Twelve weeks of hiking training improves heart rate variability and cardio-respiratory endurance in women with panic disorder

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Article Info	Abstract
	Background: Heart rate variability (HRV) as a non-invasive indicator measures the activity level of the autonomic nervous system. Exercise has significant positive effects in increasing HRV indicators, which ultimately leads to cardiovascular health. People with panic disorder (PD) generally have low HRV indices and are more exposed to cardiovascular risks. **Aim:** The aim of the present study is investigating the effect of 12 weeks of hiking training on HRV of women with PD. **Materials and Methods:** In this semi-experimental clinical trial, 18 women with PD with average panic scores (45.00±19.55) as determined by Albany Panic and Phobia Questionnaire (APPQ) in two training group (12 weeks of hiking training with 70% to 80% MHR, three sessions a week, each one an-hour, and control group (without any regular physical activity) participated randomly. HRV of subjects was measured by Holter monitoring device (with 7 leads VX3+ SN 17570 made in USA) while resting and lying back for 20 min before and after 12 weeks. **Results:** The results of covariance analysis showed that panic scores ($P≤0.001$) and HRV factors including: SDNN ($P≤0.05$), SDNN index ($P≤0.01$) and TP ($P≤0.03$) of the subjects in the training group improved significantly but HF, LF, LF/HF, did not show significant changes ($P≥0.05$). **Conclusion:** It seems that 12 weeks of hiking training improves some of the HRV indices of women, which prevents the risk of cardiovascular diseases, and also reduces the symptoms of panic in women.

1. Introduction

Heart rate variability describes the time differences between successive R-R intervals [1] and is a non-invasive, practical and repeatable indicator of the performance and activity level of the cardiac autonomic nervous systems which reacts to environmental changes. Furthermore, it is a powerful tool in studying how to modify the cardiac autonomic system and it corresponds to the balance between the sympathetic and parasympathetic nervous systems [2]. It is also a psycho-physiological phenomenon with wide consequences, including physiological, psychological and environmental factors [1]. The Autonomic Nervous System (ANS) is divided into sympathetic and parasympathetic branches. Sympathetic activity tends to increase heart rate and decrease HRV, while parasympathetic activity tends to decrease heart rate and increase HRV [3]. Heart rate varies from beat to beat mainly due to parasympathetic innervation to the heart, which is transmitted from the brain by the vagus nerve. With the loss of the vagus nerve, there is a significant decrease in HRV. Such a decrease in the parasympathetic nerve exposes the heart to unopposed stimulation by the sympathetic nervous system, which makes the heart vulnerable to arrhythmia and sudden death, and also accelerates the progression of coronary atherosclerotic disease [4].

Physical activity has been recognized as an effective strategy for improving ANS function of the heart [1] which improves HRV through increasing vagal tone and reducing cardiac sympathetic effect and regulating sympathovagal balance [5].

Exercise can lead to a decreased level of catecholamines, density of beta-adrenergic receptors and angiotensin II, and increase the availability of nitric oxide (NO) and other mediators. Angiotensin II is a peptide that increases sympathetic output and inhibits vagal activity. Also, reducing NO breakdown and enhancing endothelial NO synthase phosphorylation are indirectly involved in inhibiting sympathetic activity and increasing vagal tone. Shear stress caused by aerobic exercise augments the phosphorylation and activation of eNOS enzyme and raises its expression, which generally develops the available NO. Therefore, aerobic exercise improves the cardiac autonomic system by reducing sympathetic activity and increasing vagal tone [6].

Panic disorder (PD) is an anxiety disorder characterized by panic attacks that are preceded by anxiety accompanied by sudden and unexpected fear [7, 8]. This disorder manifests itself in women about twice as often as in men [9] and it is associated with several mental diseases such as anxiety and non-psychological diseases such as cardiovascular diseases [10].

Anxiety accelerates sympathetic drive or vagal tone and rises atherosclerotic risk and declines HRV among healthy adults [4] which is clearly visible in the patients with PD [4, 11, 13]. In PD, the autonomic mechanisms that regulate the heart in response to psychological stress are disturbed. This disturbance indicates potential inflexibility and stiffness of the heart, and reduces the change in the parasympathetic response of the heart, resulting in less ability to adapt in response to psychological stress [14]. Also, studies have shown that physical exercise may effectively reduce anxiety in patients with PD and has been investigated as a potential tool to reduce the symptoms of patients with PD [9]. It seems that the underlying mechanisms of increased cardiac risk in patients with PD reflect the direct and indirect effects of autonomic dysfunction as

well as behavioral risk factors related to an unhealthy lifestyle [15]. Usually, these people have the most visits to the doctor and emergency room that it brings a lot of financial burden for them [16].

Since indoor sports need to be paid for, we decided to use a training method that does not require spending money, in addition to having the effects of aerobic exercise. By the way, we can also benefit from the positive factors of nature and since hiking training is the most natural and common form of physical activity with moderate intensity that can exert the effects of aerobic exercise on the body [17]. Also, no research so far has investigated the effects of exercise in PD on their HRV factors, so we decided to investigate the effect of 12 weeks of hiking training on HRV of women with PD.

2. Materials and Methods
2.1. Participation
The participants in this study were women suffering from PD, from the people who were referred to the psychiatric centers of Tabriz city or through the public advertising especially in social networks. The people who had the symptoms and volunteered, filled down the Albany Panic and Phobia Questionnaire (APPQ) [16]. People whose scores in the questionnaire were above 50 out of 100 were invited to the interview and after the final approval of the psychiatrist using the Structured Clinical Interview DSM-IV, 30 people were selected as subjects. The subjects were randomly allocated in one of the two groups of training or control, n=15 for each (the sample size was estimated by G Power software). These participants didn't use any medicine and cognitive treatments and had no history of regular sports activity for at least 6 months before. Physical damage and the inability to perform exercises caused 5

subjects to be removed from the training group. The number of subjects in the training group was reduced to 10, and 6 subjects from the control group were removed from the study due to lack of cooperation. The subjects of the control group did not participate in any regular sports activities for 12 weeks.

2.2. Instrument
The HRV factors of the subjects were measured by a Holter monitoring device made in the United States with 7 leads, Model (VX3+ SN 17570). The panic scores were determined by Albany Panic and Phobia Questionnaire (APPQ). VO$_2$max was evaluated by Bruce's modified treadmill test protocol [18] by Technogym treadmill made in Italy and heart rate was monitored using Polar H10 Bluetooth heart rate sensors that showed all subjects simultaneously in the respective app. The maximum heart rate was calculated with the following formula [19]:

$$HRmax = 220 - age$$

2.3. Procedure
After selecting the samples and filling out the physical activity readiness questionnaire (PAR-Q) and the personal information form, an orientation session was assigned to the participants to familiarize them with the conditions of the tests, specify the time and duration of the exercises and how to implement the exercise program.

All the subjects signed a written consent to participate in the research and they were allowed to withdraw from the study at any time if they did not want to continue. Also, a profile sheet was considered for each subject, in which, the maximum heart rate of each person and its range of 70-80% was calculated and noted. Before starting the exercises,

anthropometric factors, VO₂max and HRV factors were measured. The exercise group did the exercises for 3 months (three sessions a week, each session one an-hour), for 12 consecutive weeks, and the control group was asked not to have any regular exercise or sports activities during this period and to continue their daily activities. After the end of the intervention and training sessions, anthropometric, VO₂max and HRV factors were measured again. The research method is shown in Figure 1 at a glance.

2.3.1. Training protocol

Hiking was performed for 12 weeks and 3 sessions of 1 hour each week. After warming up the muscles and joints of the lower limbs for 10 min, the subjects started walking on the sloping asphalt roads of Chavan areas of Tabriz (altitude 1500 m) and since the workout was aerobic based, heart rate was monitored between 70-80% of maximum heart rate. The selected routes became a little more difficult and changed every week, the first two months were in Chavan area and the last month was changed to the Aynali areas of Tabriz (1900 m high) to increase the overload. Dirt roads were also included in the route in the final week. At the end of each session, cooling down was done for 5-7 min with stretching movements. The routes were chosen by a professional mountaineer, familiar to the region.

2.3.2. The method of measuring heart rate variability (HRV)

Participants came to our laboratory, by motorized vehicle and avoiding any physical activity since they woke up, between 8.00 and 10.00 a.m. following specific study pre-conditions: (1) fasting conditions; (2) not altered sleep pattern the night before; (3) to be abstained from intake drugs or stimulant consumption, including coffee and other stimulants 24 h before; and (4) to avoid moderate-intensity physical activity (24 h) and vigorous-intensity physical activity (48 h) before the test. The environmental conditions were standardized (room temperature=22–23°C).

The assessment of the R–R signal was carried out with the participant lying on a stretcher in the supine position. To obtain a repeatable HRV measure, R–R signal recording lasted 20 min (after 10 min of acclimation). Participants were instructed not to talk or to move, and to relax as much as possible but being awake [1]. We used the Holter monitoring with 7 leads to record the R–R signal. R–R recordings were downloaded from Holter memory card by computer and were analyzed with Holter software and my Patch software.

To interpret HRV changes, time domain parameters include SDNN (standard deviation of intervals of two normal beats in milliseconds), which is the most commonly used measure for HRV [11] and tends to show vagal function [13] and SDNN index (the average standard deviation of the 5 min segments from R to R) which is an index of the same SDNN and examines it in a more detailed way, and the frequency domain parameters that include low frequency [4] (0.15-0.04 Hz) which indicates the activity of the sympathetic nerve and also the background in the activity of the parasympathetic nerve and high frequency (HF) (0.4-0.15 Hz) which mainly reflects the activity of the parasympathetic nerve and the ratio of LF to HF (LF/HF) which reflects the cardiac sympathovagal balance [11] and TP (total power or variance of all intervals of normal heartbeats in Hertz) which indicates the overall activity of the autonomic nerves was used 16 and also tends to show vagus function [13].
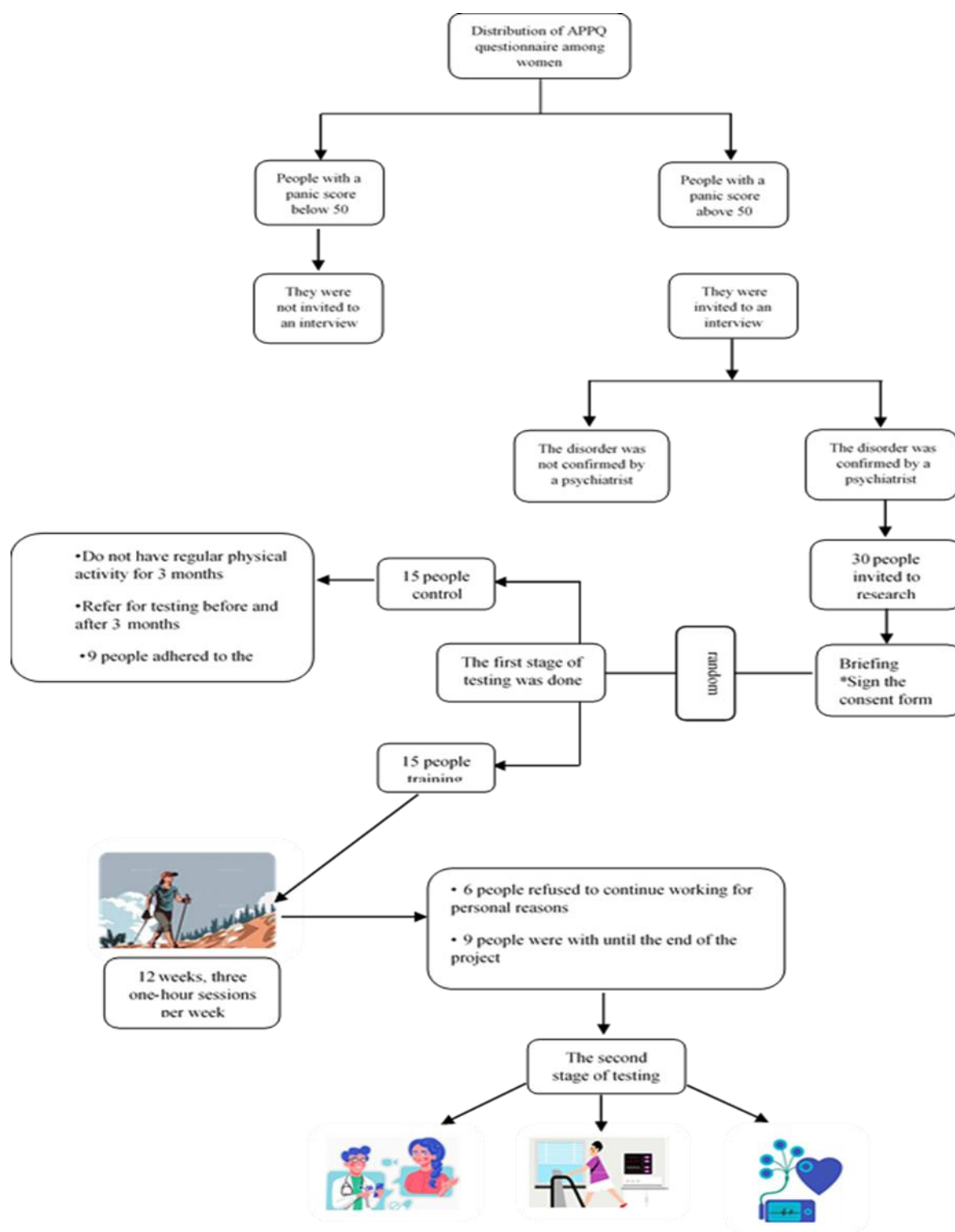
Figure 1. Flowchart of research implementation

2.4. Statistic

To analyze the collected data, in order to determine the normality of the data, the Shapiro-Wilk test was used, and to analyze the results, the covariance statistical test was used at a significance level of 0.05 under 26th version of SPSS statistical software.

3. Results

The average anthropometric indices of the

research subjects, and the panic questionnaire scores are shown in Table 1. The average HRV factors are shown in Table 2.

The analysis of the collected data using the statistical test of analysis of covariance showed that in the post-test phase, there were significant differences between the research groups in the variables of maximum oxygen consumption, panic test

score, SDNN, TP, SDNN index at a significance level of 0.05. On the other hand, in HF, LF, LF/HF variables, there were no significant difference despite some increase (Table 3). In Figure 2, the difference between the averages of the variables in the pre-test and post-test between the two groups is shown in the form of bar graphs.

**Table 1.** Average anthropometric indices of subjects.

Variable / Studied groups		Training	Control
Age (years)		46 ±8.93	45±9.30
Height (18)		160.94±6.10	163.25±2.98
Weight (kg)	Pre-test	74.13±12.75	60.40±4.08
	Post-test	74.48±12.91	60.82±5.58
BMI (kg/m^2)	Pre-test	28.63±4.42	22.70±1.98
	Post-test	29.16±4.54	22.87±2.58
Panic	Pre-test	56.66±10.12	54.00±16.32
	Post-test	36.00±17.02	54.00±18.43
VO$_2$max	Pre-test	35.91±8.09	42.77±6.75
	Post-test	44.90±5.15	41.47±6.86

Table 2. Unadjusted mean values of heart rate variability factors

Variable / Studied groups		Training	Control
HF	Pre-test	498.40 ± 480.84	847.33 ± 972.14
	Post-test	588.98 ± 808.37	502.65 ± 590.68
LF	Pre-test	1618.37 ± 1697.02	1864.12 ± 1424.77
	Post-test	1847.02 ± 1670.07	1098.15 ± 854.51
LF/HF	Pre-test	5.18 ± 5.32	4.47 ± 3.78
	Post-test	10.86 ± 15.58	3.70 ± 2.84
SDNN	Pre-test	60.77 ± 27.04	65.88 ± 22.82
	Post-test	64.11 ± 19.71	55.33 ± 20.57
SDNN index	Pre-test	52.88 ± 21.16	60.33 ± 19.0
	Post-test	61.33 ± 21.05	51.88 ± 19.29
TP	Pre-test	3060.64 ± 2051.75	3705.10 ± 2208.8
	Post-test	1636.33 ± 1915.56	2532.87 ± 1995.16

Table 3. Adjusted mean values of the research variables in the post-test, considering the pre-test values of each variable as covariates

Variable	Training	Control	P	F	ES
VO$_2$max	47.11 ± 1.34	39.26 ± 1.34	0.001	15.42	0.50
Panic	34.61 ± 3.73	55.38 ± 3.73	0.001	15.39	0.50
SDNN	65.74 ± 4.22	53.69 ± 4.22	0.05	4.04	0.21
SDNN index	63.55 ± 3.83	48.67 ± 3.83	0.01	7.37	0.33
TP	3338.38 ± 447.40	2311 ± 447.40	0.03	5.74	0.27
HF	682.56 ± 193.11	402.08 ± 193.11	0.32	1.02	0.06
LF	1899.68 ± 394.11	1045.39 ± 394.11	0.14	2.34	0.13
LF/HF	10.36 ± 3.13	4.21 ± 3.13	0.18	1.92	0.11

(A)

(B)

(C)

(D)

(E)

(F)

(G)

(H)
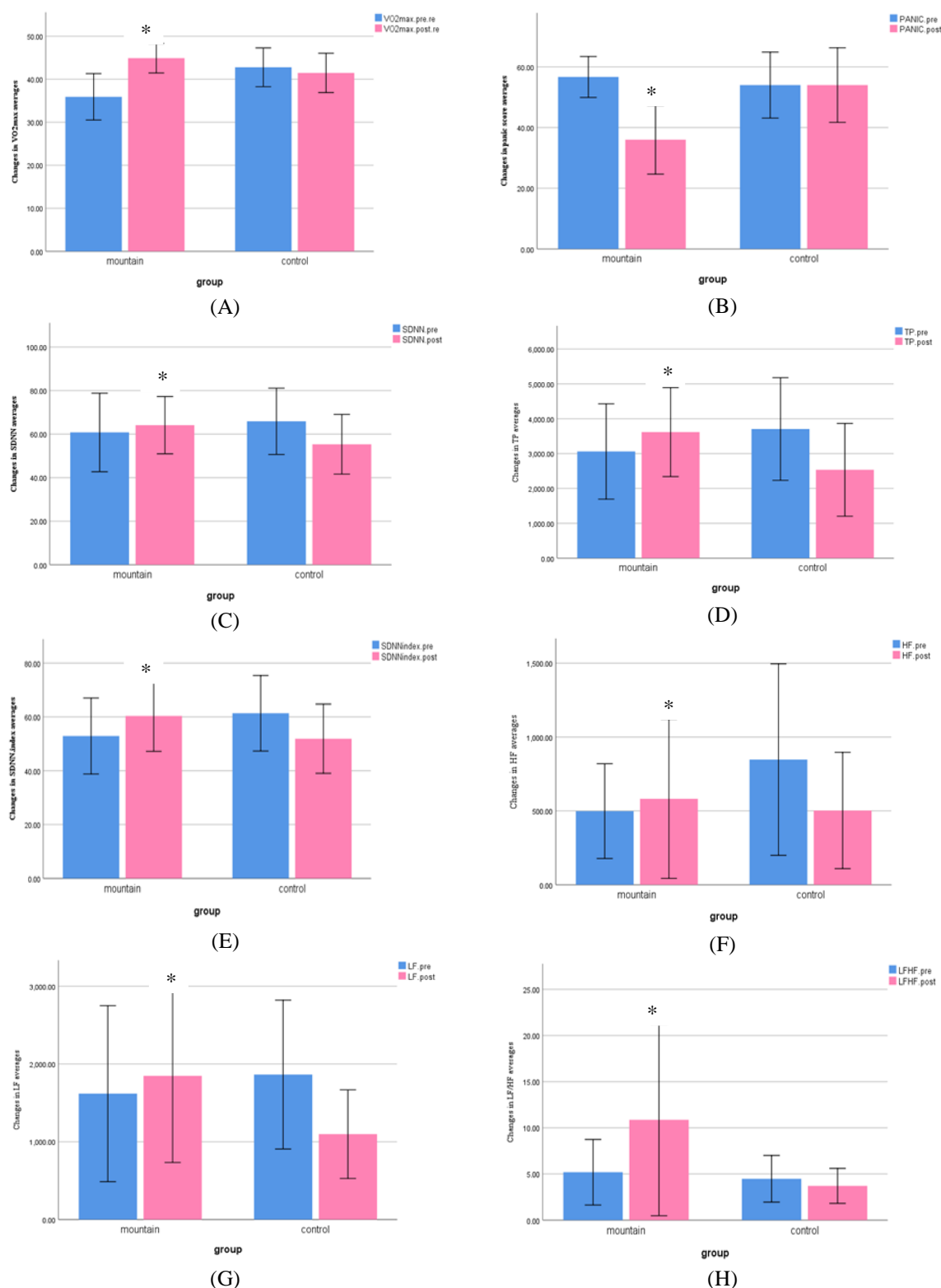
∗ Comparison with the control group

Figure 2. Changes in the averages of the variables in the pre-test and post-test between the two groups, training and control. A) Maximum oxygen consumption; B) Panic scores; C) Standard deviation of the average NN intervals (SDNN); D) Total power (TP); E) Mean of the standard deviations of all NN intervals for all 5 min segments of the entire recording (SDNN index); F) High frequency waves (HF); G) Low frequency waves (LF); H) Ratio of low frequency waves to high frequency waves (LF/HF).

4. Discussion

The ANS and its regulation, from the pathophysiological point of view, can play an essential role in the pathophysiology of PD. Increased reactivity of cardiac activity to the sympathetic system during stress can be an essential factor contributing to acute panic attacks. Patients with PD overreact to stress stimuli by sympathovagal response [14].

In fact, mental stress causes obvious autonomic imbalance in patients with PD. HRV depends on autonomic parasympathetic and sympathetic balance, and PD is associated with increased sympathetic function and decreased vagal (parasympathetic) tone. Therefore, the sympathovagal balance in PD patients will be disturbed compared to healthy individuals and the overall activity of the ANS will be reduced [11]. Therefore, one of the main axes of stress responses is ANS, and repeated activation of ANS is characterized by a diminish in HRV [4].

Physical activity is known as an effective strategy to improve cardiac ANS function [1] and improves HRV by increasing vagal tone and reducing cardiac sympathetic effect and regulating sympathovagal balance [20] Recent studies have suggested exercise as clinically effective [21], however, contradictory results are also seen in studies [22, 23, 24, 25].

Our aim of this study was to answer the question whether exercise alone can be an effective treatment method for this disorder and whether the effects of treatment appear in the HRV factors of these people.

The results of the APPQ questionnaire scores study showed that 12 weeks of hiking exercises reduced the symptoms of this disorder in women. By the way, the results of the modified Bruce test indicated that the VO$_2$max of the subjects has increased significantly after 12 weeks of hiking training which shows that the exercises have been able to increase cardiorespiratory endurance and as a result cardiovascular health. Examining HRV variables showed that the total power or variance of all normal heart rate intervals (TP) which indicates the overall activity of the ANS and reflects the vagus function [26] significantly has increased; therefore, it can be concluded that hiking training have improved the functioning of the ANS.

In addition, the results of covariance analysis showed that SDNN and SDNN index increased significantly after performing the hiking training, which indicates the improvement of the overall activity of the ANS. These findings are consistent with the results of Navarro-Lomas et al. (2022) [1] and Piralaiy et al. (2021) [20], who stated that moderate intensity aerobic exercise improves the performance of the cardiac autonomic system.

However, based on our findings, the frequency domain parameters of HRV, including HF and LF and the LF/HF ratio [11] did not show a significant difference after 12 weeks of hiking. Of course, the examination of pre-test and post-test averages shows the relative increase and improvement of these three factors in the training group, although this improvement is not significant. The enhancement of HF indicates the balance of the ANS, and HF is the most specific parasympathetic index [13]. Therefore, its increase will be in line with the changes of SDNN, SDNN index and TP, but according to the previous statements, the amount of LF and LF/HF should be reduced to express the balance of the ANS. But the noteworthy point is that there is not consensus on this issue whether

these factors indicate the sympathetic or parasympathetic nervous system. A number of researchers believe that LF also reflects parasympathetic function and is related to a combination of parasympathetic and sympathetic activities [11]. In the case of LF/HF, some researchers think that it reflects sympathetic activity [13]. So, the results obtained regarding these two variables are contradictory in most researches.

Yuan Zhang et al. (2020) did not find a significant relationship between LF and PD, as well as between HF and PD [11]. In addition, Cheng et al. (2022) stated that there is very little consistency between studies [13].

In addition, Iranpour and Bolboli (2019) concluded that aerobic exercise in men significantly increases LF, HF and LF/HF compared to the control group and aerobic exercise in water [26]. HRV factors can be influenced by many factors (what happened at the moment, a few hours before and the day before) that all these factors could not be under the control of the researchers of this research. Even though the things mentioned in the research method were emphasized, there were still many factors beyond the control of the researchers that could affect the HRV factors. Therefore, it seems that more studies with high statistical samples in women and 24-hour examination of HRV factors is needed to be able to express the definitive response of HRV factors to exercise in people with PD.

5. Conclusions

According to the results of the present study, it can be said that 12 weeks of hiking training has improved the symptoms of panic in women, and this improvement can also be seen in the HRV factors of the subjects and it has been able to improve SDNN, SDNN index and TP factors.

Conflict of interest

The authors declared no conflicts of interest.

Authors' contributions

All authors contributed to the original idea, study design. Dr. Lotfali Bulbali compiled the initial version and Dr. Mustafa Khani did the statistical analysis and compiled the final version. Dr. Roghia Afrondeh was involved in revising the article and Dr. Mehta Skandrenjad was involved in ideation of the article. Nahid Ashkriz implemented the design, coached the participants, obtained the measurements, and wrote the paper.

Ethical considerations

The authors have completely considered ethical issues, including informed consent, plagiarism, data fabrication, misconduct, and/or falsification, double publication and/or redundancy, submission, etc. This study was approved by Tabriz University's Research Ethics Committee (IR.TABRIZU.REC.1402.003).

Data availability

The dataset generated and analyzed during the current study is available from the corresponding author on reasonable request.

noted that this article is derived from the doctoral dissertation approved by University of Mohaghegh Ardabili [27].

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