The lower heart rate response in this group likely reflects better cardiovascular efficiency and lower peripheral vascular resistance, consistent with the relatively lower ACE enzyme activity in allele I carriers.

These physiological conditions are known to contribute to reduced cardiovascular workload during submaximal exercise and more efficient autonomic regulation in response to endurance-based exercise.

The findings presented in the Table confirm the role of angiotensin-converting enzyme (ACE) gene polymorphisms in modulating heart rate dynamics, particularly during exercise following a fartlek intervention. The results of this study indicate that individuals with the ACE II genotype exhibit different heart rate response patterns than individuals with other genotypes. These differences reflect variations in autonomic nervous system control and cardiovascular regulation.

Consistent with these findings, several previous studies have reported an association between ACE gene polymorphisms, including the I allele, and improved endurance performance, which is indirectly related to cardiovascular responses in athletes (Alves et al., 2018; Gasser et al., 2022). Furthermore, aerobic exercise has been shown to positively impact heart rate variability, an important indicator of autonomic function and cardiovascular health (Andrade et al., 2023; Basri & Turki, 2025; Gasser et al., 2023). However, the specific influence of ACE gene polymorphisms on heart rate dynamics during submaximal exercise requires further study to obtain more conclusive conclusions. The interplay between genetic predisposition and exercise-induced physiological adaptations illustrates the complexity of cardiovascular and autonomic regulatory mechanisms in response to physical stress.

Physiological studies have shown that lower ACE activity, commonly associated with the presence of the I allele, can affect cardiovascular responses, including heart rate variability (Montes-de-Oca-García et al., 2021; Soares et al., 2023). Improved aerobic fitness has also been reported to correlate with a reduced heart rate response during submaximal exercise, reflecting improved cardiovascular performance (Han et al., 2021; Nakahara et al., 2021; Nindorera et al., 2025). Thus, reduced heart rate demands during submaximal exercise underscore the importance of cardiovascular and autonomic regulation in improving exercise efficiency, while highlighting the potential role of genetic factors, such as the I allele of the ACE gene, in influencing these physiological responses.

The results of this study are consistent with previous reports showing more favorable endurance adaptations in individuals with the ACE II genotype. These findings also extend existing understanding by demonstrating genotype-specific heart rate dynamics in the context of exercise in adolescents. Importantly, the results of this study confirm that genetic factors act as modulators of exercise responses, not as the sole determinant of successful adaptation to physical exercise.

5. Conclusion

Three months of fartlek training significantly improved cardiovascular efficiency, as demonstrated by a decrease in heart rate during submaximal exercise, in adolescent boys. This adaptation occurred across all ACE genotypes, but was more pronounced in individuals with the ACE II genotype. These findings suggest that ACE gene polymorphisms contribute to individual variations in cardiovascular responses and act as biological modulators of adaptation to endurance training in the adolescent population.

- ***Preprint Declaration***

  Not applicable

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TABLE AND FIGURE

Table 1. Heart Rate Dynamics During a 6-Minute Cycle Ergometer Exercise According to

Gen	Observ.	HR-CE 1 Mean±SD	HR-CE 2 Mean±SD	HR-CE 3 Mean±SD	HR-CE 4 Mean±SD	HR-CE 5 Mean±SD	HR-CE 6 Mean±SD
II	Pre	122.0±10.9	132.8±12.7	138.5±12.9	142.2±13.3	147.0±11.9	150.0±16.2
	Post	109.1±14.5	119.3±14.9	126.7±14.7	132.0±14.3	136.8±12.9	141.7±15.5
	Change	12.9±3.6	13.3±2.2	11.8±1.1	10.2±1.0	10.2±1.0	8.3±0.7
	P*	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
NON II	Pre	124.0±12.8	132.0±13.8	138.8±13.9	144.0±14.1	150.1±12.9	155.5±11.8
	Post	112.4±13.7	120.9±13.6	128.5±12.9	133.9±12.7	140.9±11.6	147.3±10.1
	Change	11.6±0.9	11.1±0.2	10.3±1.0	10.1±1.4	9.1±1.3	8.2±1.7
	P*	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Total	Pre	123.1±12.0	132.3±13.2	138.7±13.6	143.4±13.7	148.8±12.5	153.0±14.1
	Post	110.9±14.0	120.3±14.1	127.7±13.6	133.0±13.3	139.2±12.3	144.9±12.8
	Change	12.2±2.0	12.0±0.9	11.0±0.0	10.4±0.4	9.6±0.2	8.1±1.3
	P*	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

ACE Gene Polymorphism After a 3-Month Fartlek Training Program

HR-CE: Heart Rate during Cycle Ergometer exercise

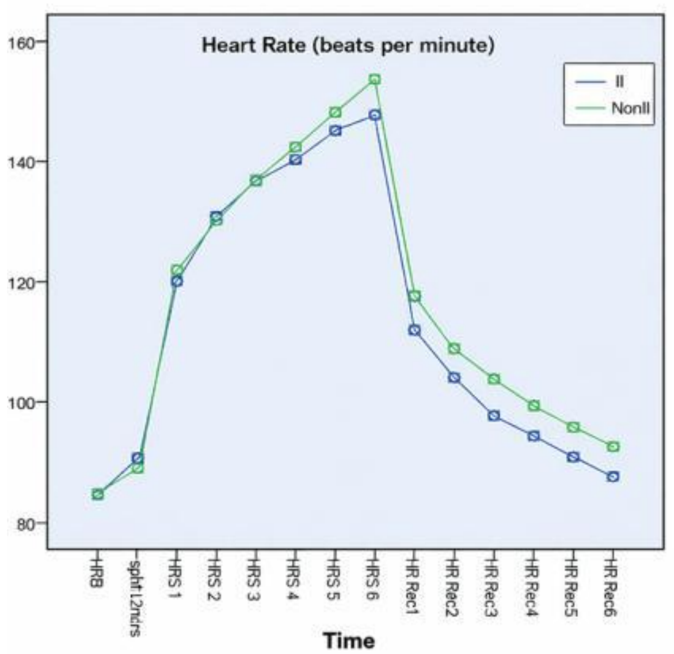

Figure 1. Heart Rate Responses During a 6-Minute Cycle Ergometer Exercise According to ACE Gene Polymorphism After a 3-Month Fartlek Training Program