THE VALIDITY OF ELECTROCARDIOGRAPHIC QTC INTERVAL IN PREDICTING LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN HYPERTENSIVE PATIENTS

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ABSTRACT

Background

The QT interval extends from the onset of the QRS complex to the end of the T wave. Thus, it includes the total duration of ventricular activation and recovery and, in a general sense, reflects the duration of the ventricular action potential. The QT interval on electrocardiography is temporally aligned with diastolic dysfunction.

Objectives

To determine the significance of corrected QT (QTc) interval prolongation in predicting left ventricular diastolic dysfunction in hypertensive patients.

Patients and Methods

A cross-sectional study was conducted in the echocardiography department of SHAR teaching hospital from December 2018 to May 2019, on subjects diagnosed as hypertension; twelve lead electrocardiography was done to obtain QTc using Bazett formula. Echocardiography was performed using M mode, two-dimensional image, pulse wave, and tissue Doppler to calculate left ventricular diastolic dysfunction according to the published guideline.

Results

In this study, 64 patients who have met the inclusion and exclusion criteria were enrolled, 45.3 %(n=29) were male and 54.7 %(n=35) were female. 25 subjects (39.1%) met the criteria of diastolic dysfunction, and 39 subjects (60.9%) had a normal diastolic function. The mean QTc value of the diastolic dysfunction group was 459.2 ± 14.7 ms, while the mean QTc of normal diastolic function group was 402.8 ± 26.4 ms (P-value <0.001). The diagnostic value of the prolonged QTc interval (QTc >450 ms in male and > 460 ms in female) in determining diastolic dysfunction is 68 % sensitivity, 97.4% specificity, 94.4% positive predictive value, 82% negative predictive value and 85.9% accuracy. Among all variables; only ejection fraction (EF)%, echocardiographic LVH, tricuspid regurgitation (TR) velocity, E/e' and left atrial volume index (LAVI) had statistically significant relation to QTc.

Conclusion

Electrocardiographic QTc interval is a simple but useful and accurate measurement for predicting diastolic dysfunction in hypertensive patients providing its high sensitivity and specificity.

Keywords: *Diastolic dysfunction; QTc interval; Hypertension.*

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INTRODUCTION

Diastolic function measurement is a crucial part of the routine evaluation especially in patients with suspected heart failure symptoms and preserved ejection fraction [(1)]. Coordination of left ventricular ejection, relaxation, and structure is the basic requirement for a normal, active process of diastolic function [(2)]. Impairment of left ventricular relaxation, and increased left ventricular chamber stiffness, which increases cardiac filling pressures, is the main perturbation that results in left ventricular diastolic dysfunction [(1)].

Several pathologies, that affect left a ventricular function or produce left ventricular hypertrophy or fibrosis, were known to cause diastolic dysfunction including hypertension, diabetes mellitus, ischemia, myocarditis, toxins, and infiltrative cardiomyopathies [(2)].

Ventricular diastolic dysfunction that is present at rest or induced by stress (from exercise, tachycardia, or hypertension) is a central mechanism in heart failure with a preserved ejection fraction. The main pathophysiological disturbances leading to heart failure with a preserved ejection fraction remains unclear, but traditionally it has been referred to hypertensive left ventricular remodeling [(3)].

In comparison to systolic dysfunction, left ventricular diastolic dysfunction has the same diagnostic and prognostic value [(4)]. Assessment for diastolic dysfunction grade has superior ability than left ventricular ejection fraction for predicting mortality in patients with heart failure [(2)].

The QT interval extends from the onset of the QRS complex to the end of the T wave on the surface electrocardiogram. Thus, it includes the total duration of ventricular depolarization and repolarization [(5)]. It is thought that the corrected QT (QTc) interval on an electrocardiogram is closely correlated with diastolic dysfunction, giving the temporal relation of electrical repolarization and mechanical relaxation in diastole so prolongation of the QTc interval is associated with worsening in diastolic dysfunction [(4)]. Despite the significance of diastolic dysfunction, there is a limited number of studies on the ability of electrocardiography to evaluate the presence or absence of diastolic dysfunction. Also, whether a normal electrocardiogram excludes diastolic dysfunction is unknown [(6)].

Furthermore, this study was conducted to assess the diagnostic value of QTc in predicting left ventricular diastolic dysfunction.

PATIENTS AND METHODS

This is a cross-sectional observational study; it was performed at the echocardiography department of SHAR teaching hospital from December 2018 to May 2019. Hypertensive patients undergoing echocardiography testing for any reason were enrolled in the study.

Patients with bundle branch block, arrhythmias, severe mitral and aortic valve disease, and patients receiving drug that is known to prolong QT interval, and 5-reduced left ventricular ejection fraction (EF < 50%).

We documented the history of diabetes mellitus, ischemic heart disease, hypertension, and its duration, smoking status, medication used, height, weight, BMI, and blood pressure measurement.

Hypertension was defined as systolic BP value ≥140 mmHg and /or diastolic BP value ≥ 90 mmHg according to the published guideline [(7)].

All patients underwent 12-lead electrocardiographic examination using (General Electric MAC 1600 ECG machine, Germany). The electrocardiograms were analyzed by a single reader for calculating QT interval, QTc using Bazett formula, and electrocardiographic criteria for left ventricular hypertrophy. We depend on both the limb and precordial lead voltages, or a combination of the two, to define LV hypertrophy based on Sokolow-Lyon voltages criteria ($SV_1+RV_5 > 3.5$ mV or RaVL > 1.1 mV) [(8)].

QTc intervals of 450 ms and 460 ms are defined as the upper limits of normal for adult men and women, respectively [(5)].

Echocardiography examination was performed using echocardiography (General Electric Vivid E9 with heart probe M5S-D, Canadian ICES-001), all patients underwent M-mode and 2-dimensional echocardiography, mitral inflow pattern using pulse wave Doppler echocardiography and pulse wave tissue Doppler echocardiography of the septal and lateral mitral annulus.

Left ventricular ejection function (LVEF) was calculated using M-mode echocardiography as a difference between end-diastolic volume and end-systolic volume divided by end-diastolic volume. For measuring echocardiographic left ventricular hypertrophy. We used both septal and posterior Left ventricular wall thickness to define left ventricular hypertrophy (mild:1-1.2 cm, moderate:1.3-1.5 cm, severe: ≥1.6 cm for women and mild: 1.1-1.3 cm, moderate: 1.4-1.6 cm, and severe: ≥1.7 cm for men) [9].

Left atrial volume (LAV) measured by biplane area-length method, then LAV indexed to body surface area to calculate left atrial volume index (LAVI) [10].

Diastolic dysfunction was defined when patient has at least three out of the four following criteria: 1- average E/e' >14, 2- septal e'< 7 cm/s or lateral e' velocity < 10 cm/s, 3- TR velocity > 2.8 m/s, 4- LAVI > 34 m/m^2.

For grading diastolic dysfunction based on the mitral inflow pattern, patients with E/A ≤ 0.8 and E velocity ≤ 50 cm/s are considered as grade I diastolic dysfunction, those with E/A ≤ 0.8 and E velocity > 50 cm/s or E/A >0.8 - <2 as grade II diastolic dysfunction, while those with E/A ≥ are regarded as grade III diastolic dysfunction. [1]

After data collection and before data entry and analysis, the questions of the study were coded. Data entry performed via using an excel spreadsheet then the statistical analysis was performed by the SPSS program, version 21. The data presented in tabular forms showing the frequency and relative frequency distribution of different variables Compliance of quantitative random variables with the Gaussian curve. The QTc variable was not normally distributed so when the Mean QTc interval of different groups as Bar chart. P values of 0.05 were used as a cut off point for the significance of statistical tests.

RESULTS

In this study, 64 patients who have met the inclusion and exclusion criteria were enrolled, 45.3%(n=29) were male and 54.7%(n=35) were female. Depending on the new definition of diastolic dysfunction published by the recent American society of echocardiography (ASE) guideline. [1] 25 subjects (39.1%) met the criteria of diastolic dysfunction, and 39 subjects (60.9%) had a normal diastolic function.

The mean QTc value of diastolic dysfunction group was 459.2 ± 14.7 ms, while the mean QTc of normal diastolic function group was 40 2.8 ± 26.4 ms with P value (<0.001), Table1.

The diagnostic value of the prolonged QTc interval (QTc >450 ms in male and > 460 ms in female) in determining diastolic dysfunction is 68 % sensitivity, 97.4% specificity, 94.4% positive predictive value, 82% negative predictive value and 85.9% accuracy, Table 2. There was also a graded increase in the QTc interval with increasing diastolic dysfunction grades with statistically significant value (P-value = < 0.001), Figure 1.

The relation of patients demographics and medical illness to QT c is shown in Table 3, where Age, Gender, Duration of HT, DM, and IHD did not show statistically significant relation to the presence or absence of Prolonged QTc.

The rate of echocardiographic parameters of diastolic dysfunction and electrocardiographic LVH criteria among patients with prolonged and normal QTc is shown below, Where EF%, echocardiographic LVH, TR velocity, E/e' and LAVI had a statistically significant relation to QTc, Table 4.

Table 1. Mean QTc value of the normal diastolic function and diastolic dysfunction group.

QTc/Diastolic dysfunction	QTc Mean ± SD	P-value
Diastolic dysfunction		
Yes	459.2±14.7	< 0.001
No	402.8±26.4	

Table 2. The diagnostic value of the prolonged QTc interval.

QTc/ Diastolic dysfunction		Diastolic dysfunction		Total
		Yes	No	
QTc interval	Prolonged	17	1	18
	Normal	8	38	46
Total		25	39	64
Sensitivity	68.0%			
Specificity	97.4%			
PPV	94.4%			
NPV	82.6%			
Accuracy	85.9%			

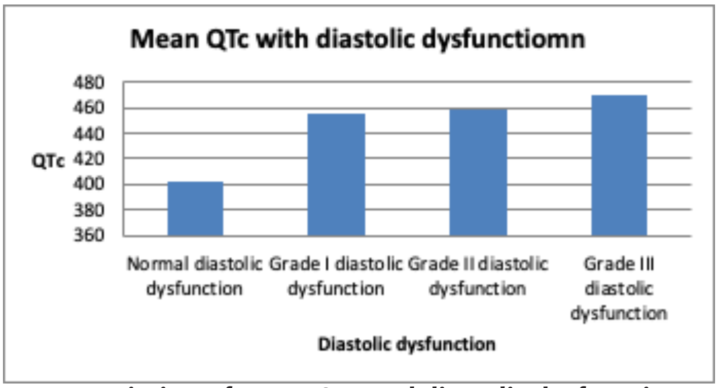

Figure 1. Association of mean QTc and diastolic dysfunction grades (P value = <0.001).

Table 3. The relation of patients demographics and medical illness to QTc interval.

Demographic features and Medical illness		QTc interval		Total	P-value
		Prolonged	Normal		
Age	35 - 45 years	2	9	11	0.48
	46 - 55 years	4	14	18	
	56 - 65 years	7	17	24	
	> 65 years	5	6	11	
Gender	Male	20	9	29	0.64
	Female	26	9	35	
Hypertension duration	1 - 2 years	6	18	24	0.49
	3 - 5 Years	4	10	14	
	6 - 10 Years	6	8	14	
	> 10 years	2	10	12	
DM	Yes	6	10	16	0.34
	No	12	36	48	
IHD	Yes	4	6	10	0.36
	No	14	40	54	
Controlled HT	Yes	6	19	25	0.56
	No	12	27	39	

Table 4. The rate of echocardiographic parameters of diastolic dysfunction and electrocardiographic LVH criteria with QTc interval.

Echocardiographic and ECG findings		QTc interval		Total	P-value
		Prolonged	Normal		
LVH (ECG)	Yes	7	11	18	0.23
	No	11	35	46	
LVH (Echo)	Yes	18	37	55	0.043
	No	0	9	9	
LVH severity	I	9	27	36	0.49
	II	6	7	13	
	III	3	3	6	
TR velocity	Less than 2.8	5	34	39	0.001
	More than 2.8	13	12	25	
EF %	Mean ± SD	62.2 ± 8.1	65.2 ± 3.7		0.045
E wave	Mean ± SD	0.79 ± 0.2	0.71 ± 0.17		0.11
E/A ratio	Mean ± SD	0.94 ± 0.43	0.85 ± 0.27		0.32
Dec T	Mean ± SD	191.1 ± 33.7	211.6 ± 49.0		0.32
Septal e' (m/s)	Mean ± SD	0.09 ± 0.13	0.06 ± 0.02		0.19
Lateral e'(m/s)	Mean ± SD	0.14 ± 0.19	0.08± 0.02		0.06
E /e' ratio	Mean ± SD	17.64 ± 7.35	11.06 ± 5.03		< 0.001
Average e'	Mean ± SD	0.07 ± 0.11	0.07 ± 0.02		0.84
LAVI (ml/m2)	Mean ± SD	45.5 ± 15.36	30.04 ± 10.92		< 0.001

DISCUSSION

Diastolic dysfunction is the result of abnormal myocardial relaxation and left ventricular stiffness during a cardiac cycle and this phase is correlated temporally with the QT interval on the electrocardiography. Little information is available in the literature regarding the association of electrocardiographic QTc interval with echocardiographic diastolic dysfunction. Given the diagnostic and prognostic implications of left ventricular diastolic dysfunction, predicting diastolic dysfunction by measuring electrocardiographic QTc interval may be of paramount importance during daily practice [(4)].

In this study, 64 patients with hypertension who underwent comprehensive doppler and tissue doppler echocardiography, the sensitivity and specificity of electrocardiographic QTc interval in assessing diastolic dysfunction was 68 % and 97.4 % respectively, this is almost comparable to the result obtained by Hamid *et al* [(4)] where sensitivity and specificity of QTc interval in predicting diastolic dysfunction was found out to be 71.11% and 80.83%, respectively. While Wilcox *et al* [(6)] reported the sensitivity and specificity of QTc interval in predicting diastolic dysfunction was 73% and 74%, respectively.

Normal aging is associated with several physiologic alterations in the cardiac function especially slowing of myocardial relaxation which may cause diastolic dysfunction. Therefore, age should be considered when evaluating diastolic function variables [(1)]. In the present study, neither age nor sex was significantly different between non-diastolic and diastolic dysfunction group probably due to small study size, our results also agree with Gunduz *et al* [(11)] who observed no significant differences regarding age and sex in patients with and without diastolic dysfunction.

In interpreting the result of this study, we have detected the mean QTc value of diastolic dysfunction group was 459.2 ± 14.7 ms, while mean QTc of normal diastolic function group was 402.8 ± 26.4 ms with P value (<0.001), this result is similar to study done by Sheila *et al* [(12)] which showed the mean QTc interval in the normal group was 404.5 ms, whereas in the group with diastolic dysfunction was 442.4 ms ($p < 0.001$).

Another study conducted by Wilcox *et al* [6] found that there is a graded increase in QTc interval with increasing diastolic dysfunction grade supporting the result that we have noticed in our study, in which there progressive increase of QTc interval with worsening diastolic dysfunction grade, starting with a mean QTc of (403 ms) in normal diastolic function group to mean QTc of (456 ms) in grade I, mean QTc of (459 ms) in grade II and mean QTc of (469 ms) in grade III diastolic dysfunction (Paper 2).

Among the echocardiographic parameters of diastolic dysfunction, LAVI, E/e' and TR velocity were the parameters shown to have a statistically significant association with the QTc interval, our result match with the study of Sheila *et al* [12] who reported LAVI values and E/e ratio was higher in the group with diastolic dysfunction but did not show TR velocity to be statistically different between non- diastolic and diastolic dysfunction group.

It is important to mention that cut-off point of QTc interval to define as prolonged QTc in our study is much higher than other studies, also, we calculated the diastolic dysfunction according to the recent American society of echocardiography guideline which depends on multiple parameters to signify a patient as diastolic dysfunction, whereas the previous study they relied upon one parameter to stratify a patient as having diastolic dysfunction or not, these might be the reasons why we have got the higher specificity of QTc interval in predicting diastolic dysfunction.

In conclusion, electrocardiographic QTc interval is a simple but useful and accurate measurement for predicting diastolic dysfunction in hypertensive patients providing its high sensitivity and specificity.

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