RESEARCH ARTICLE

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Convenient Novel Method for Diagnosing Diastolic Dysfunction: Electrocardiographic Diastolic Index

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Abstract

Background and Aim: Left ventricular diastolic dysfunction (LVDD) is the primary pathophysiology in patients with preserved ejection heart failure. Hypertension (HT) results in myocardial structural changes and accelerates the progression to LVDD. Electrocardiographic diastolic index (EDI) calculated from electrocardiogram parameters can provide information about the correlation between hypertrophy of the left ventricle and LVDD. We investigated the predictor of EDI in detecting LVDD in patients followed up with HT.

Materials and Methods: This study included 202 consecutive patients with HT between January 2022 and March 2022. The patients were classified without and with LVDD. The EDI is created as (V5-R amplitude + V1-S amplitude x aVL-R amplitude/PWL-I amplitude). The prediction value of the EDI for LVDD was evaluated by curve analysis of the receiver operating curve. Multivariate and univariate logistic regression analyzes were used to evaluate the free predictors of LVDD. Two multivariate models were used (model I: EDI as a continuous variable and model II: EDI as a categorical variable).

Results: The patients were classified into two groups by showing LVDD. The average age of the study population was 50 ± 14 years, and 57.4% of the patients were female. The patient EDI value was 8.5 ± 7.3. The EDI value of the first group was remarkably lower than that of the second group. When the limit value of EDI is greater than 7.4 mV, it predicts LVDD with 63.6% sensitivity and 79.8% specificity. In univariate logistic regression analysis, the presence of LVDD was associated with EDI. Two different multivariate regression models were constructed to evaluate EDI as both a continuous variable and a categorical variable. EDI was determined as an independent predictor of LVDD in both models.

Conclusion: The EDI is an essential assessment tool in predicting DD in patients who are followed up with HT because it is a cheap, accessible, and easy-to-use formula.

Keywords: Diastolic dysfunction, electrocardiographic diastolic index, hypertension

INTRODUCTION

Diastolic dysfunction (DD) is a relaxation defect of the left ventricular myocardium.[1] It can show a broad clinical course, simple impaired myocardial relaxation to end-stage heart failure (HF).[2] In recent years, it has emerged as an essential factor in the pathogenesis of HF.[3] Left ventricular diastolic dysfunction (LVDD) is the primary pathophysiology in patients with HF with preserved ejection fraction (HFpEF).[4] Recent studies have shown that increased myofilament sensitivity to calcium plays a role in DD, but more molecular and clinical studies are needed.[5]

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Hypertension (HT) is one of the most common chronic diseases in developed countries. Higher blood pressure complications result in myocardial structural changes and accelerate the progression to HF.[6] DD is commonly observed in patients with dysregulated blood pressure.[7] In summary, high blood pressure causes myocardial structural changes and these changes cause DD and subsequently HFpEF. For this reason, DD can be considered an intermediate clinical stage in the progression to HF. Early diagnostic methods can detect the development of DD and slow the progression to HF.

Many patients with DD are asymptomatic before clinical symptoms of HF.[3] Consequently, cost-effective diagnostic methods come to the fore in diagnosing DD. It has been shown that transthoracic echocardiography (TTE) can detect DD in the early stage of HT before the development of left ventricular hypertrophy (LVH).[7] Tissue Doppler examination, which can be performed in TTE, provides information about the left ventricle's early and late relaxation functions and the presence of DD.

Electrocardiogram (ECG) can give information about the relationship between LVH and the presence of DD.[8] The Sokolow-Lyon voltage criterion is used as an ECG parameter to predict HT and related LVH, and DD.[9] However, the relationship between electrocardiographic diastolic index (EDI) and DD has been investigated in recent years.[10] Various studies on the relationship between ECG and DD are under scope because it is both easily accessible and cost-effective in predicting DD.

In this study, we investigated the predictor of EDI in detecting DD in patients followed up with HT.

MATERIALS AND METHODS

The single-center retrospective observational study included 202 consecutive patients with HT who applied to the cardiology policlinic between January 2022 and March 2022. Baseline clinical characteristics and clinical information were recorded. Patients with lower left ventricular ejection fraction (LVEF) than 55%, congenital heart disease, infiltrative cardiomyopathy, coronary artery disease, chronic kidney disease, previous thromboembolic event, presence of valve diseases, bundle branch blocks, atrial fibrillation, bradyarrhythmia, tachyarrhythmia, and missing data in the hospital recording system were excluded from the study. The patients were divided into groups with and without DD by TTE parameters. Baseline characteristics, TTE and ECG findings, and EDI was compared between the two groups.

This study was approved by the University of Health Sciences Turkey, Ankara City Hospital Ethics Committee (number: E1-22-2587, date: 20.04.2022). HT was defined as resting blood pressure above 140/90 mmHg at least twice or current use of antihypertensive medication.

TTE was performed using a Philips EPIQ7 (Philips Healthcare) ultrasound device. LVEF was calculated by the modified Simpson method.[11] E wave, A wave, tissue Doppler annular velocities, and left atrial diameter were recorded with TTE by the American Society of Echocardiography (ASE) guidelines.[12] According to the recommendations of the ASE, segmental wall movements of the left ventricle were evaluated from the apical four-chamber, three-chamber, and two-chamber windows in the left lateral decubitus position. The left ventricular end-diastolic and end-systolic diameters was measured in M mode on parasternal long-axis images. The lateral E-value was determined by tissue Doppler examination.

Standard 12-lead ECG (filter 40 Hz, 25 mm/s, 10 mm/mV) was recorded in all patients. ECGs were scanned at 300 dpi, and all images were magnified 5x. The P wave amplitude in the lead I (PWLI) was measured from the peak of the P wave to the isoelectric line of the TP interval (Figure 1). The amplitude of the R wave in aVL and the Sokolow-Lyon voltage (sum of the amplitudes of the S wave in V1 and the R wave in V5) were calculated (Figure 1). The EDI is expressed as [aVL R amplitude × (V1S amplitude + V5R amplitude)/PWLI amplitude].[10] The EDI values of the patients were calculated by two experienced cardiologists who were unaware of the patients' TTE parameters.

Statistical analysis

The data were analyzed using the SPSS 22.0 Statistical Package Program for Windows (SPSS; IBM, Armonk, New York, USA). A Kolmogorov-Smirnov test was used to assess the normality of distribution. Continuous variables were presented as mean ± standard deviation (normal distribution) or median ± interquartile ranges (without normal distribution) and categorical variables as the number of patients and percentages.

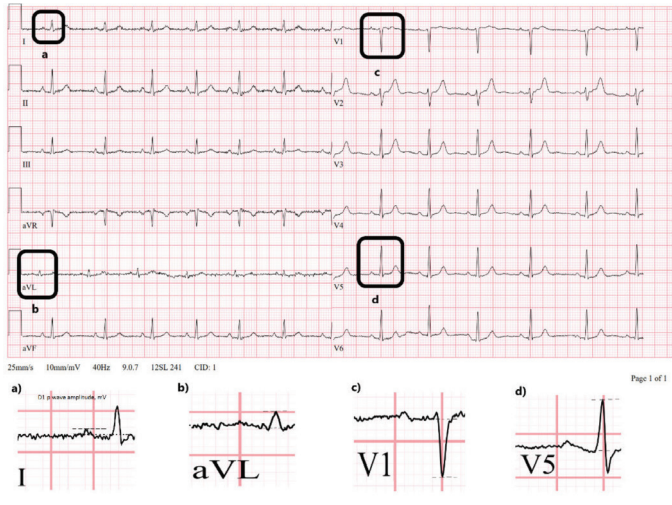

Figure 1: Electrocardiographic parameters of the EDI formula [aVL R amplitude × (V1S amplitude + V5R amplitude)/ P wave amplitude in the lead I amplitude]

A comparison between groups was made with the Student's t-test for normally distributed variables and a Mann-Whitney U test for the variables without a normal distribution. Categorical data from both groups were compared using the χ^2 or Fisher's exact test.

The prediction value of the EDI for LVDD was evaluated by receiver operating curve (ROC) curve analysis and area under the curve (AUC) values. The cutoff value was calculated according to the Youden index. A *P* value lower than 0.05 (using a two-sided test) was considered significant.

Univariate and multivariate logistic regression analyses were used to evaluate the independent predictors of LVDD. Variables displaying $P < 0.05$ in the univariate analysis were used in a multivariate logistic regression analysis. Two multivariate models were used (model I: EDI as a continuous variable and model II: EDI as a categorical variable).

RESULTS

Two hundred two patients followed with a diagnosis of HT were included in the study. Basal characteristics are given in Table 1. The patients were divided into two groups according to the presence of LVDD (105 patients without LVDD, group 1; 97 patients with LVDD, group 2).

The mean age of the study population was 50 ± 14 years, and 57.4% of the patients were female. Patients in group 2 had a higher age ($P = 0.19$), more frequent diabetes diagnosis ($P = 0.023$), and a higher body mass index (BMI) value ($P = 0.005$) compared to group 1. Left ventricular end-diastolic and end-systolic diameter measurements were similar between the two groups. Interventricular septum thickness (IVST) and posterior wall thickness (PWT) were found to be significantly higher in group 2 (respectively; $P < 0.01$, $P = 0.02$). Higher LVEF ($P = 0.032$) and larger left atrial diameter ($P = 0.031$) was found in group 2. Lower E wave (peak early filling velocity during atrial

Table 1: Baseline clinical characteristics, echocardiographic, and electrocardiographic findings of all patients

	All populations (*n*=202)	LVDD (-) (*n*=105)	LVDD (+) (*n*=97)	*P*-value
Age, years	50±14	47±14	53±13	0.019
Male, n (%)	86 (42.6)	35 (33.3)	51 (52.6)	0.007
Female, n (%)	116 (57.4)	70 (66.7)	46 (47.4)	0.007
Diabetes mellitus, n (%)	33 (16.3)	11 (10.5)	22 (22.7)	0.023
Smoking, n (%)	93 (46)	44 (41.9)	49 (50.5)	0.259
BMI, kg/m^2	30±10	28.5±11	32±9	0.005
Echocardiography parameters				
LVEDD, mm	46±3	46±3	46±3	0.124
LVESD, mm	29±4	28±3	29±4	0.051
IVST, mm	1.0±0.2	1.0±0.1	1.1±0.2	<0.001
PWT, mm	1.0±0.1	1.0±0.10	1.0±0.11	0.002
LVEF, %	61±5	62±5	60±3.5	0.032
LA, mm	35±3	35±4	36±4	0.031
E, cm/sn	70 ± 10	80 ± 10	70 ± 10	<0.001
A, cm/sn	60 ± 20	60 ± 10	80 ± 30	<0.001
E/A ratio	1.2±0.5	1.4±0.3	0.9±0.5	<0.001
E' Lateral, cm/sn	10±4	12±2	8±2	<0.001
Electrocardiography parameters				
D1 P wave amplitude, mV	0.1±0.06	0.1±0.04	0.1±0.05	0.181
aVL R amplitude, mV	0.4±0.3	0.3±0.3	0.5±0.3	<0.001
V1S amplitude, mV	0.7±0.3	0.7±0.4	0.7±0.5	0.043
V5R amplitude, mV	1.0±0.6	1.0±0.5	1.1±0.7	0.093
V1S amplitude + V5R amplitude, mV	1.7±0.7	1.7±0.7	2.0±0.9	0.005
EDI	8.5±7.3	5.2±3.7	10.6±8.5	<0.005

Data are presented as mean ± standard deviation for normal distribution or median ± interquartile range for not-distribution normality or n (%).

BMI: Body mass index, LVEDD: Left ventricular end-diastolic dimension, LVESD: Left ventricular end-systolic dimension, IVST: Interventricular septum thickness, PWT: Posterior wall thickness, LVEF: Left ventricular ejection fraction, LA: Left atrial, EDI: Electrocardiographic diastolic index

systole), higher A wave (late peak filling velocity during atrial systole), decreased E/A ratio, and decreased lateral E' wave were observed in group 2 ($P < 0.001$ for all parameters). While there was no significant difference between PWLI and V5R amplitude in both groups, aVR amplitude was higher in group 2 than in group 1 ($P < 0.001$). When V1S and V1S + V5R amplitudes were compared, it was observed that patients in group 2 were significantly higher than those in group 1 (respectively; $P = 0.043$, $P = 0.005$). The EDI value of the patients included in the study was 8.5 ± 7.3. The EDI value in group 2 was significantly higher than that in group 1 ($P < 0.005$).

ROC analysis was performed to test the optimal cut-off value reliability of EDI in group 2. The AUC of EDI in predicting LVDD was found to be 0.773 [95% confidence interval (CI):0.708 - 0.839; $P < 0.001$] (Figure 2). When the cutoff value of the EDI is greater than 7.4 mV, it predicts LVDD with 63.6% sensitivity and 79.8% specificity.

First, the factors affecting the presence of LVDD were examined by univariate logistic regression analysis. In univariate logistic regression analysis, the presence of LVDD was associated with EDI (OR:1,248, 95% CI:1,159-1,345, $P < 0.001$), age [OR:1,025, 95% CI:1,005-1.047), $P = 0.016$], presence of diabetes [OR:2,507, 95% CI:1,144-5,495, $P = 0.022$] and BMI [OR:1,060, 95% CI:1,015-1.106, $P = 0.009$] (Table 2).

Multivariate logistic analysis was used to investigate the effect of significant parameters in univariate logistic regression analysis for predicting the presence of LVDD. Two different models were constructed to evaluate EDI as both a continuous variable and a categorical variable. EDI was determined as an independent predictor of LVDD in both models (Table 3).

DISCUSSION

Our study is an investigation presenting an ECG index to predict DD in patients with HT. This study shows that the EDI formula is a simple and easily applicable tool for DD estimation.

ECG is easier to reach than an echocardiography device. Therefore, more patients can be scanned for DD using the ECG index. According to ECG findings, it can be referred to an advanced center in terms of definitive diagnosis at an earlier stage. In this way, worsening can be prevented by applying the necessary medications in the earlier period.

A higher EDI value was found in patients with LVDD than in those without LVDD. In our study, IVST, and PWT were significantly higher in the LVDD patient group. However, a larger left atrial diameter was found in patients with LVDD. aVL R amplitude was found to be higher in patients with LVDD. A higher EDI value predicted LVDD, and the optimal cutoff value was calculated at 7.4 mV. These results show that changes in cardiac diastolic parameters can be detected in the 12-lead

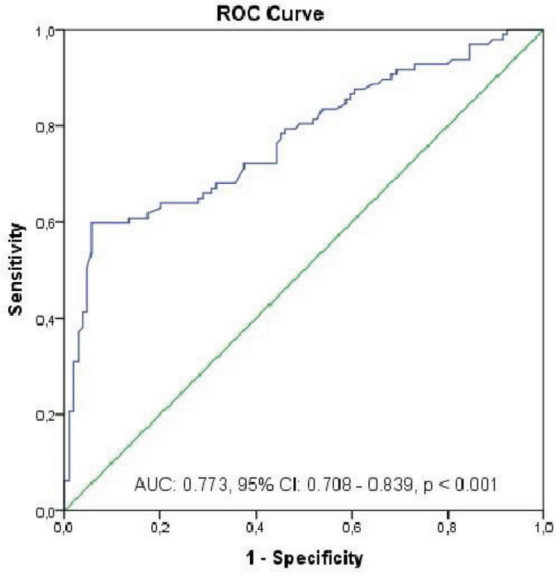

Figure 2: A receiver operating curve (ROC) analysis showed that the optimal cut-off value of the electrocardiographic diastolic index to predict diastolic dysfunction was 7.4 mV with 63.6% sensitivity and 79.8% specificity [area under the curve (AUC) 0.773; 95% confidence interval (CI) 0.708-0.839; $P < 0.001$].

Table 2: Univariate logistic regression analysis for left ventricular diastolic dysfunction

	Odds ratio (95% CI)	*P*-value
EDI	1,248 (1,159-1,345)	<0.001
Age	1,025 (1,005-1,047)	0.016
DM	2,507 (1,144-5,495)	0.022
BMI	1,060 (1,015-1,106)	0.009

CI: Confidence interval, EDI: Electrocardiographic diastolic index, DM: Diabetes mellitus, BMI: Body mass index

Table 3: Multivariate logistic regression analysis for left ventricular diastolic dysfunction

	Odds ratio (95% CI)	*P*-value
Model 1		
EDI	1,253 (1,161-1,352)	<0.001
Age	1,015 (0.986-1,044)	0.322
DM	2,666 (1,071-6,638)	0.035
BMI	1,025 (0.968-1,086)	0.395
Model 2		
EDI >7.4	7,262 (3,771-13,985)	<0.001
Age	1,012 (0.986-1,040)	0.369
DM	2,263 (0.986-1,040)	0.078
BMI	1,033 (0.987-1,091)	0.247

CI: Confidence interval, EDI: Electrocardiographic diastolic index, DM: Diabetes mellitus, BMI: Body mass index

surface ECG in the patient population without coronary artery disease followed by HT.

In conditions of pressure overload owing to systemic HT, the left ventricle undergoes extensive growth, leading to LVH. LVH is seen as an increased voltage on ECG. The excess myocardial collagen present in hypertensive LVH is suggested to result from several alterations. These changes lead to DD and subsequently to HFpEF.[13]

Atrial dilatation reflects atrial remodeling due to HT.[14] ECG changes related to atrial dilatation, such as broad P wave and prolongation of the PR interval, can be observed on surface ECGs.[15] A previous study has shown that the initial P wave in lead V1 was associated with atrial dilatation, confirmed by cardiac magnetic resonance examination.[16] P wave amplitude in D1 constitutes an essential component of EDI to evaluate the relationship between left atrial dilatation and DD.[10] Left ventricular filling restriction and decreased LV function are ventricular structural changes caused by HT.[14,17] These changes can result in increased LVH markers in the ECG.[18] LVH appears to be both a cause and a result of DD in HT patients without coronary artery disease. The Sokolow-Lyon voltage criteria are commonly used in ECG for detecting LVH.[19] Using R amplitude in aVL, a component of the Cornell and Sokolow-Lyon voltage criteria, in the EDI calculation is intended to increase the DD estimation.[10] The research also confirmed the relationship between LVH and DD.[10]

Krepp et al.[8] evaluated the relationship between patients' ECG, TTE, and diastolic functions. They divided the patients into two groups diagnosed with and without DD in TTE. In this study, isovolumetric relaxation time, deceleration time, and the left atrial volume index were also calculated in TTE. ECG examination, Cornell criterion, and Sokolow-Lyon voltage criteria were calculated. In our study, evaluating the components of both criteria in a single formula in the electrocardiographic examination increased the index predictiveness.

Another study divided patients into three equal groups according to their EDI.[10] Baseline features, ECG, and TTE findings were compared in these patient groups. The mean age of the patient population was 62.8 ± 8.9 years, and the female sex ratio was 24.5%. In our study, the mean age was 50 ± 14 years, and the female sex ratio (57.4%) was higher. Our study divided the patients into two groups according to their TTE findings. The relationship between DD and EDI was examined. Hayıroğlu et al.[10] found that the optimal threshold value of EDI was determined as 8.53 mV with a sensitivity of 70% and a specificity of 70%. In our study, this value was determined as 7.4 mV with sensitivity of 63.6% and specificity of 79.8%.

In this study, the EDI value was significantly higher in patients with LVDD, suggesting that ECG can be used as a critical diagnostic parameter in predicting DD.

Study limitations

There are several limitations to our study. First, it is a retrospective and single-center trial. Therefore, it has limited value in terms of generalizability. As this is a retrospective study, the etiology of HFpEF (such as amyloidosis) is not identified as an underlying factor. Using TTE as an imaging modality involves subjective evaluation elements. In addition, TTE measurements can be affected by variables such as respiration and heart rate. However, ECG measurements have limitations in terms of standardization because computerized measurement techniques are not used. More patients are needed to classify DD and to determine its relationship with ECG findings more clearly.

CONCLUSION

EDI is an essential assessment tool in predicting DD in patients who are followed up with HT because it is a cheap, accessible, and easy-to-use formula.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Ankara City Hospital Ethics Committee (number: E1-22-2587, date: 20.04.2022).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.O.Ö., C.Ç., Concept: M.O.Ö., Design: M.O.Ö., O.M., Data Collection or Processing: M.O.Ö., Ö.Ç.K., Analysis or Interpretation: Ö.Ç.K., C.Ç., Literature Search: M.O.Ö., O.M., Writing: M.O.Ö., C.Ç.

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