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ORIGINAL ARTICLE

Impact of three types of resistance, aerobic, and combined exercises on serum levels of cardiac biomarkers in active older adults

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ABSTRACT

This study explored the impact of eight weeks of resistance, aerobic, and combined exercises on serum levels of Growth Differentiation Factor-15 (GDF-15) and N-terminal pro-brain natriuretic peptide (NT-proBNP) in active older men. Thirty-six participants were randomly divided into three groups (resistance, aerobic, and combined exercise), and serum levels were measured using ELISA kits before and after the exercise protocols. The results revealed a significant 6.4% increase in GDF-15 levels following aerobic exercise, while resistance exercise caused an 18.05% decrease. No notable change was observed in the combined exercise group for GDF-15. For NT-proBNP, aerobic and combined exercises led to reductions of 34.1% and 24.8%, respectively, while resistance exercises resulted in a 37.7% increase. These findings indicate that resistance exercises can reduce GDF-15 levels, which contrasts with the general view that aerobic exercises alone benefit cardiac health. Additionally, aerobic and combined exercises were effective in lowering NT-proBNP levels, whereas resistance exercises had the opposite effect.
Keywords: Sport health, Resistance exercise, Aerobic exercise, Combined exercise, GDF-15, NT-proBNP, Elderly.

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INTRODUCTION

There has been a growing emphasis on maintaining a healthy lifestyle, with numerous studies conducted in health, fitness physiology, and exercise physiology. These studies have focused on various aspects, including nutrition, daily physical exercise, metabolism, cardiovascular diseases, and the consequences and adaptations of exercise.

Physical activity is a powerful non-pharmacological solution for heart problems and related diseases, particularly in older adults. For instance, regular exercise can prevent obesity, heart attacks, hypertension, and arteriosclerosis. Sedentary behaviour can exacerbate these conditions. (Fleg, 2012). Studies have also indicated that aerobic exercise can positively change blood pressure, insulin levels, body weight, blood glucose, insulin resistance, cholesterol, and triglyceride levels (Christenson et al., 2010). As a result, exercise therapy has been recommended as an effective intervention for cardiovascular problems and for improving risk factors, particularly in the older population who may face challenges in managing obesity, hypertension, and diabetes through medications. (Lok et al., 2013).

Previous research has demonstrated the significant role that regular physical activity, encompassing both aerobic and strength training, plays in the non-pharmacological prevention and treatment of cardiovascular issues. This includes improving risk factors such as hypertension, fasting glucose, lipid profile, and obesity (Punia et al., 2016). The determinants of health and mobility in the older participants consist of a combination of primary factors, including genetics and secondary characteristics. Based on previous research findings, it can be concluded that due to the decline in the function of various body organs, the older population is more susceptible to diseases than young and middle-aged individuals. Common diseases that pose a threat to the health of older people include hypertension, diabetes, cardiac arrhythmias, heart failure, falls, osteoporosis, atherosclerosis, and various types of cancer (Fadavi-Ghaffari et al., 2019). Cardiac biomarker Growth Differentiation Factor-15 (GDF-15) also provides prognostic information in these groups (Christenson et al., 2010). GDF-15 belongs to the Transforming Growth Factor (TGF) family and functions as a bone morphogenic protein expressed in the heart, pancreas, prostate, liver, and kidney (Ding et al., 2009).

GDF-15 is prominently expressed in cardiomyocytes after ischemia/reperfusion. In human and murine hearts, increased GDF-15 expression has been observed within hours after myocardial infarction and remains elevated for several days in the infarcted myocardium. Although there is disagreement regarding the site of GDF-15 secretion from cardiomyocytes, the infarcted area has been identified as the primary source of GDF-15. GDF-15 plays a crucial cardioprotective role in the adult heart by activating the Smad2, Smad3, and ALK4/5/7 receptors. Under normal conditions, GDF-15 is not expressed in the heart; however, its levels rapidly increase in response to injuries such as excessive pressure, heart failure, recurrent ischemia/reperfusion, and atherosclerosis (Kempf et al., 2016). GDF-15 has been identified as a predictor of cardiovascular diseases such as heart failure, which is influenced by exercise and physical activity (Abete et al., 2013).

Biomarkers for diagnosing heart failure and monitoring disease progression, such as Natriuretic Peptide type B (BNP) and NT-proBNP, are well-established in clinical guidelines worldwide. These circulating hormone peptides are synthesized and released in response to increased stress on the heart wall due to volume overload or excessive pressure, as well as other conditions like myocardial ischemia or inflammation (Viviane et al., 2004). Plasma concentrations of these hormones rise in patients with left ventricular dysfunction, both systolic and diastolic, and are often used in the clinical diagnosis of heart attacks. NT-proBNP levels increase in response to various signals, including excessive myocardial strain (Serrano-Ostáriz et al., 2011). It is utilized for predicting heart failure in both elderly and non-elderly populations after adjusting for common clinical risk factors and structural and functional cardiac disorders in the elderly and non-elderly populations (Christenson et al., 2010).

Therefore, NT-proBNP and GDF-15 biomarkers are useful indicators of heart damage. Additionally, it has been established that these two markers increase in conditions preceding heart damage, serving as predictive markers for cardiac injury (Jurczyluk et al., 2003). Despite the identification of new biomarkers (NT-proBNP, GDF-15) in the clinical field for predicting cardiac events, the response of these variables to various physical exercises remains unclear. Consequently, given this information and emphasizing the importance of sports exercises as one of the most well-known interventions for treating and preventing age-related disorders.

MATERIALS AND METHODS

Participants

The study population consisted of older men who volunteered and attended an introductory session, during which comprehensive information about the research topic, objectives, and interventions was provided. Initial screening involved evaluations of health status, including the absence of cardiovascular diseases, diabetes, hypertension, non-smoking status, non-alcohol consumption, no medication use, and no regular physical activity in the past year, with participants aged between 55 and 70 . After obtaining informed consent and confirming participants' health status, particularly their suitability for engaging in a regular exercise program (verified by a physician), 36 individuals were purposefully selected and randomly assigned to one of three groups: 1) Resistance training, 2) Aerobic exercise, or 3) Combined exercise. Ethical approval for the study was granted by Islamic Azad University Science and Research Branch, with the ethical code IR.SSRC.REC.1399.070.

Measurement of serum levels of GDF-15 and NT-proBNP

Serum levels of Growth Differentiation Factor 15 (GDF-15) and N-terminal pro b-type Natriuretic Peptide (NT-proBNP) were measured using a sandwich ELISA method. The specific kits (Human Growth Differentiation Factor 15 ELISA Kit) were obtained from Cusabio, China. Blood samples were collected by trained medical personnel from the Tehran Noor Laboratory. Blood was drawn into vacutainer tubes and allowed to clot for 30 minutes at room temperature. Serum was then separated by centrifugation at 3000 rpm for 15 minutes. The serum was stored at -20°C until analysis. The ELISA procedure was conducted following the manufacturer's instructions provided in the kit brochure, including calibration and validation steps to ensure accuracy. The sensitivity and specificity of the ELISA kits used were verified according to the manufacturer's specifications.

Experimental approach

The research employed a semi-experimental design with a pre-test–post-test framework. Pre-test assessments were conducted one week prior to implementing the research protocol, which included measurements of body composition, physical fitness, and biochemical evaluations. Body composition variables measured included height (using a wall-mounted stadiometer), weight (with a calibrated scale), body mass index (BMI), body fat percentage (measured using the Jackson and Pollock method), muscle mass, and waist-to-hip ratio. Exercise intensity was assessed using the Borg Rating of Perceived Exertion (RPE) scale, with exercises designed and implemented based on the scale's intensity and duration. Aerobic capacity was evaluated using the Queen’s step test. Participants underwent an eight-week intervention with three exercise sessions per week. Forty-eight hours after the final session, body composition, physical fitness, and biochemical measurements were repeated. Following the intervention, participants completed a four-week no-exercise period before post-test data collection.

Resistance training protocol

Following the initial measurements (pre-test), individuals in the resistance training group (RT) performed resistance exercises three times a week for eight weeks. The exercise protocol included a 10-minute warm-up, a main session comprising eight movements (leg press, leg extension, leg curl, calf raise, bench press, rowing, triceps pushdown, and biceps curl) with three sets of 10 repetitions at 70% of 1RM, and a 10-minute cool-down with stretching exercises. The intensity and duration were gradually increased during the first two weeks to minimize muscle soreness and reduce injury risk (Viviane et al., 2004; Rangers et al., 2019).

Aerobic training protocol

For the aerobic exercise group, a protocol of continuous exercises, including brisk walking, gentle jogging, and ultimately running at near maximum heart rate, was designed. The exercise protocol was based on the principles, guidelines, and recommendations of the American College of Sports Medicine (ACSM) for the older population and was informed by previous studies. Each session began with 5 minutes of gentle stretching, followed by a 10-minute warm-up period of slow jogging and another 5-minute warm-up to increase the heart rate to approximately 120 beats per minute. The main exercise session lasted about 30 minutes and included brisk walking, gentle jogging, and high-intensity running—the resistance training lasted eight weeks with three sessions per week. A Polar heart rate monitor (model Pox 1000) was used to maintain the correct heart rate range (Lok et al., 2013).

Table 1. Aerobic exercise protocol.

Week 1	**Week 2**	**Week3**	**Week4**
20 minutes running at 45% HRR	25 minutes running at 45% HRR	30 minutes running at 45% HRR	30 minutes running at 55% HRR
Week 5	**Week 6**	**Week 7**	**Week 8**
30 minutes running at 55% HRR	30 minutes running at 65% HRR	30 minutes running at 65% HRR	30 minutes running at 55% HRR

Combined training protocol

Based on previous research, the exercise protocol consisted of combined endurance and resistance training. Each session included a 10-minute warm-up and 40–50 minutes of the main exercise. The main exercise session comprised 15 minutes of endurance training in the first week, gradually increasing to 20 minutes by the eighth week. After a two-minute rest period, resistance training was performed for 25 minutes in the first week, extending to 30 minutes by the eighth week. Finally, a 10-minute cool-down period was used to complete each session. (Fábio et al., 2011).

Statistical analysis

Descriptive statistics were used to summarize the characteristics of the participants and the collected data. The Kolmogorov-Smirnov (K-S) test was employed to assess data normality, and Levene's test was used to check for homogeneity of variances.

Upon confirming normality and homogeneity, one-way analysis of variance (ANOVA) was conducted. Post-hoc comparisons were performed using Scheffe's test. The analysis was structured in a 3x2 format (three groups and two measurement time points) for each dependent variable. Significant interactions between time and group were further analysed with simple ANOVA and Scheffe's post-hoc test. Paired t-tests were used to assess within-group changes over time.

Statistical analyses were performed using SPSS version 24, with a significance level set at $p \leq .05$.

Table 2. Combined exercise protocol.

Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
10 minutes of warm-up	10 minutes of warm-up	10 minutes of warm-up	10 minutes of warm-up	10 minutes of warm-up	10 minutes of warm-up	10 minutes of warm-up	10 minutes of warm-up
15 minutes of treadmill running at 55% of maximum heart rate	16 minutes of treadmill running at 55% of maximum heart rate	16 minutes of treadmill running at 60% of maximum heart rate	17 minutes of treadmill running at 60% of maximum heart rate	18 minutes of treadmill running at 65% of maximum heart rate	18 minutes of treadmill running at 70% of maximum heart rate	19 minutes of treadmill running at 70% of maximum heart rate	20 minutes of treadmill running at 75% of maximum heart rate
Bench press: 40% × 2 × 15	Bench press: 40% × 2 × 16	Bench press: 45% × 2 × 15	Bench press: 50% × 2 × 16	Bench press: 60% × 2 × 15	Bench press: 65% × 3 × 12	Bench press: 70% × 3 × 10	Bench press: 75% × 3 × 10
Quadriceps: 40% × 2 × 15	Quadriceps: 40% × 2 × 16	Quadriceps: 45% × 2 × 15	Quadriceps: 50% × 2 × 16	Quadriceps: 60% × 2 × 15	Quadriceps: 65% × 3 × 12	Quadriceps: 70% × 3 × 10	Quadriceps: 75% × 3 × 10
Hamstrings: 40× 2 × 15	Hamstrings: 40% × 2 × 16	Hamstrings: 45% × 2 × 15	Hamstrings: 50% × 2 × 16	Hamstrings: 60% × 2 × 15	Hamstrings: 65% × 3 × 12	Hamstrings: 70% × 3 × 10	Hamstrings: 75% × 3 × 10
Biceps: 40% × 2 × 15	Biceps: 40% × 2 × 16	Biceps: 45% × 2 × 15	Biceps: 50% × 2 × 16	Biceps: 60% × 2 × 15	Biceps: 65% × 3 × 12	Biceps: 70% × 3 × 10	Biceps: 75% × 3 × 10
Lat pull-down: 40% × 2 × 15	Lat pull-down: 40% × 2 × 16	Lat pull-down: 45% × 2 × 15	Lat pull-down: 50% × 2 × 16	Lat pull-down: 60% × 2 × 15	Lat pull-down: 65% × 3 × 12	Lat pull-down: 70% × 3 × 10	Lat pull-down: 75% × 3 × 10
10 minutes of cool-down	10 minutes of cool-down	10 minutes of cool-down	10 minutes of cool-down	10 minutes of cool-down	10 minutes of cool-down	10 minutes of cool-down	10 minutes of cool-down

RESULTS

Table 1 presents the participants' characteristics. The results of the one-way analysis of variance (ANOVA) for age, height, weight, and body mass index (BMI) did not show any significant differences among the participants in the three groups ($p > .05$). Therefore, the participants in the three groups exhibited homogeneity in these factors, indicating variance inhomogeneity among the groups.

Table 3. Individual characteristics of study participants by exercise group.

Group	Age (years)	Weight (kg)	Height (cm)	BMI
Resistance	6.5 ± 3.3	69.1 ± 8.6	164.8 ± 4.6	25.74 ± 3.2
Aerobic	71.4 ± 4.1	71.8 ± 7.2	166.26 ± 6.3	25.81 ± 2.8
Combined	68.6 ± 2.9	73.4 ± 9.5	171.34 ± 4.9	25.1 ± 2.9

One-way analysis of variance (ANOVA) (F) was used to analyse the data and determine differences in the effects of the three exercise methods. The results of the F-test did not show a significant difference between the data of the three groups in the pre-test ($p > .05$). Therefore, the participants in the three groups were homogeneous.

For the post-test analysis, the data obtained in the three groups were evaluated using the F-test, which revealed a significant difference between the three groups ($p = .001$). Post hoc Scheffe's test was used to determine the source of the difference, and the results indicated a significant difference between all three groups (combination resistance, combination aerobic, and aerobic resistance) ($p = .001$).

A paired t-test was used to analyse the time effects within each group. The results indicated a significant difference in the post-test data compared with the pre-test data in both the aerobic and resistance training groups. Specifically, a substantial decrease in serum GDF-15 levels was observed after resistance training, whereas a significant increase was observed after aerobic exercise. However, the changes observed after the combined training were not statistically significant. One-way analysis of variance (ANOVA) was used to analyse group effects. The results revealed no significant differences among the three groups during the pre-test stage. However, there was a significant difference among the aerobic, resistance, and combined training groups in the post-test stage. The post-hoc Scheffe test was used to determine the source of differences, indicating significant differences between the combined and aerobic and resistance groups.

Table 4. Follow-up test results of groups.

		Total scores	Freedom degrees	Mean Scores	F Score	Significance level
Pre-test	Between groups	25.167	2	12.583	1.580	.221
	Within groups	262.833	33	7.965		
	Total	288.000	35			
Post-test	Between groups	3421.056	2	1710.528	143.785	.000
	Within groups	392.583	33	11.896		
	Total	3813.639	35			

The percentage of change in each group after the training period also indicated a 16.15% decrease in post-test data compared to pre-test data in the resistance training group and a 16.5% increase in the mean post-test data compared to pre-test data in the aerobic training group. However, the changes in the combined treatment group were not statistically significant.

Table 5. Interactive effect of time and group on GDF_15.

	Pre-test	Post-test	Within group observation (*p*-value)
Aerobic	651.91 ± 2.67	693.16 ± 2.36	.001 ◦
Resistance	652.25 ± 2.66	614.66 ± 2.64	.001 ◦
Combined	653.83 ± 3.09	655.00 ± 3.97	.331
p-value	.786	.001 •	

Note. ◦ - Within-group difference. • - Between-group difference.

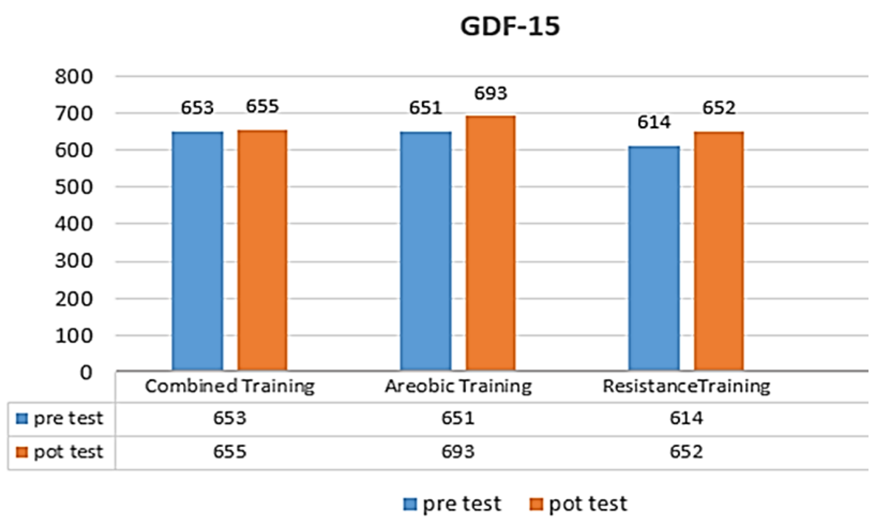

Figure 1. The effect of resistance, aerobic, and combined exercise on GDF_15.

For the statistical analysis of NT-proBNP levels, a paired t-test was used to assess the effect of time within each group. The results indicated significant differences in the post-test data compared to the pre-test data in all three groups: aerobic, resistance, and combined. Specifically, the aerobic and combined groups experienced a significant decrease, whereas the resistance group showed a significant increase.

Additionally, one-way analysis of variance (ANOVA) was used to analyse the group effect statistically. The results revealed no significant differences among the three groups during the pre-test phase. However considerable; during the post-test phase, a significant difference was observed between the aerobic, resistance, and combined groups. Post hoc tests were conducted to determine the specific location of the differences, which indicated a significant difference between the resistance group and the aerobic and combined groups. However, no significant differences were observed between the effects of aerobic and combined exercises.

The percentage changes in each group after the exercise intervention also indicated an increase in post-test data compared with pre-test data in the resistance training group. Conversely, there was a decrease in the post-test data compared to the pre-test data in the aerobic and combined training groups. Specifically, the resistance training group showed a 37.7% increase after eight weeks of training, while the changes in the aerobic training and combined training groups decreased by 34.1% and 24.8%, respectively.

Table 6. Interaction effect of time and group on NT-proBNP.

	Pre-test	Post-test	Within Group Significance (p)
Aerobic	167.58 ± 2.71	110.33 ± 3.49	.001 ◦
Resistance	167.25 ± 1.91	230.16 ± 3.73	.001◦
Combined	169.50 ± 3.52	127.16 ± 2.28	.001 ◦
Inter-group	.924 •	.001 •	-

Note. ◦ - Within-group difference. • - Between-group difference.

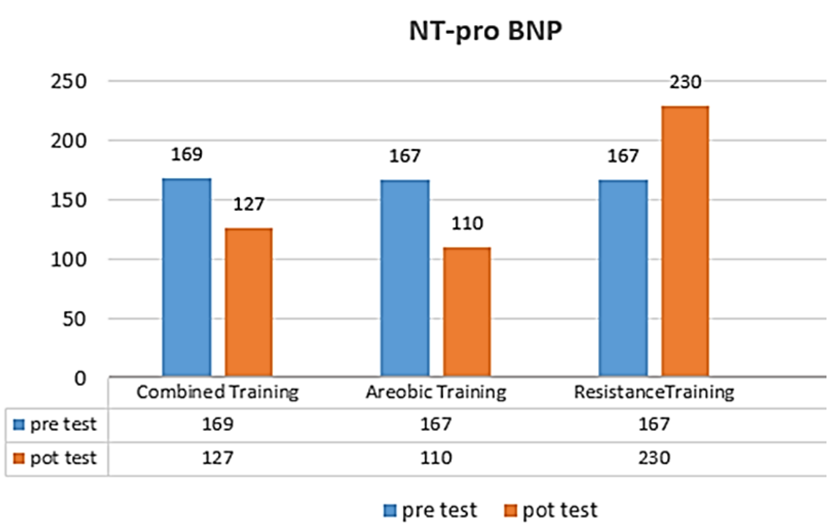

Figure 2. The Effect of resistance, aerobic, and combined exercise on NT-proBNP.

DISCUSSION

The primary objective of this study was to evaluate the distinct effects of resistance, aerobic, and combined exercises on the serum levels of growth differentiation factor 15 (GDF-15) and N-terminal pro-brain natriuretic peptide (NT-proBNP) in active older men.

Consistent with Galliera et al.'s (2014) findings, this study also reported a significant increase in the levels of GDF-15 following aerobic exercises, including both a period of aerobic training and a single session of maximal rugby activity. Similarly, the study by Rangers et al. (2019) also reported a significant decrease in the levels of GDF-15 after an eight-week resistance training program.

It is important to note that Hoffman et al. (2015) reported that serum levels of GDF-15 are higher in older adults than in younger individuals and that there is an inverse relationship between GDF-15 levels and muscle mass, as well as a positive correlation with age. Furthermore, the findings of Xie et al. (2019) suggest that increased levels of GDF-15 are associated with a higher risk of cardiovascular disease and mortality. Therefore, it can be inferred that implementing resistance exercises may increase muscle mass, resulting in a significant decrease in GDF-15 levels, given the inverse relationship between muscle mass and GDF-15 levels.

It is important to note that this study focused on the effects of resistance, aerobic, and combined exercises on the serum levels of GDF-15 and NT-proBNP in active older men, and no changes were made to the information, citations, or references.

Given the link between high levels of GDF-15 and increased cardiovascular mortality, elevated levels of this biomarker in serum blood indicate cardiac damage. The results of the current study imply that, despite previous research, resistance exercises have a more significant positive impact on the GDF-15 factor than aerobic exercise, contrary to the common belief in society. In terms of reducing serum levels of GDF-15, aerobic exercise is more effective in improving cardiac risk factors and reducing the likelihood of cardiovascular mortality in older individuals. After aerobic exercises, there was a significant increase of 16.50%, while after resistance exercises, there was a decrease of 16.15%. No significant change was observed after the combined exercises.

Regarding NT-proBNP, the findings of this study align with the research of Bordbar et al. (2013), who reported an increase in this factor after resistance training and a decrease after aerobic exercises, consistent with the rise seen after resistance exercises. Furthermore, this study's results are consistent with the research of Arbab et al. (2016), which demonstrated a significant reduction in NT-proBNP after combined (resistance-endurance) exercises . However, conflicting results can be seen in the research of Rangers et al. (2019), which reported a decrease in NT-proBNP after eight weeks of resistance training, as well as in the studies of Serrano et al. (2011) and Valls et al. (2014), which showed no significant change in NT-proBNP after resistance exercises. In contrast, Favio et al. (2008) demonstrated that in basketball and football athletes, NT-proBNP significantly increases indicating a significant decrease of 34.1% and 24.8% after aerobic and combined exercises, respectively, and a substantial increase of 37.7% after resistance exercises.

Study limitation

The present study had several limitations. Firstly, it was conducted over a defined temporal scope, specifically from the second half of 2019 to the first half of 2020, and involved participants from Zanjan Province. The study focused on examining the effects of aerobic, resistance, and combined exercise on biochemical and metabolic markers of heart health. Uncontrollable limitations include participant attrition, where some individuals dropped out of the exercise program or had issues with blood sample collection. Additionally, despite providing dietary guidelines and lifestyle recommendations, there was insufficient control over participants' nutrition and sleep. The potential use of medications by participants, which was not reported or controlled, also represents a limitation. Furthermore, variability in participants' emotional and psychological states during the exercise protocol and blood sample collection was not controlled. Lastly, there was the potential for unavoidable measurement errors by the researcher, exercise implementers, and laboratory personnel.

CONCLUSION

The current study's results suggest that although previous research has found aerobic exercises positively impact cardiac factors, resistance training is more effective in improving risk factors, mainly by reducing serum GDF-15 levels. Furthermore, aerobic and combined exercises were shown to decrease NT-proBNP levels, while resistance exercises led to an increase in this factor. These findings imply that the common perception in the community regarding the benefits of aerobic exercises on cardiac health may be partially accurate.

AUTHOR CONTRIBUTIONS

H. N., A. S., H. R., and H. H., contributed equally to the study. H.N., conceptualized the study, designed the research methodology, and supervised the overall project. Conducted data analysis and interpretation of results. Drafted and revised the manuscript for intellectual content. A.S., contributed to the development of the research design and methodology. Assisted in data collection and performed statistical analysis. Reviewed and edited the manuscript for clarity and accuracy. H.R., participated in the recruitment of participants and facilitated data collection. Provided critical insights into the interpretation of findings and contributed to manuscript revisions. H. H., assisted in the literature review and theoretical framework of the study. Contributed to the drafting of sections of the manuscript and ensured compliance with ethical standards in research. All authors have read and approved the final manuscript and agree with the authorship order.

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DISCLOSURE STATEMENT

No potential conflict of interest was reported by the authors.

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