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Original Article

The change of heart rate recovery index and Tpeak-end interval values according to age range in healthy men and women

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Abstract

Background: As age progresses, vagal activity decreases and sympathetic activity increases in both men and women. The purpose of the current study was to examine variations in the Tpeak-end interval and heart rate recovery index (HRR-i) values according to age range in men and women.

Methods: A total of 1481 subjects, including 758 males and 723 females, was included in the study. The study was conducted between March 2013 and January 2020. The effort test was performed and a retrospective study was performed on patient records that were interpreted as negative. The Tpeak-end (Tp-e), QT, corrected QT (QTc), Tp-e/QT, and Tp-e/QTc values were calculated on basal ECGs in the exertion test records. The 1st, 2nd, and 3rd-min HRR-i data were calculated by subtracting the 1st, 2nd, and 3rd-min HR from the peak HR, and then compared.

Results: The Tp-e, QT, QTc values increased as the age range increased in both groups, while the HRR-i data decreased as the age range increased. Values between 70 and 79 years of age appeared similar. It was found that there was a significant negative correlation between the Tp-e interval and the 1st-min HRR-i values.

Conclusions: As the age range increased, the HRR-i values decreased and the Tp-e interval increased.

Keywords: aging; electrocardiography; exercise; heart rate

1. Introduction

As age increases, vagal activity decreases in both men and women, and sympathetic activity increases. Heart rate variability (HRV) and HR recovery index (HRR-i) values are simple methods used to evaluate autonomic functions [1-3]. HRR-i values are calculated by subtracting the HRs during the 1st, 2nd, and 3rd recovery phases from the HR at the peak exercise level. The HRR-i is not routinely used.

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Although it is used directly to assess autonomic functions, a decreased HRR-i is closely related to increased cardiovascular mortality and morbidity [4,5]. Autonomic functions play an important role in regulating and controlling cardiovascular functions. Therefore, deterioration in autonomic functions causes cardiovascular mortality and morbidity [6,7].

An increase in sympathetic activity or a decrease in parasympathetic activity can cause malignant ventricular arrhythmias, even in healthy individuals. As is known, during the exercise test, sympathetic activity increases and parasympathetic activity is relatively depressed. While vagal activity is responsible for the reduction of the HR in the 1st min of the recovery phases, in general, the decrease in the HR occurs due to the decrease in the sympathetic activity in the 2nd and 3rd stages. Hence, rhythm disturbances and sudden cardiac death usually occur after heavy exertion [8]. Despite markers showing autonomic functions, HRV has been shown to decrease with age [9], It has not yet been investigated how HRR-i data change with age in men and women and how it relates to repolarization markers.

Electrophysiological findings of men and women differ from each other clinically. This includes both autonomic functions and repolarization markers. This information explains why malignant ventricular arrhythmias are different in men and women [10]. Many predictors have been studied to identify high-risk patients for malignant ventricular arrhythmias. The most important of these are the Tp-e interval, Tp- e/QT and Tp-e/QTc ratios, T wave alternans, late ventricular potentials, QT interval elongation, QT dispersion, and T wave heterogeneity. However, the Tp-e interval and Tp-e/QT and Tp-e/QTc ratios are repolarization markers and significant elongations in their values have been closely associated with malignant ventricular arrhythmias [11-14]. The current study aimed to investigate how the HRR-i values, Tp- e, QT, QTc interval, and Tp-e/QT and Tp-e/QTc values changed with age in healthy men and women, and compare these values and determine the relationship between them.

2. Methods

2.1. Study population

This study was conducted retrospectively based on hospital records. A total of 1481 patients, 758 men, and 723 women, who applied to the cardiology outpatient clinic between March 2013 and January 2020 with atypical chest pain, and who had a negative exercis e test, was included in the study. The group of men was named group 1 and the group of women was named group 2. While the average age of group 1 was 46.42 ± 22.56 years, the average age of group 2 was 45.67 ± 21.62 years. There was no statistically significant d ifference between the mean ages of groups 1 and 2 ($p > 0.05$). Each group was divided into 6 subgroups, comprising individuals aged 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, and 70-79 years. Effort test data were compared according to these sub-age groups. In group 1, there were 154 men aged 20-29 years, 155 men aged 30-39 years, 145 men aged 40-49 years, 139 men aged 50-59 years, 99 men aged 60-69 years, and 66 men aged 70-79 years. In group 2, there were 149 women aged 20-29 years, 151 women aged 30-39 years, 144 women aged 40-49 years, 133 women aged 50-59 years, 91 women aged 60-69 years, and 55 women aged 70-79 years. Additionally, there were no statistically significant differences between the mean ages of each sup-group. Physical examination, effort test, and blood data of each group were evaluated and compared among themselves.

2.2. Exclusion criteria

Having a systemic disease, such as hypertension or diabetes mellitus, if any murmur was heard during the routine physical examination, if there were signs of stasis, having a left or right bundle branch block on the electrocardiogram, if any electrolyte disturbance was detected, if a positive test required coronary angiography on the exercise test, the presence of anemia or polycythemia, a previous history of coronary angiography, having a pacemaker, having been previously diagnosed with cancer and therefore being treated, having basal HR below 60 beats/min or over 100 beats/min, being a smoker, taking any medication that affects the heart for any reason, having been diagnosed with the chronic obstructive pulmonary disease at any time and getting treatment for this reason, having any central nervous system disease such as dementia or Parkinson's.

2.3. Treadmill exercise test (TET)

All of the participants were subjected to a TET according to the Bruce protocol after a 5-min rest [15]. Participants with a measured arterial blood pressure above 140/90 mmHg were excluded from the study. Participants who reached less than 88% of the target HR were also excluded (target HR = 220 – age). Calculations were made based on the basal resting, peak exercise, 1st-, 2nd-, and 3rd-min recovery HRs. Moreover, the Tpeak-end (Tp-e), QT, corrected QT (QTc), Tp-e/QT, and Tp-e/QTc values were calculated on the basal resting ECG. Basal HR, peak HR, 1st-, 2nd-, and 3rd-min recovery HR data of the participants were recorded. The 1st-min HR was extracted from the peak HR of the participants, the 1st-min HRR-i was calculated, the 2nd recovery HR was subtracted, the 2nd-min HRR-i, and the 3rd recovery HR were extracted, and the 3rd-min HRR-i data were calculated.

The Tp-e and QT intervals were calculated on the basal resting ECG using a digital caliper with a precision of 1/100 mm (TorQ; 150 mm, digital caliper LCD). The Tp-e interval is defined as the time from the peak of the T wave to the point where it returned on the isoelectric line. The Tp-e interval V2-5 was calculated in the left anterior derivations. It was examined in 3 consecutive beats in a single lead and averaged for the Tp-e interval. The value in millimeters was found in milliseconds and recorded by multiplying by 40 because the ECG speed was 25 mm/s.

The QT interval is defined as the time between the start of the Q wave and the end of the T wave. The QT interval was calculated in at least 9 leads and at least 3 consecutive beats, and the averages of these measurements were taken as the QT interval. The QTc interval was calculated using the Bazzet formula. The Tp-e/QT ratio was obtained by dividing the Tp-e interval value by the QT interval value and the Tp-e/QTc value by dividing the Tp-e interval value by the QTc value, and comparisons were performed.

2.4. Statistical analysis

Continuously defined values were written as the mean ± standard deviation, and categorically defined values were written as a percentage. The student t-test was used to compare continuous variables, while the Fisher exact test or chi-square test was used to compare categorically given values. The unpaired t-test was used for the variables of two separate independent groups and the paired t-test was used for two different variables of the same group that were not always independent. The Pearson correlation test was used to determine the correlation between the variables. $P < 0.05$ was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics 20.0 (IBM Corp., Armonk, NY, USA).

2.5. Ethical approval

All procedures performed in studies involving human participants were conducted following the ethical standards of the National Health and Medical Research Council of Turkey, and the 1964 Helsinki declaration and its later comparable ethical standards. Written permission was obtained from the Hospital Management (Protocol Number: 22568850-799). Informed patient consent was obtained from each subject.

3. Results

There were no significant differences between the groups in terms of the basal clinical and sociodemographic findings [Table 1].

Table 1. Basal clinical findings and sociodemographic properties of the groups

Variable	Men (group 1, n = 758)	Women (group 2, n = 723)	T-value	P-value
Age, years	46.42 ± 22.56	45.67 ± 21.62	0.65	0.51
BMI, kg/m²	25.8 ± 3.1	25.9 ± 2.8	0.65	0.51
Systolic BP, mmHg	121.4 ± 11.7	120.9 ± 11.6	0.82	0.40
Diastolic BP, mm Hg	78.9 ± 12.1	79.2 ± 11.7	0.48	0.62
Hemoglobin, g/dL	14.3 ± 1.7	14.2 ± 2.1	1.00	0.31
TC, mg/dL	171.8 ± 28.6	172.1 ± 31.5	0.19	0.84
LDL, mg/dL	136.7 ± 22.5	137.3 ± 31.8	0.42	0.67
Triglyceride, mg/dL	171.5 ± 33.7	170.5 ± 36.2	0.55	0.58
HDL, mg/dL	32.9 ± 4.9	33.2 ± 5.4	1.12	0.26
Calcium, mg/dL	9.2 ± 1.4	9.1 ± 1.5	1.32	0.18
Sodium, mEq/L	140.8 ± 1.3	140.7 ± 1.5	1.37	0.17
Potassium, mEq/L	4.3 ± 0.9	4.2 ± 1.1	1.91	0.06
TSH, mIU/L	3.3 ± 1.3	3.2 ± 0.9	1.71	0.08

BMI: Body mass index; BP: Blood pressure; TC: Total cholesterol; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; TSH: Thyroid-stimulating hormone; sPAP: Systolic pulmonary arterial pressure.

With regards to individuals aged 20-29 years, the basal and peak HRs in groups 1 and 2 were similar. Moreover, the basal Tp-e, QT, and QTc, and Tp-e/QT and Tp-e/QTc values were significantly higher in group 2 than in group 1. In addition, the 1st-, 2nd-, and 3rd-min

recovery HR values were significantly higher in group 1 than in group 2; however, the 1st-, 2nd-, and 3rd-min HRR-i values were significantly lower in group 1 than in group 2 [Table 2].

Table 2. Comparison of the TET-values of the groups for individuals aged 20-29 years

Variable	Group 1 (n = 154)	Group 2 (n = 149)	T-value	P-value
Age, years	25.39 ± 2.10	24.91 ± 3.08	1.58	0.11
Basal Tp-e, ms	70.04 ± 8.41	78.44 ± 8.04	8.88	**<0.0001**
Basal QT, ms	324.64 ± 22.56	341.23 ± 27.84	5.70	**<0.0001**
Basal QTc, ms	388.79 ± 26.47	413.88 ± 29.51	7.79	**<0.0001**
Basal Tp-e/QT	0.24 ± 0.02	0.22 ± 0.02	12.34	**<0.0001**
Basal Tp-e/QTc	0.20 ± 0.02	0.19 ± 0.01	5.47	**<0.0001**
Basal HR, b/m	75.87 ± 8.55	75.93 ± 9.81	0.055	0.95
Peak HR, b/m	177.07 ± 5.74	176.91 ± 7.84	0.20	0.83
1st-min recovery HR, b/m	123.95 ± 6.91	114.22 ± 5.43	13.59	**<0.0001**
2nd-min recovery HR, b/m	106.20 ± 7.28	98.33 ± 5.41	10.65	**<0.0001**
3rd-min recovery HR, b/m	79.40 ± 4.84	71.41 ± 4.30	9.46	**<0.0001**
HRR-i in the 1st-min, b/m	54.51 ± 4.66	65.07 ± 7.04	15.25	**<0.0001**
HRR-i in the 2nd-min, b/m	73.19 ± 5.89	79.34 ± 4.23	10.41	**<0.0001**
HRR-i in the 3rd min, b/m	102.59 ± 1.21	113.41 ± 7.43	17.83	**<0.0001**

Tp-e: Tpeak-end interval; HR: Heart rate, b/m: Beats/min; HRR-i: HR recovery index.

Table 3. Comparison of the TET-values of the groups for individuals aged 30-39 years

Variable	Group 1 (n = 155)	Group 2 (n = 151)	T-value	P-value
Age, years	36.24 ± 3.10	36.04 ± 2.81	0.58	0.55
Basal Tp-e, ms	76.41 ± 9.12	80.04 ± 9.03	7.17	**<0.0001**
Basal QT, ms	331.84 ± 26.48	345.78 ± 31.41	4.20	**<0.0001**
Basal QTc, ms	399.74 ± 25.76	417.56 ± 39.51	4.68	**<0.0001**
Basal Tp-e/QT	0.22 ± 0.02	0.23 ± 0.0	4.37	**<0.0001**
Basal Tp-e/QTc	0.19 ± 0.01	0.20 ± 0.01	8.74	**<0.0001**
Basal HR, b/m	76.41 ± 9.12	77.03 ± 8.84	0.88	0.38
Peak HR, b/m	168.84 ± 6.28	169.33 ± 3.41	0.84	0.40
1st-min recovery HR, b/m	118.34 ± 5.36	107.24 ± 5.34	9.82	**<0.0001**
2nd-min recovery HR, b/m	98.36 ± 5.76	94.28 ± 3.01	7.69	**<0.0001**
3rd-min recovery HR, b/m	78.46 ± 6.24	72.33 ± 5.36	9.16	**<0.0001**
HRR-i in the 1st-min, b/m	50.75 ± 4.42	63.22 ± 5.07	22.79	**<0.0001**
HRR-i in the 2nd-min, b/m	71.04 ± 5.81	79.24 ± 5.33	12.79	**<0.0001**
HRR-i in the 3rd min, b/m	95.44 ± 4.84	104.61 ± 3.84	17.26	**<0.0001**

Tp-e: Tpeak-end interval; HR: Heart rate, b/m: beats/min; HRR-i: HR recovery index.

With regards to individuals aged 30-39 years, the basal and peak HRs in groups 1 and 2 were similar. Moreover, the basal Tp-e, QT, and QTc, and Tp-e/QT and Tp-e/QTc values were significantly higher in group 2 than in group 1. In addition, the 1st-, 2nd-, and 3rd-min recovery HR values were significantly higher in group 1 than in group 2: however, the 1st-, 2nd-, and 3rd-min HRR-i values were significantly lower in group 1 than in group 2 [Table 3].

Table 4. Comparison of the TET-values of the groups for individuals aged 40-49 years

Variable	Group 1 (n = 145)	Group 2 (n = 144)	T-value	P-value
Age, years	44.81 ± 2.34	44.91 ± 3.89	0.27	0.78
Basal Tp-e, ms	77.81 ± 6.84	81.24 ± 5.35	4.85	**<0.0001**
Basal QT, ms	339.74 ± 23.44	349.79 ± 32.51	3.01	**0.002**
Basal QTc, ms	423.86 ± 28.74	436.41 ± 31.41	3.54	**0.0005**
Basal Tp-e/QT	0.22 ± 0.02	0.23 ± 0.02	4.25	**<0.0001**
Basal Tp-e/QTc	0.18 ± 0.01	0.19 ± 0.01	8.50	**<0.0001**
Basal HR, b/m	74.89 ± 8.71	75.34 ± 7.35	0.29	0.73
Peak HR, b/m	161.38 ± 3.61	160.84 ± 3.04	1.40	0.16
1st-min recovery HR, b/m	113.08 ± 5.81	111.44 ± 5.71	2.24	**0.01**
2nd-min recovery HR, b/m	96.05 ± 3.84	94.35 ± 4.08	3.64	**0.0003**
3rd-min recovery HR, b/m	69.45 ± 3.45	74.33 ± 3.71	2.62	**0.0092**
HRR-i in the 1st-min, b/m	48.74 ± 5.81	53.74 ± 4.22	8.36	**<0.0001**
HRR-i in the 2nd-min, b/m	69.49 ± 4.84	71.42 ± 5.84	3.06	**0.0024**
HRR-i in the 3rd min, b/m	88.45 ± 5.01	95.27 ± 3.71	7.36	**<0.0001**

Tp-e: Tpeak-end interval; HR: Heart rate, b/m: beats/min; HRR-i: HR recovery index.

Table 5. Comparison of the TET-values of the groups for individuals aged 50-59 years

Variable	Group 1 (n = 139)	Group 2 (133)	T-value	P-value
Age, years	54.99 ± 3.09	55.34 ± 3.72	0.84	0.39
Basal Tp-e, ms	81.44 ± 7.41	83.07 ± 7.74	2.86	**0.0045**
Basal QT, ms	348.74 ± 29.82	355.61 ± 29.84	1.89	0.056
Basal QTc, ms	435.82 ± 29.45	443.78 ± 26.41	2.34	**0.012**
Basal Tp-e/QT	0.23 ± 0.02	0.23 ± 0.01	0.00	1
Basal Tp-e/QTc	0.18 ± 0.02	0.18 ± 0.01	0.00	1
Basal HR, b/m	75.01 ± 9.07	75.44 ± 3.93	0.50	0.61
Peak HR, b/m	157.41 ± 3.84	156.34 ± 5.81	1.79	0.07
1st-min recovery HR, b/m	115.84 ± 8.31	113.31 ± 3.74	3.21	**0.001**
2nd-min recovery HR, b/m	96.71 ± 7.71	90.84 ± 6.27	4.54	**<0.0001**
3rd-min recovery HR, b/m	77.81 ± 8.34	71.63 ± 5.74	7.19	**<0.0001**
HRR-i in the 1st-min, b/m	44.71 ± 5.01	49.34 ± 4.43	4.56	**<0.0001**
HRR-i in the 2nd-min, b/m	66.08 ± 4.89	69.44 ± 3.95	6.21	**<0.0001**
HRR-i in the 3rd min, b/m	84.85 ± 4.03	88.37 ± 4.07	7.16	**<0.0001**

With regards to individuals aged 40-49 years, the basal and peak HRs in groups 1 and 2 were similar. Moreover, the basal Tp-e, QT, and QTc, and Tp-e/QT and Tp-e/QTc values were significantly higher in group 2 than in group 1. In addition, the 1st-, 2nd-, and 3rd-min recovery HR values were significantly higher in group 1 than in group 2; however, the 1st-, 2nd-, and 3rd-min HRR-i values were significantly lower in group 1 than in group 2 [Table 4].

Table 6. Comparison of the TET-values of the groups for individuals aged 60-69 years

Variable	Group 1 (n = 99)	Group 2 (n = 91)	T-value	P-value
Age, years	65.73 ± 3.41	64.51 ± 3.45	0.52	0.59
Basal Tp-e, ms	81.04 ± 7.74	82.24 ± 7.75	1.27	0.20
Basal QT, ms	355.74 ± 31.52	359.77 ± 33.81	0.85	0.39
Basal QTc, ms	443.86 ± 25.86	448.63 ± 31.29	1.14	0.25
Basal Tp-e/QT	0.22 ± 0.02	0.22 ± 0.02	0.00	1
Basal Tp-e/QTc	0.18 ± 0.02	0.18 ± 0.02	0.00	1
Basal HR, b/m	75.08 ± 8.31	74.82 ± 8.71	0.25	0.80
Peak HR, b/m	155.08 ± 3.45	153.35 ± 3.43	1.74	0.08
1st-min recovery HR, b/m	117.81 ± 5.04	114.42 ± 4.35	5.92	**<0.0001**
2nd-min recovery HR, b/m	95.52 ± 7.82	91.37 ± 3.84	5.51	**<0.0001**
3rd-min recovery HR, b/m	78.53 ± 5.84	74.47 ± 4.70	6.30	**<0.0001**
HRR-i in the 1st-min, b/m	39.31 ± 3.84	43.37 ± 5.24	3.72	**0.0002**
HRR-i in the 2nd-min, b/m	62.08 ± 3.36	65.22 ± 4.87	6.21	**<0.0001**
HRR-i in the 3rd min, b/m	77.05 ± 5.09	82.28 ± 3.71	9.64	**<0.0001**

Tp-e: Tpeak-end interval; HR: Heart rate, b/m: beats/min; HRR-i: HR recovery index.

Table 7. Comparison of the TET-values of the groups for individuals aged 70-79 years

Variable	Group 1 (n = 66)	Group 2 (55)	T-value	P-value
Age, years	76.01 ± 3.22	75.91 ± 3.84	0.15	0.87
Basal Tp-e, ms	86.03 ± 7.74	86.34 ± 9.81	0.19	0.84
Basal QT, ms	361.81 ± 31.59	361.56 ± 33.89	0.04	0.96
Basal QTc, ms	451.86 ± 35.63	452.01 ± 33.59	0.02	0.98
Basal Tp-e/QT	0.23 ± 0.02	0.23 ± 0.03	0.00	1
Basal Tp-e/QTc	0.19 ± 0.02	0.19 ± 0.02	0.00	1
Basal HR, b/m	76.01 ± 3.22	75.77 ± 7.84	0.65	0.51
Peak HR, b/m	151.04 ± 3.77	151.34 ± 8.38	0.24	0.80
1st-min recovery HR, b/m	117.54 ± 4.91	116.27 ± 3.85	1.59	0.11
2nd-min recovery HR, b/m	93.04 ± 8.71	94.37 ± 4.07	0.55	0.57
3rd-min recovery HR, b/m	76.09 ± 5.51	77.39 ± 5.52	1.29	0.19
HRR-i in the 1st-min, b/m	33.41 ± 3.41	34.01 ± 3.04	1.02	0.30
HRR-i in the 2nd-min, b/m	58.07 ± 5.43	58.34 ± 7.04	0.23	0.81
HRR-i in the 3rd min, b/m	69.08 ± 7.41	69.37 ± 7.86	0.30	0.75

Tp-e: Tpeak-end interval; HR: Heart rate, b/m: beats/min; HRR-i: HR recovery index.

With regards to individuals aged 50-59 years, the basal and peak HRs, basal QT, and Tp-e/QT and Tp-e/QTc values were similar in both groups. Moreover, the basal Tp-e and QTc values were significantly higher in group 2 than in group 1. In addition, the 1st-, 2nd-, and 3rd-min recovery HR values were significantly higher in group 1 than in group 2; however, the 1st-, 2nd-, and 3rd-min HRR-i values were significantly lower in group 1 than in group 2 [Table 5].

With regards to individuals aged 60-69 years, the basal Tp-e, QT, and QTc, Tp-e/QT and Tp-e/QTc, and basal and peak HR values were similar in both groups. Moreover, in group 1, while the 1st-, 2nd-, and 3rd-min recovery HR values were significantly higher than in group 2, the 1st-, 2nd-, and 3rd-min HRR-i values were significantly lower than in group 2 [Table 6].

With regards to individuals aged 70-79 years, the basal Tp-e, QT, and QTc, Tp-e/QT and Tp-e/QTc, 1st-, 2nd-, and 3rd-min recovery HR, and 1st-, 2nd-, and 3rd-min HRR-i values were similar in both groups [Table 7].

In groups 1 and 2, there were statistically significant negative correlations between the Tp-e and HRR-i values at the 1st-min recovery stage of the TET ($r = 0.11$ and $p = 0.0024$, $r = 0.09$ and $p = 0.0154$, respectively). However, there were no significant correlations between the Tp-e and HRR-i at the 2nd- and 3rd-min recovery of the TET in groups 1 and 2 (at the 2nd-min recovery: $r = 0.05$ and $p = 0.169$, $r = 0.03$ and $p = 0.420$, and at the 3rd-min recovery: $r = 0.04$ and $p = 0.2713$, $r = 0.02$ and $p = 0.5913$, respectively).

4. Discussion

In the current study, the HRR-i, Tp-e, QT, and QTc interval, and Tp-e/QT and Tp-e/QTc values differed significantly between the men and women, except in individuals aged 70-79 years. Moreover, as the age range increased in both the men and women, the HRR-i values decreased significantly and most of the repolarization markers increased progressively. Moreover, there was a statistically significant negative correlation between the Tp-e interval and 1st-min HRR-i values, while there was no significant correlation between the 2nd- and 3rd-min HRR-i values.

Cardiovascular diseases are the most common diseases with mortality and morbidity worldwide. Autonomic functions and cardiovascular system functions are both complex and intertwined important conditions. One of the most used methods to detect autonomic functions is TET. As it is known, in maximal TET, sympathetic system increases and decreases in parasympathetic system activation occur up to the peak exercise level, while in recovery phases, there is a decrease in sympathetic system activation and reactivation of the parasympathetic system. These two branches in the recovery phase, namely reducing the activation of the sympathetic system and increasing the activation of the parasympathetic system, are essential for autonomic functions. Since malignant ventricular arrhythmias are directly related to sympathetic nervous system activation or reduction of parasympathetic system activation, any imbalance in the autonomic system is particularly effective in the emergence of these malignant ventricular arrhythmias after exercise. For this reason, the vast majority of malignant ventricular arrhythmias occur immediately after intense exercise [8].

The HRR-i value is obtained by subtracting the 1st, 2nd, and 3rd recovery HR values from the peak HR on the TET, and it is used to detect autonomic functions [16]. In addition, when HRR-i values are lower than normal or expected, whether there is an underlying structural heart disease or not, this is closely related to increased cardiovascular mortality and morbidity [17].

There is a variety of HRR-i cutoff points available in the scientific literature to determine the delay in 1st-min HR recovery. In the study of Bellefleur et al. [18], the cutoff point used to characterize the delay in the HRR-i was below or equal to 14 beats/min, but most studies have used the cutoff point of below or equal to 12 beats/min [19]. The most widely used way to assess delayed 1st-min HRR-i is through a maximum exercise test performed on a treadmill.

It is known that a rapid decrease in HR in the 1st recovery minute immediately after peak exercise is associated with vagal reactivation, whereas a decrease in HR in the 2nd and 3rd min is due to the withdrawal of the sympathetic system activation [20]. Significant delays in these decreases are closely related to increased cardiovascular and all-cause deaths [21]. In particular, in the study of Cole et al., it was closely associated with increased cardiovascular and all-cause deaths in patients with lower HRR-i values in the 1st min [6]. In their study, 2428 patients who underwent TET were followed-up for 6 years. Values below 12 beats/min were determined as an abnormal HRR-i value. Moreover, 213 of 639 patients whose 1st-min HRR-i value was below 12 beats/min died due to any reason after these 6 years of follow-up. This rate was found to be significantly higher than the group with an HRR-i value above 12 beats/min.

HRR-i is a cheap, simple, and useful method that reflects the parasympathetic system very well, which clinicians can use not only for heart diseases but for many system diseases. The relationship of autonomic dysfunction with malignant ventricular arrhythmias has been strongly proven to date. While there are very complex methods to measure autonomic functions, the HRR-i stands out as an easy, inexpensive, and feasible method. Other complex methods are required to have both expensive and specialized equipment. A simple TET and HRR-i, which is calculated very easily, can be applied very easily and cheaply in the detection of high-risk patients.

In electrophysiological studies, it was found that the repolarization findings of women and men were different. One of which was the Tp-e interval [10,22]. To date, many studies have been conducted that revealed the relationship between repolarization anomalies and

malignant ventricular arrhythmias. In electrophysiological studies, significant prolongation of ventricular repolarization times was found to be closely related to significantly increased malignant ventricular arrhythmias, with or without underlying structural heart disease [23,24]. For this reason, many repolarization predictors have been explored beforehand to detect a high-risk population for malignant ventricular arrhythmias. Some of these include the Tp-e interval, QT elongation, Tp-e7QT and Tp-e/QTc rates, microvolt T wave alternans, T wave heterogeneity, T wave area dispersion, V index, and late ventricular potentials.

Some of the most emphasized markers over the last 10 years have been the Tp-e interval, and Tp-e/QT and Tp-e/QTc ratios. Although some researchers have the opinion that the Tp-e interval does not show the total ventricular repolarization dispersion, significant prolongations, especially in the Tp-e interval, were found to be associated with significantly increased malignant ventricular arrhythmias [24,25]. The relationship between a changing ventricular repolarization time and changing cardiac autonomic functions with significantly increased malignant ventricular arrhythmia is well known [26]. In another study, the Tp-e interval was prolonged by stimulating sympathetic ganglia [27]. Thus, the Tp-e interval was proven to be prolonged with increasing sympathetic activity and decreasing vagal activity. In yet another study, the cut-off point of the Tp-e interval for the malign ventricular arrhythmias in the general normal population was 113.6 ms [28]. The rates of malignant ventricular arrhythmia in ICD patients with a Tp-e/QT ratio above 0.25 were reported to be statistically significantly higher than those with a Tp-e/QT ratio below 0.25 by Barbhaiya et al. [11]. Moreover, in many diseases with a high risk of sudden cardiac death and malignant ventricular arrhythmia, the Tp-e interval and Tp-e/QT and Tp-e/QTc ratios were significantly higher than in the control group [12,14,29].

It is well known that the risk of malignant ventricular arrhythmia increases with or without underlying structural heart disease. Many mechanisms have been proposed to explain the risk of malignant ventricular arrhythmia increasing with age. The most emphasized of these is that the sensitization of beta-adrenergic receptors in the heart decreases as age increases. Among its mechanisms are prolonged action potential duration and effective refractory period, myocardial fibrosis, amyloid infiltration, scarring on the background of the ischemia, increased tension, and permanent electrical remodeling. All of these mechanisms may increase the risk of malignant ventricular arrhythmia by causing repolarization heterogeneity in the aging heart [30].

4.1. Study limitations

If the number of individuals in this study had been a bit higher, healthier data could have been obtained. In addition, 24-h Holter monitoring could not be performed. If 24-h Holter monitoring was performed and the data were confirmed with the HRV data, more healthy data could be obtained. Additionally, if the Tp-e interval and Tp-e/QT and Tp-e/QTc ratios had been supported by other T wave predictors, such as T wave alternans or T wave heterogeneity, the data would have been healthier.

4.2. Conclusion

As a result, in the current study, it was found that the Tp-e interval, QT, QTc, and Tp-e/QT and Tp-e/QTc ratios changed with age in healthy men and women, and this difference became non-significant, specifically in the age range of 70-79 years. In particular, a significant relationship was found between the Tp-e interval and HRR-i values in the 1st-min recovery phase. These results can help to explain why the increased risk of malignant ventricular arrhythmia increases, with or without underlying structural heart disease.

Conflict of interest

The authors declare that there are no conflicts of interest.

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