The predictive value of heart rate turbulence for ventricular systolic dysfunction and prognosis in the peri-infarction period

Kalp hızı türbülansının peri-infarktüs dönemde sol ventrikül disfonksiyonu ve prognoz açısından öngördürücü değeri

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Objectives: This study was conducted to investigate the relationship between heart rate turbulence (HRT) and acute left ventricular systolic dysfunction due to ST-segment elevation acute myocardial infarction (STEMI).

Study design: The study included 50 consecutive patients with acute STEMI. All the patients received thrombolytic therapy on admission and underwent transthoracic echocardiographic (TTE) examination at the 24th hour of hospitalization. The patients were divided into two groups according to whether they had decreased or normal left ventricular ejection fraction (LVEF). There were 25 patients (mean age 48±9 years; LVEF: <55%) in group 1, and 25 patients (mean age 52±9 years; LVEF: ≥55%) in group 2. All the patients underwent 24-hour Holter monitoring after TTE to derive the two HRT parameters, turbulence onset (TO) and turbulence slope (TS), showing early acceleration and late deceleration phases, respectively.

Results: Patients in group 1 exhibited a significantly higher mean TO (0.74±1.82% *vs* -2.35±1.48%, p<0.05) and a significantly lower LVEF (39.1±6.7% *vs* 57.2±5.3%, p<0.05). The other Holter and echocardiographic variables did not differ significantly between the two groups (p>0.05). An abnormal TO value (≥0%) was found to have sensitivity and specificity of 88% (p<0.05) in predicting acute left ventricular systolic dysfunction (LVEF<55%) during the peri-infarction period of STEMI.

Conclusion: Impaired TO may be used as a useful predictor of left ventricular systolic dysfunction and poor prognosis in the peri-infarction period of STEMI.

Key words: Echocardiography; electrocardiography; heart rate; myocardial infarction; prognosis; ventricular dysfunction, left; ventricular premature complexes/physiopathology.

Amaç: Bu çalışmada, ST-segment yükselmeli miyokard infarktüslü (STEMI) hastalarda kalp hızı türbülansı (KHT) ile sol ventrikül sistolik disfonksiyonu arasındaki ilişki araştırıldı.

Çalışma planı: Çalışmaya STEMI ile başvuran ardışık 50 hasta alındı. Yatışta trombolitik tedavi uygulandıktan 24 saat sonra hastalar transtorasik ekokardiyografi ile değerlendirildi. Hastalar, sol ventrikül ejeksiyon fraksiyonunun (EF) düşük (<%55) veya normal (≥%55) olmasına göre iki grupta incelendi. Grup 1'de 25 hasta (ort. yaş 48±9), grup 2'de 25 hasta (ort. yaş 52±9) vardı. Transtorasik ekokardiyografi ile değerlendirme sonrasında tüm hastalara 24 saatlik Holter monitörizasyonu uygulanarak, buradan elde edilen verilerden KHT'ye ait iki parametre, erken akselerasyonu gösteren türbülans başlangıcı ve geç deselerasyonu gösteren türbülans eğimi hesaplandı.

Bulgular: Grup 1'deki hastalarda ortalama türbülans başlangıç değeri anlamlı derecede yüksek (%0.74±1.82 ve -%2.35±1.48, p<0.05), sol ventrikül EF'si anlamlı derecede düşük (%39.1±6.7 ve %57.2±5.3, p<0.05) bulundu. Holter izleme ve ekokardiyografik değerlendirmeye ait diğer veriler iki grup arasında anlamlı farklılık göstermedi (p>0.05). Akut sol ventrikül sistolik disfonksiyonunu öngörmede (EF <%55) türbülans başlangıcına ait anormal değerlerin (≥%0) duyarlılık ve özgüllüğü %88 bulundu (p<0.05).

Sonuç: Akut STEMI'de, bozulmuş türbülans başlangıç değeri, sol ventrikül sistolik disfonksiyonunu ve prognozu öngörmede yararlı bir parametre olarak kullanılabilir.

Anahtar sözcükler: Ekokardiyografi; elektrokardiyografi; kalp hızı; miyokard infarktüsü; prognoz; ventrikül disfonksiyonu, sol; ventrikül erken kompleksi/fizyopatoloji.

Heart rate turbulence (HRT) represents a short fluctuation in sinus cycle length after a ventricular premature beat (VPB). Impaired HRT may be encountered in some cardiac conditions including heart failure and has a predictive value in the estimation of mortality and sudden cardiac death.[1] It comprises two distinct phases: turbulence onset (TO) and turbulence slope (TS), which denote early acceleration and late deceleration phases, respectively. Even though the absolute mechanism of HRT has not been established, physiological early acceleration and late deceleration after a VPB may be due to hemodynamic alterations and subsequent autonomic nervous system activation.[2,3]

This study was conducted to compare patients with and without acute left ventricular systolic dysfunction due to acute myocardial infarction with ST-segment elevation, particularly with regard to the HRT parameters (TO and TS) along with basic clinical and echocardiographic parameters.

PATIENTS AND METHODS

Fifty consecutive patients admitted to our center with a diagnosis of acute ST-segment elevation myocardial infarction (STEMI) were included in the study. All cases received thrombolytic therapy on admission and underwent transthoracic echocardiographic (TTE) examination at the 24th hour of hospitalization. On basis of echocardiographic findings, patients were divided into two groups according to whether they had decreased or normal left ventricular ejection fraction (LVEF). Group 1 consisted of 25 patients (mean age 48±9 years) with an LVEF <55%, and group 2 included 25 patients (mean age 52±9 years) with an LVEF ≥55%. Soon after TTE, all the patients underwent 24-hour Holter monitoring.

The two groups were compared with regard to the HRT parameters (TO and TS) along with basic clinical parameters including heart rate, conventional echocardiographic parameters including left ventricular end-diastolic diameter, left atrial diameter, LVEF, and some laboratory parameters including peak serum concentrations of creatine kinase MB and cardiac troponin I.

For determination of accompanying risk factors, hypercholesterolemia was defined as a total plasma cholesterol level of ≥200 mg/dl, or a low-density lipoprotein cholesterol level of ≥130 mg/dl, or the use of cholesterol lowering drugs at the time of the study. Hypertension was defined as the detection of systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg in at least two separate readings, or being on an antihypertensive medication. Smoking was defined as the presence of incessant smoking for at least a year at the time of the study.

Echocardiographic examinations were made using the Vivid 4 System (VingMed, Horten, Norway) with a 3 MHz transducer according to the recommendations[4] of the American Society of Echocardiography. Left ventricular end-diastolic diameter and left atrial diameter were measured via M-mode from the parasternal long-axis view. Left ventricular ejection fraction was measured via the modified Simpson's method. Color Doppler was used for the evaluation of valvular regurgitation. Heart rate was measured just prior to TTE via auscultation. Echocardiographic and clinical parameters were expressed as the mean value obtained from three consecutive measurements.

Parameters of HRT (TO and TS) were obtained from 24-hr Holter recordings. Analysis of HRT was performed on sequences of sinus RR intervals after a VPB, with the sinus rhythm being free from any arrhythmia or artefact just before and after the VPB. Of the two HRT components after a VPB, TO represents the initial acceleration (shortening of RR intervals) and TS represents the subsequent deceleration (prolongation of RR intervals).[5] To calculate TO (%) (normal <0), the difference between the sum of the first two RR intervals after the compensatory pause following a VPB and the sum of the last two RR intervals preceding the VPB is divided by the sum of the last two RR intervals preceding the VPB.[5] Turbulence slope (normal >2.5 ms/RR interval number)[5] was accepted as the steepest regression line between the RR interval count and the duration. The average of HRT values measured for all convenient VPBs were accepted as the final HRT values characterizing the patient. Due to the fact that HRT usually diminishes (less negative TO, lower TS) at higher heart rates, sinus rhythms with heart rates of >80/min before VPB were not taken into account.

The presence of any potential cause of impaired HRT was accepted within the exclusion criteria, including history of congestive heart failure (CHF), moderate or severe degrees of any valvular regurgitation, previous myocardial infarction, diabetes mellitus, and obstructive sleep apnea. Patients with persistent or recurrent ischemic symptoms and signs

Table 1. Clinical and echocardiographic features of patients

	Group 1 (n=25)			Group 2 (n=25)			
	n	%	Mean±SD	n	%	Mean±SD	p
Mean age (years)			48±9			52±9	>0.05
Gender							>0.05
Male	15	60.0		14	56.0		
Female	10	40.8		11	44.0		
Hypercholesterolemia	15	60.0		14	56.0		>0.05
Smoking	14	56.0		13	52.0		>0.05
Hypertension	9	36.0		10	40.0		>0.05
Heart rate before TTE (beat/min)			86±14			85±13	>0.05
Left ventricular end-diastolic diameter (cm)			4.80±0.74			4.72±0.63	>0.05
Left atrial diameter (cm)			3.64±0.48			3.72±0.41	>0.05
Left ventricular ejection fraction (%)			39.1±6.7			57.2±5.3	<0.05
Peak creatine kinase MB (IU/l)			156.5±53.5			152.7±45.3	>0.05
Peak cardiac troponin I (ng/ml)			7.64±4.1			7.49±5.3	>0.05
Turbulence onset (%)			0.74±1.82			-2.35±1.48	<0.05
Turbulence slope (ms/beat)			12.8±6.4			13.6±5.7	>0.05

Group 1: Decreased left ventricular ejection fraction; Group 2: Normal left ventricular ejection fraction; TTE: Transthoracic echocardiography.

including reinfarction after the 24th hour (during Holter recording), those with mechanical complications of STEMI, and those with pacemaker rhythm, atrial fibrillation, left or right bundle branch block on the initial ECG, or having VPB numbers of less than 10 during the 24-hr Holter monitoring were also excluded.

Parametric data were expressed as mean ± standard deviation, and categorical data as percentages. Statistical procedures were performed using the SPSS 10.0 statistical package. Parametric data were compared by the Student's t-test, and categorical data via the chi-square test. A *p* value of less than 0.05 was considered significant.

RESULTS

The two groups did not differ significantly with regard to the general, laboratory, and clinical features (p>0.05; Table 1).

Among the Holter and echocardiographic features, patients in group 1 exhibited a significantly higher mean TO value (0.74±1.82% *vs* -2.35±1.48%, p<0.05) and a significantly lower LVEF value (39.1±6.7% *vs* 57.2±5.3%, p<0.05).

The other Holter and echocardiographic variables did not differ significantly between the two groups (p>0.05). An abnormal TO value (≥0%) was found to have sensitivity and specificity of 88% (p<0.05) in predicting acute left ventricular systolic dysfunction (LVEF<55%) during the peri-infarction period of STEMI.

DISCUSSION

Heart rate turbulence (HRT) is a relatively novel parameter of baroregulatory system and is defined as a short fluctuation in sinus cycle length after a VPB. In normal state, the cardiac response to a VPB is an immediate acceleration (2 to 3 beats) followed by a subsequent deceleration (maximum RR interval by about the 9th to 10th beat) and restoration of the baseline heart rate (before the 20th beat). HRT comprises Two counteracting phases of HRT, TO and TS, normally represent the post VPB acceleration and deceleration in heart rate, respectively. In normal state, a VPB usually causes a rapid fall in systolic and diastolic blood pressure leading to early acceleration (decreased vagal tonus) (TO).[6] This acceleration phase is followed by an increase in blood pressure and subsequent deceleration (TS).[6] Normal TO and TS indicate intact autonomic control and baroregulatory mechanism. Higher baseline heart rates (above 80/min) may result in false positive results (less negative TO and lower TS). Gender has no effect on HRT parameters, whereas TS is generally higher among younger population.[7] The concept of HRT was first introduced by Schmidt et al.[5] who regarded HRT as a predictor of mortality after myocardial infarction. Impaired HRT may also be encountered in CHF and is closely associated with hemodynamic changes, sympathetic system activation, and impaired baroregulatory mechanism.[6] Impaired HRT was found to have a predictive value in CHF with regard to disease progression and fatal

ventricular arrhythmias.[8] Impaired HRT may be encountered in other conditions including diabetes mellitus,[9] essential hypertension,[10] obstructive sleep apnea syndrome,[11] and mitral valve prolapsus[12] probably due to hemodynamic changes and impaired baroregulatory mechanism associated with these conditions.

Patients presenting with CHF due to STEMI have increased risk for death.[13] Early mortality risk in STEMI is generally associated with the extent of myocardial damage, and the consequent hemodynamic compromise[14] leading to CHF. In other terms, systolic dysfunction manifested as reduced LVEF on TTE during the peri-infarction period of STEMI portends poor prognosis.

Left ventricular systolic dysfunction in the early stage of STEMI is generally associated with significant hemodynamic changes including highly elevated left ventricular end-diastolic pressure and reduced peripheral perfusion. These significant hemodynamic changes may result in malfunction of baroregulatory mechanism, which also potentially underlies the concept of impaired HRT. In this study, patients with reduced LVEF were found to have significantly impaired TO values in comparison to those with normal LVEF during the peri-infarction period of STEMI. In addition, an abnormal TO value (≥0) was found to have sensitivity and specificity of 88% p<0.05) in predicting acute left ventricular systolic dysfunction and associated poor prognosis during the peri-infarction period of STEMI.

In conclusion, this study demonstrated significantly impaired TO in patients with STEMI, which was accompanied by acute left ventricular systolic dysfunction detected on TTE during the peri-infarction period. The abnormal TO value (≥0) was also found to have remarkable sensitivity and specificity in the distinction of cases with STEMI associated with left ventricular systolic dysfunction, which is considered a strong indicator of poor prognosis and mortality. Thus, in addition to clinical and echocardiographic findings, impaired TO may be used as a useful predictor of left ventricular systolic dysfunction and poor prognosis in the peri-infarction period of STEMI.

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