

## Evaluation of Left Ventricular Systolic Functions of Patients with Exaggerated High Blood Pressure Response to Treadmill Exercise Test with Two-Dimensional Longitudinal Strain Imaging

### ABSTRACT

**Background:** An exaggerated hypertensive response (EHR) during exercise is linked to increased cardiovascular risk and mortality. This study aims to assess structural and functional cardiac changes, along with subclinical myocardial damage, using transthoracic echocardiography (ECHO) and 2D longitudinal strain analysis in patients showing a hypertensive response to treadmill exercise.

**Methods:** Patients without known chronic diseases, presenting to the Cardiology Department at Health Sciences University Gülhane Training and Research Hospital, were divided into 2 groups based on their blood pressure response during treadmill exercise: exaggerated hypertensive response (EHR, n = 42) and normal response (control, n = 44). Left ventricular longitudinal strain was assessed using transthoracic echocardiography, and global longitudinal strain (GLS) was calculated as the average from all segments. Data analysis was performed using SPSS 26.

**Results:** No significant differences were found between the groups regarding baseline demographic and laboratory parameters ( $P > .05$  for all). However, the EHR group exhibited significantly higher interventricular septum thickness, mitral A velocity, and mitral annulus velocity ( $a'$ ), while mitral annulus velocity ( $e'$ ) was significantly lower ( $P < .05$  for all). Additionally, left ventricular (LV) mass index, left atrial volume index, mitral E/ $e'$  ratio, deceleration time, and relative wall thickness (RWT) were higher in the EHR group, while the mitral E/A ratio was lower ( $P < .05$  for all). The GLS was also significantly lower in the EHR group ( $P < .05$ ).

**Conclusion:** Left ventricular geometry parameters, such as LV mass index and RWT, and GLS findings indicating subclinical cardiac damage, were significantly altered in the EHR group, suggesting a higher risk of LV hypertrophy and myocardial dysfunction.

**Keywords:** Exercise, hypertension, left ventricular systolic function, two-dimensional longitudinal strain, speckle tracking

### INTRODUCTION

The exercise stress test (EST) is a widely used noninvasive method for detecting exercise-induced myocardial ischemia, arrhythmias, and evaluating cardiopulmonary functional capacity. Since the 1960s, EST has been an important diagnostic tool, particularly in the assessment of obstructive coronary artery disease (CAD) and exercise-induced myocardial ischemia. While EST is favored for its low cost, accessibility, and safety, its sensitivity is reported to be around 60-70% and specificity between 70-80%.<sup>1</sup> Despite its limitations in ruling out obstructive CAD, hemodynamic parameters such as electrocardiogram (ECG) changes, exercise duration, metabolic equivalents (METs), heart rate (HR), and blood pressure (BP) recorded during the test provide valuable insights for assessing cardiovascular risk and prognosis. Therefore, EST remains one of the first-line tests for patients who are able to exercise and have an interpretable baseline ECG.<sup>2</sup>

During exercise, the increase in cardiac output due to heightened sympathetic tone and the increased oxygen demands of working muscles leads to a normal

### ORIGINAL INVESTIGATION

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physiological rise in systolic blood pressure (SBP). However, in some individuals, an exaggerated rise in SBP occurs independent of underlying cardiovascular disease. This condition is defined as an exaggerated hypertensive response (EHR) to exercise. Individuals with EHR, despite being normotensive at rest, are associated with the future development of hypertension, end-organ damage, cardiovascular risk factors, as well as increased morbidity and mortality. While EHR is generally considered an abnormal response in most studies, there is conflicting evidence suggesting it may be clinically insignificant in some cases. Furthermore, information about its causes, pathophysiology, and the necessity for treatment or follow-up remains limited.<sup>3</sup>

Speckle tracking echocardiography (STE) is a valuable tool for the early detection of subclinical cardiac damage, as it allows for precise evaluation of myocardial fiber motion and deformation. The early detection of subclinical cardiac damage is crucial for optimizing clinical management and preventing future adverse events. The aim of our study is to assess the presence of subclinical cardiac damage in normotensive individuals exhibiting an EHR during EST using both conventional and 2-dimensional (2D)-STE parameters. Our study is among the first to demonstrate the presence of subclinical cardiac damage in individuals with EHR using the 2D-STE imaging technique.

## METHODS

### Study Population

Our study is an observational case-control study conducted at the Cardiology Department of Gülhane Training and

Research Hospital between August 2022 and December 2022. Participants were consecutively selected from patient records until the required sample size was reached, and those meeting the inclusion criteria were enrolled in the study. All participants underwent comprehensive clinical evaluations, including BP profiling, anthropometric measurements, resting transthoracic echocardiography (ECHO), and treadmill exercise testing. Ethical approval for the study was obtained from the Gülhane Training and Research Hospital Ethics Committee (2022/83), and all procedures were conducted in accordance with the Helsinki Declaration. Informed consent was obtained from all participants during the initial visit.

### Inclusion Criteria

- Individuals presented to the cardiology clinic with appropriate indications for exercise stress testing; they were normotensive at rest but exhibited an exercise-induced hypertensive response (defined as an increase in SBP of at least 60 mm Hg in men, 50 mm Hg in women, or exceeding the 90<sup>th</sup> percentile:  $\geq 210$  mm Hg in men,  $\geq 190$  mm Hg in women).
- Participants with a negative cardiovascular stress test.
- Those with an average resting SBP  $< 140$  mm Hg and diastolic blood pressure (DBP)  $< 90$  mm Hg based on repeated measurements.
- Individuals who consented to participate in the study.

### Exclusion Criteria

- Individuals under 18 or over 70 years of age.
- Participants with a left ventricular (LV) ejection fraction below 55% on ECHO.
- Those with a positive EST (suggestive of coronary artery disease).
- Individuals with a history of diabetes, cardiovascular disease, valvular disease, or other significant systemic illnesses, or those on relevant medications.
- Patients with atrial fibrillation, bundle branch block, or other arrhythmias.
- Participants with psychiatric conditions affecting decision-making capacity might interfere with study participation.

## METHODS

All participants underwent a comprehensive clinical examination following a detailed inquiry into their medical history to assess cardiovascular risk factors and existing health conditions. During the examination, HR and arterial BP measurements were taken. Additionally, body weight and height were measured, and body mass index (BMI) was calculated and recorded. Arterial BP measurements were performed using a digital BP monitor (Omron HEM-7155T-EBK, M4 Intelli IT, Omron Healthcare, Kyoto, Japan) in accordance with the 2019 guidelines of the European Society of Cardiology for BP management. Participants were also instructed on home BP monitoring, and out-of-office BP measurements were taken in the morning and evening for 3 consecutive days to rule out masked hypertension. The average of the home BP measurements was calculated and analyzed as resting BP. No artificial intelligence (AI)-based tools, such as large language

## HIGHLIGHTS

- Clinical significance and mechanisms of exaggerated hypertensive response (EHR): "The clinical significance of an EHR during exercise is underscored by its association with endothelial dysfunction in younger individuals and arterial stiffness in older adults, suggesting a link to increased cardiovascular risk."
- Impact of EHR on cardiac structure and function: "Our findings indicate that individuals with EHR exhibit significantly altered cardiac structure and function, evidenced by less negative global longitudinal strain values and increased parameters such as LVMI and RWT, highlighting the presence of subclinical cardiac damage."
- Assessment of blood pressure changes during exercise testing: "Evaluating blood pressure changes during exercise testing is crucial, as EHR can unmask hypertension not detected in routine office measurements and aid in cardiovascular risk stratification."
- Treatment strategies and future research: "Given the absence of clear guidelines, treating individuals with subclinical cardiac damage identified by EHR with cardioprotective agents such as angiotensin receptor blockers or beta blockers warrants consideration, and underscores the need for extensive, multicenter, randomized controlled trials."

models (LLMs), chatbots, or image generation technologies were utilized in the development of this manuscript.

### Echocardiographic Examination

Transthoracic 2D-ECHO recordings of all participants in our study were obtained using a Philips Epiq 7 (Philips Medical Systems, Bothell, WA) device with a 3.5 MHz transducer and evaluated by 2 operators (X and X), who were blinded to the participants' BP responses during exercise. Left ventricular global longitudinal strain (LV-GLS) was assessed using STE. Apical 2-, 3-, and 4-chamber views were acquired and analyzed offline using commercial software (QLAB 13, TOMTEC/Philips, Andover, MA, USA) in accordance with the guidelines. Regional LV function was evaluated both visually and quantitatively with a 17-segment polar plot (Bulls' eye) displaying color-coded peak systolic strain values. Additionally, key parameters such as left ventricular ejection fraction (LVEF), left ventricular mass index (LVMI), relative wall thickness (RWT), diastolic function, and left atrial volume index (LAVI) were calculated according to the guidelines of the American Society of Echocardiography.

### Exercise Stress Test

Participants in this study underwent a symptom-limited exercise test using a treadmill stress system (GE Case, GE Medical Systems, Freiburg, Germany) following the modified Bruce protocol. A 12-lead ECG was recorded throughout the EST. During the test, participants achieved at least 85% of their age-predicted maximum HR. Blood pressure measurements were taken at 3 minute intervals during exercise. To minimize measurement errors, the arm used for BP measurement was supported on the shoulder of the operator conducting the test.

Exaggerated hypertensive response was defined as an increase in SBP of at least 60 mm Hg in men and 50 mm Hg in women from baseline SBP or exceeding the 90<sup>th</sup> percentile (men: SBP  $\geq$  210 mm Hg; women:  $\geq$  190 mm Hg). The test was terminated if there were no symptoms and the participant reached more than 90% of the target HR, if SBP exceeded 250 mm Hg, if there was a decrease of 10 mmHg or more in SBP, if the participant could not continue due to fatigue, or if ischemic ECG changes developed.

### Data Analysis

The sample size for this study was calculated through power analysis using G\*Power version 3.1.9.7, based on an effect size of 0.75, a significance level of 0.05, and a statistical power of 95%, in accordance with the standards for independent *t*-tests. This calculation determined that 40 participants per group were needed, yielding a total of 80 participants. Descriptive statistics for the study variables included frequency, percentage, mean, and standard deviation. Prior to conducting group comparisons, the assumption of normal distribution was tested using the Shapiro–Wilk test. If the assumption of normality was satisfied, independent *t*-tests were used for group comparisons; if the assumption was violated, the Mann–Whitney *U* test was applied. All statistical analyses were conducted using SPSS version 26 (SPSS for Mac OS, SPSS Inc., Chicago, IL, USA). A *P*-value of less than .05 was considered statistically significant.

## RESULTS

As shown in Table 1, there were no statistically significant differences in basal demographic and biochemical laboratory parameters between the patient and control groups examined in this study (*P* > .05 for all).

Table 2 demonstrates that the peak SBP of participants in the EHR-positive group was 205.81 ( $\pm$ 9.49) mm Hg and the peak-DBP was 93.52 ( $\pm$ 5.26) mm Hg, both of which were significantly higher compared to the control group (*P* < .05 for all). Additionally, the achieved HR measurements in the patient group were significantly lower at 153.24 ( $\pm$ 12.51) compared to the control group (*P* < .05). No other statistically significant differences were observed between the patient and control groups in other measurements (*P* > .05 for all).

Table 3 shows that in the patient group, measurements such as IVS thickness at 10.06 ( $\pm$ 1.54) mm, mitral A-velocity at 69.63 ( $\pm$ 16.36) cm/s, lateral mitral annulus velocity (a') at 10.84 ( $\pm$ 3.16) cm/s, and septal mitral annulus velocity (a') at 10.08 ( $\pm$ 2.19) cm/s were significantly higher compared to the control group (*P* < .05 for all). Additionally, the lateral mitral annulus velocity (e') at 12.02 ( $\pm$ 3.21) cm/s and septal mitral annulus velocity (e') at 8.95 ( $\pm$ 2.13) cm/s were significantly lower in the patient group compared to the control group (*P* < .05 for all). Additionally, the mitral E/A measurement in the patient group was 1.19 ( $\pm$ 0.33), which was significantly lower than in the control group (*P* < .05). Furthermore, the mean segmental strain resulting in a global longitudinal strain (GLS) of  $-18.89$  ( $\pm$ 2.48)% was significantly lower compared to  $-22.32$  ( $\pm$ 1.44)% in the control group (*P* < .05). Participants in the patient group had significantly higher measurements of LVMI at 81.90 ( $\pm$ 15.36) g/m<sup>2</sup>, LAVI at 22.57 ( $\pm$ 8.04) mL/m<sup>2</sup>, mitral E/e' ratio at 7.70 ( $\pm$ 1.79), deceleration time (DT) at 160.52 ( $\pm$ 38.57) ms, and RWT at 0.47 ( $\pm$ 0.06) compared to the control group (*P* < .05 for all). No other statistically significant differences were found between the

**Table 1. Demographic and Biochemical Data of Patient and Control Groups**

Parameters	Control (n=44)		EHR (n=42)		P
	n	(%)	n	(%)	
Sex					.455 <sup>X</sup>
Men	27	61,4	29	69,0	
Women	17	38,6	13	31,0	
Smoking	17	38.64	18	42.86	.858 <sup>T</sup>
	<b>Mean</b>	<b>(<math>\pm</math>SD)</b>	<b>Mean</b>	<b>(<math>\pm</math>SD)</b>	<b>P</b>
Age (years)	48.69	6.89	49.86	10.97	.053 <sup>T</sup>
BMI (kg/m <sup>2</sup> )	26.43	4.54	27.75	4.08	.161 <sup>T</sup>
GFR (mL/minute/1.73 m <sup>2</sup> )	83.65	16.93	81.83	14.69	.231 <sup>U</sup>
Total cholesterol (mg/dL)	194.50	32.99	204.36	34.82	.181 <sup>T</sup>
LDL (mg/dL)	114.23	21.91	115.90	26.64	.081 <sup>T</sup>
HDL (mg/dL)	52.95	10.51	48.61	11.49	.071 <sup>T</sup>

<sup>X</sup>Chi-square test; <sup>T</sup>Independent samples *t*-test; <sup>U</sup>Mann–Whitney *U* test. BMI, body mass index; GFR, glomerular filtration rate, LDL, low density lipoproteins.

**Table 2. Hemodynamic Responses to Exercise Testing in Patient and Control Groups**

Parameters	Control (n = 44)		EHR (n = 42)		P
	n	(±SD)	n	(±SD)	
METs	11.06	1.15	10.79	1.10	.314 <sup>U</sup>
Peak HR (bpm)	159.36	11.09	153.24	12.51	.018 <sup>T</sup>
Resting SBP, (mm Hg)	116.73	10.61	118.21	10.02	.231 <sup>U</sup>
Resting DBP, (mm Hg)	75.52	7.15	76.83	6.51	.210 <sup>U</sup>
Peak SBP, (mm Hg)	142.70	12.10	205.81	9.49	< .001 <sup>U</sup>
Peak DBP, (mm Hg)	86.27	7.88	93.52	5.26	< .001 <sup>U</sup>

<sup>X</sup>Chi-square test; <sup>T</sup>Independent samples t-test; <sup>U</sup>Mann-Whitney U test. BPM, beats per minute; DBP, diastolic blood pressure; HR, heart rate; METs, metabolic equivalent.

patient and control groups in other measurements ( $P > .05$  for all).

## DISCUSSION

High BP is one of the modifiable and significant risk factors for cardiovascular morbidity and mortality. Office BP measurements are widely used and validated for cardiovascular risk assessment; however, they may not fully reflect the true BP levels and variability experienced in daily life.<sup>4</sup> Factors

such as diet, medication use, exercise, circadian rhythm, and stress can influence BP fluctuations, which should be closely monitored. Intermittent BP elevations and BP variability are considered independent risk factors that can negatively impact cardiac function and lead to target organ damage, regardless of average BP levels.<sup>4</sup> In relation to BP variability, some individuals may exhibit normal resting BP but experience an abnormal increase in SBP during exercise. This condition is referred to as an EHR to exercise.<sup>3</sup>

In recent years, the pathophysiology and clinical significance of EHR have remained subjects of debate due to the differing findings presented by various studies. In previous studies in the literature, researchers have arbitrarily used different threshold values for peak BP. This has led to inconsistent outcomes regarding the relationship between EHR and adverse events.<sup>5</sup> However, recent studies using standardized reference values have increasingly shown that EHR is associated with masked hypertension, future hypertension, morbidity, and mortality.<sup>3</sup> Furthermore, some common pathophysiological mechanisms have been identified in individuals with EHR that could be linked to adverse cardiovascular outcomes. These mechanisms include microvascular dysfunction, endothelial dysfunction, arterial stiffness, increased angiotensin II levels, reduced nitric oxide (NO) levels, and heightened sympathetic tone.<sup>6</sup> In a study conducted by Wilson et al<sup>7</sup>, normotensive individuals at rest with EHR demonstrated significantly higher peripheral vascular resistance at all stages of exercise. Additionally, young individuals with EHR, who had no known cardiovascular risk factors, were found to have reduced nitric oxide activity and release. Based on these findings, endothelial dysfunction is suggested as a primary cause of EHR in younger individuals.<sup>8</sup> In contrast, arterial stiffness plays a more critical role in older individuals. As arterial stiffness increases with age, it leads to reduced arterial compliance, impaired BP regulation, and abnormal increases in systolic BP during exercise.<sup>6</sup>

The primary aim of this study is to compare normotensive individuals with an EHR to those with a normal BP response, using conventional and 2D-STE parameters, to evaluate potential subclinical cardiac damage. There are 2 key points that distinguish our study from previous research. First, previous studies have generally not considered out-of-office BP measurements, which could have led to undiagnosed masked hypertension. In our study, participants were instructed to monitor their BP at home, allowing us to exclude masked hypertension.<sup>5</sup> Second, while earlier studies have primarily used only conventional echocardiographic parameters to assess subclinical cardiac damage, we employed both conventional and STE parameters. This makes our study the second of its kind in the literature, with a larger sample size compared to the previous study.<sup>9</sup>

Two dimensional-speckle tracking echocardiography is a relatively new imaging technique that assesses myocardial function independent of rotational movements. Its applicability and benefits have been demonstrated in various conditions, particularly in hypertension patients, where it can detect impaired myocardial deformation despite normal

**Table 3. Conventional Echocardiography Findings in Patient and Control Groups**

Parameters	Control (n = 44)		EHR (n = 42)		P
	Mean	(±SD)	Mean	(±SD)	
IVSd (mm)	9.42	1.32	10.06	1.54	.043 <sup>U</sup>
PWT (mm)	9.89	1.22	10.39	1.06	.069 <sup>U</sup>
LVEDD (mm)	30.03	4.46	28.74	4.97	.209 <sup>T</sup>
LVEDD (mm)	45.51	3.60	45.20	3.86	.702 <sup>T</sup>
LA (mm)	31.56	4.78	33.01	4.23	.210 <sup>U</sup>
LAVI, (ml/m <sup>2</sup> )	18.41	4.38	22.57	8.04	.005 <sup>U</sup>
Peak E (cm/sn)	82.47	14.17	81.93	18.88	.782 <sup>U</sup>
Peak A, (cm/sn)	58.26	13.07	69.63	16.36	.001 <sup>T</sup>
E/e <sup>†</sup> ratio	6.20	1.51	7.70	1.79	< .001 <sup>T</sup>
E/A ratio	1.54	0.82	1.19	0.33	< .001 <sup>U</sup>
DT (msn)	135.2	28.3	160.52	38.57	.001 <sup>T</sup>
RWT	0.41	0.05	0.47	0.06	< .001 <sup>T</sup>
EDV (ml)	96.42	22.33	95.31	23.46	.824 <sup>T</sup>
ESV (ml)	36.38	10.69	40.46	11.52	.092 <sup>T</sup>
LVM (g)	146.2	35.09	161.36	38.32	.059 <sup>T</sup>
LVMi (g/m <sup>2</sup> )	73.59	12.85	81.9	15.36	.008 <sup>T</sup>
EF (%)	62.82	4.04	61.98	4.59	.169 <sup>T</sup>
GLS, (%)	-22.32	1.44	-18.89	2.48	.001 <sup>T</sup>

<sup>T</sup>Independent samples t-test, <sup>U</sup>Mann-Whitney U test. A, atrial kick mitral inflow velocity; DT, deceleration time; E, early mitral inflow velocity; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; GLS, global longitudinal strain; IVS, interventricular septum; LA, left atrium; LAVI, left atrium volume index; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVMi, left ventricular mass index; PWT, posterior wall thickness; RWT, relative wall thickness.



ejection fraction.<sup>10</sup> In this study, it was observed that the GLS values in individuals with EHR were significantly less negative compared to those with a normal BP response, indicating deformation in the LV. Longitudinal muscle fibers are located in the subendocardium, making them more sensitive to increased intracardiac pressures and more exposed to stress compared to circumferential fibers.<sup>9</sup> As the BP increases, the workload on the LV and left atrium (LA) also increases. Initially, this results in physiological adaptation, leading to LV hypertrophy, but over time, persistent workload may cause myocardial fibrosis. Thus, it was considered that conventional echocardiographic parameters indicating LV and LA geometry and size, such as LVMI, RWT, IVSd, and LAVI, were significantly elevated in individuals with EHR. Additionally, LV diastolic dysfunction was significantly higher in those with EHR compared to normotensive controls. In conclusion, our study demonstrated subclinical myocardial impairment in normotensive individuals with EHR when both conventional and strain parameters were evaluated.

When evaluating other studies in the literature, individuals with EHR were observed to have a higher prevalence of diastolic dysfunction and abnormalities in LV geometry and LV hypertrophy parameters compared to those with a normal BP response.<sup>11,12</sup> However, some studies have not reported statistically significant differences in diastolic dysfunction and LV remodeling between individuals with EHR and those with a normal exercise response.<sup>13,14</sup> We believe that these inconsistencies across studies may stem from factors such as the use of different exercise test modalities, the lack of standardized threshold values for diagnosing EHR, variations in the timing of BP measurements during different stages of the exercise test, differences in exercise test protocols across clinics, and the small sample sizes with diverse demographic characteristics typically studied.<sup>3</sup> In our study, individuals with an EHR during the most intense phase of the EST were examined using the modified Bruce protocol.

The treatment of individuals with normotension at rest but exhibiting an EHR remains controversial. Current hypertension guidelines lack specific recommendations regarding the diagnosis and management of a hypertensive response during exercise.<sup>5</sup> Available evidence suggests that angiotensin II plays a crucial role as a neurohormonal regulator of vascular and myocardial responses to physical activity. Thus, angiotensin receptor blockers or angiotensin-converting enzyme inhibitors may represent therapeutic options for patients exhibiting EHR. Additionally, considering the increased sympathetic tone during exercise, beta-blockers may also be a preferred treatment option.<sup>6</sup> However, in a study conducted by Chant et al<sup>15</sup>, an elevated BP response was observed during exercise even in patients taking antihypertensive medications with well-controlled resting BP. This phenomenon was thought to be partially related to enhanced metaboreflex sensitivity. In conclusion, further research is needed to explore the potential benefits of non-pharmacological interventions based on aggressive lifestyle modifications and pharmacological interventions, such as cardioprotective angiotensin receptor blockers or angiotensin-converting enzyme inhibitors, in these individuals.

### Study Limitation

A significant limitation of this study is that it was conducted at a single center and involved a relatively small sample size. The primary reason for the low number of patients in the groups is the exclusion of individuals with comorbid diseases and those using pharmacological agents that could affect LV systolic function. Left ventricular deformation is a complex, 3-dimensional movement, and longitudinal strain analysis represents only one aspect of this process. Another limitation of our study is that only GLS measurements were performed on the patients, while radial and circumferential strain measurements were not conducted. We believe that future studies incorporating 3-dimensional circumferential, longitudinal, and radial strain analyses could yield more comprehensive findings.

### CONCLUSION

In our study, normotensive individuals with an EHR demonstrated significant findings consistent with LV deformation through GLS analysis, our primary outcome measure, alongside conventional parameters. The main conclusion drawn from this study is that the presence of EHR, as suggested in most previous research, has negative effects on cardiac structure and function. Findings indicating subclinical cardiac damage may help clarify the increased cardiovascular risk in patients with EHR. Additionally, these findings may provide critical insights into the early diagnosis of hypertension, target organ damage, and increased cardiovascular risk in these patients. It is essential that individuals with EHR be evaluated for masked hypertension through out-of-office BP measurements. Although there is no consensus on the diagnosis, follow-up, and treatment strategies for patients with EHR, the current findings suggest subclinical LV damage, indicating the need for close cardiovascular risk monitoring in these patients. Larger, multicenter, randomized controlled trials with extended follow-up periods are necessary to establish more precise diagnostic and therapeutic approaches for patients presenting with EHR.

The clinical definition and significance of an EHR during exercise remain inadequately elucidated, necessitating further research to clarify its implications for cardiovascular risk stratification and management.

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**Ethics Committee Approval:** This study was approved by the Gülhane Training and Research Hospital Ethics Committee on 01.07.2022, with decision number 2022/83.

**Informed Consent:** Informed consent was obtained from all participants.

**Peer-review:** Externally peer reviewed.

**Author Contributions:** Concept – M.G.; Design – M.G.; Supervision – M.G., M.Ç.; Resources – M.G.; Materials – M.G.; Data Collection and/or Processing – M.G.; Analysis and/or Interpretation – M.G., M.Ç.; Literature Search – M.G.; Writing – M.G.; Critical Review – M.G., M.Ç.

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