ORIGINAL ARTICLE

Validity of Electrocardiographic QT Interval in Predicting Left Ventricular Diastolic Dysfunction in Patients with Suspected Heart Failure

Hamid Sharif Khan, Imran Iftikhar and Qaiser Khan

ABSTRACT

Objective: To determine the validity of electrocardiographic QT interval in predicting left ventricular diastolic dysfunction in patients with suspected heart failure using echocardiogram as the gold standard.
Study Design: Cross-sectional validation study.
Place and Duration of Study: AFIC-NIHD, Rawalpindi, from December 2012 to June 2013.
Methodology: Patients with suspected heart failure undergoing 12-lead electrocardiogram and echocardiography were inducted. All electrocardiograms were analyzed by a single trained reader unaware of the echocardiographic findings. QTc interval was calculated according to the published guidelines. All patients underwent a complete M mode, 2 dimensional, Doppler, and tissue Doppler echocardiography using aiE33 ultrasound system and diastolic dysfunction was calculated.
Results: Three hundred patients were studied. Descriptive statistics of age was 61.42 years ±10.43. Of all the patients 218 patients (72.7%) were male and 82 patients were female (27.3%). Mean QT interval (msec) was 427.29 ±54.69. One hundred and eighty patients (60.0%) had diastolic dysfunction and 120 patients (40%) had no diastolic dysfunction. The sensitivity of electrocardiographic QTc interval in predicting diastolic dysfunction was 71.11% and specificity was 88.11%.
Conclusion: Prolonged electrocardiographic QTc interval in patients with suspected heart failure is a useful tool in predicting diastolic dysfunction.

Key Words: *Diastolic dysfunction. Heart failure. QT interval.*

INTRODUCTION

Diastolic heart failure (HF) is a progressive disorder characterized by impaired left ventricular (LV) relaxation, increased LV stiffness, increased interstitial deposition of collagen, and modified extracellular matrix proteins. Diastolic HF, also referred to as HF with normal ejection fraction, currently accounts for 40% to 50% of all HF cases and has a prognosis, which is as ominous as that of systolic HF.[1] It is now apparent that the diagnostic and prognostic significance of left ventricular (LV) diastolic dysfunction (DD) is as important as systolic dysfunction.[2] When diagnosed using the echocardiography, diastolic dysfunction can help diagnose heart failure and is associated with increased all cause mortality.[3] Echocardiography is the standard tool for diagnosing diastolic dysfunction. There are various echocardiographic parameters that help in diagnosing and grading the severity of diastolic dysfunction.[4] The sensitivity and specificity of various echocardiographic parameters in assessing diastolic dysfunction was found to be 95% and 100%, respectively in one study.[5] The role of electrocardiogram in diagnosing and grading severity of diastolic dysfunction is not well understood. However, electrocardiographic findings that can predict diastolic dysfunction on echocardiography are important, giving the diagnostic and prognostic implications of diastolic dysfunction.[6] It is believed that QTc interval on an electrocardiogram is closely associated with diastolic dysfunction, giving the temporal alignment of electrical repolarization and mechanical relaxation in diastole so lengthening in the QTc interval is associated with worsening in diastolic dysfunction. In one study, a prolonged QTc interval (> 435 msec) had a sensitivity of 73% and specificity of 74% in detecting overall diastolic dysfunction.[7]

Electrocardigraphic QT prolongation is not commonly used in assessing diastolic dysfunction and echocardiography is routinely used to asses it. Since echocardiogram is not easily available in all clinical settings and, if available, requires an experienced operator in assessing diastolic dysfunction; the electrocardographic QT interval prolongation, if found valid, would prove to be a valuable tool in diagnosing the diastolic dysfunction in suspected heart failure patients in such clinical settings.

The aim of the study was to assess the validity of electrocardiographic QT interval in assessing the severity of diastolic dysfunction in suspected heart failure patients.

Department of Cardiology, Armed Forces Institute of Cardiology (AFIC), Rawalpindi.

Correspondence: Dr. Hamid Sharif Khan, Department of Cardiology, Armed Forces Institute of Cardiology (AFIC)/ NIHD, Rawalpindi.
E-mail: hamid_sharif10@hotmail.com

Received: February 08, 2015; Accepted: January 26, 2016.

METHODOLOGY

The study was carried out at Armed Forces Institute of Cardiology (AFIC), Rawalpindi, from December 2012 to June 2013. Patients presenting in outpatient department with suspected heart failure and undergoing echocardiography were included in the study.

Chronic heart failure was suspected if the person has at least two typical symptoms and signs of heart failure including breathlessness, fatigue and fluid retention (ankle edema, basal crepts) and presence of at least one risk factor in their medical or social history.[8] QT interval > 435 msec was taken diagnostic of diastolic dysfunction.[9] Diastolic dysfunction was defined as abnormal myocardial relaxation and occurs when the events during diastole are prolonged, slowed, or are incomplete. Cases with Ea (tissue velocity during early diastole) of less than 8 cm/s at the lateral mitral valve annulus were considered to have diastolic dysfunction.[10] The diastolic dysfunction was graded echocardiographically as in Table I.

The study was explained to the patients and informed consent taken. All patients underwent 12-lead electrocardiography using Mortara instrument ELI 250. All electrocardiograms were analyzed by a single trained reader unaware of the echocardiographic findings. QTc interval was calculated according to the published guidelines.[5] All patients underwent a complete M mode, 2-dimensional, Doppler, and tissue Doppler echocardiography using aiE33 ultrasound system (Phillips Medical System, Andover, Massachusetts) and diastolic dysfunction was calculated.

The data was collected on a pre-tested questionnaire by the investigator after taking informed consent from the patients. Each participant was alloted an identification number and confidentiality of the participant was safeguarded. The procedure was conducted by the investigator of the study.

Data was entered and analysed in Statistical Package for Social Sciences (version 10.0). Mean ± S.D for quantitative variables like age and QT interval was calculated. Frequency was calculated as percentages for true positive. A 2 x 2 table was constructed to calculate sensitivity, specificity, positive predictive value (PPV) and negative predicitive value (NPV) keeping echocardiography as the gold standard.

RESULTS

A total of 300 patents were studied. The mean age was 61.42 ±10.43. Of all the patients, 218 patients (72.7%) were male and 82 patients were female (27.3%). Mean QT interval was 427.29 ±54.69 msec.

One hundred and eighty patients (60.0%) had diastolic dysfunction and 120 patients (40%) had no diastolic dysfunction. Of the 180 patients who had diastolic dysfunction, 111 patients (61.6%) had grade I diastolic dysfunction, 37 patients (20.5%) had grade II diastolic dysfunction and 32 patients (17.7%) had grade III diastolic dysfunction.

In ROC analysis, AUC (area under curve) for the electrocardiographic QTc interval was 0.813 ($p < 0.001$). The standard area is 0.025 and 95% Confidence interval between 0.763 and 0.862. A cut off QTc between 414 msec and 418 msec represent sensitivity and specificity close to 80%.

DISCUSSION

Heart failure continues to be a challenge for physicians due to its complex nature, various etiologies, and numerous management and prognostic strategies. Over the past decade, diastolic dysfunction has been more studied and recognized; however, there are few studies comparing various electrocardiographic parameters with degree of diastolic dysfunction in suspected heart failure patients.

Diastolic dysfunction mostly refers to abnormal myocardial relaxation during a cardiac cycle and this phase being represented by the QT interval on the electrocardiography. The QTc interval was compared to the severity of diastolic dysfunction on echocardiography. A few studies in the literature have compared electrocardiographic QTc interval with echocardiographic diastolic dysfunction.[11]

The mean age in this study was more than 50 years, i.e. 61.42 years, which was similar to the one in a study conducted at Karachi Institute of Heart Diseases in 2010.[12] It was predictable as prevalence of diastolic dysfunction increases with age.[13]

The mean QT interval in the study population was found to be 427.29 seconds. Zareba *et al*. had a similar finding of an increased QTc interval in patients of heart failure with diastolic dysfunction.[14] This finding conforms to the

Table I: Grades of diastolic dysfunction.[4]

	Normal (adult)	Delayed relaxation grade 1	Pseudonormal filling grade 2	Restrictive filling grade 3 (reversible to grade 2 with Valsalva manoeuvre) grade 4 (irreversible to grade 2 with Valsalva manoeuvre
E:A	> 1	< 1	1 - 2	> 2
E deceleration time (ms)	220	> 220	150 - 200	< 150
IVRT (ms)	< 220	> 100	60 - 100	< 60
Ea (cm/s) at lateral mitral annulus	> 8	< 8	< 8	< 8

Ea : Tissue velocity during early diastole

fact that prolonged QTc interval signifies abnormal myocardial relaxation in patients of heart failure with diastolic dysfunction.

In a sample of 300 consecutive patients who underwent comprehensive Doppler and tissue Doppler echocardiography for a clinical suspicion of HF, the most significant finding was strong association of prolonged electrocardiographic QTc interval with a reduced septal E' velocity, a marker of abnormal relaxation and DD. The sensitivity and specificity of electrocardiographic QTc interval in assessing diastolic dysfunction was found out to be 71.11% and 80.83%, respectively. Similar results were obtained by Wilcox *et al*. where the sensitivity and specificity of QTc interval in predicting diastolic dysfunction was 73% and 74%, respectively.[15]

Table II: Baseline characteristics of patients.

Characteristic	
Age (years)	61.42 ±10.43
Gender	
Male	218 (72.7%)
Female	82 (27.3%)
QTc interval msec (mean)	427.29 ±54.69
Diastolic dysfunction	180 (60.0%)
Grade I	111 (61.6%)
Grade II	37 (20.5%)
Grade III	32 (17.7%)

Table III: Validity results*.

	Echocardiography positive for diastolic dysfunction (+)	Echocardiography negative for diastolic dysfunction (-)
Electrocardiogram positive for diastolic dysfunction (+)	128 (a)	23 (b)
Electrocardiogram positive for diastolic dysfunction (-)	52 (c)	97 (d)

** adjusted for age, gender, ACE inhibitor use, QRS duration*
Sensitivity : a/a+c x 100 : 128/180 : 71.11%
Specificity :d/d+b x 100 : 87/110 : 80.83%
Accuracy : a+d/a+b+c+d x 100 : 75.00%
Positive Predictive Value (PPV): a/a+b x 100 : 128/151 : 84.76%
Negative Predictive Value : d/c+d x 100 : 97/149 : 65.10%

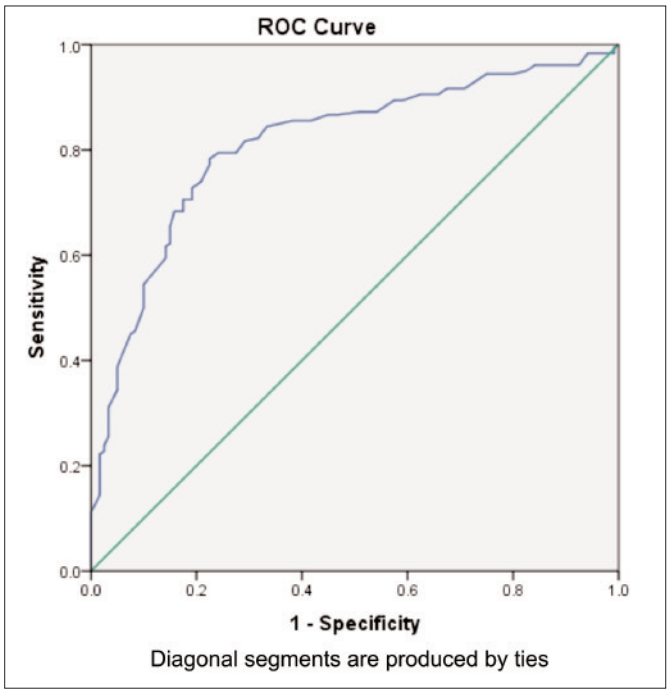

Figure 1: ROC Curve.

The electrocardiographic findings that can predict left ventricular diastolic dysfunction on echocardiography are important, given the diagnostic and prognostic implications of left ventricular diastolic dysfunction.[16,17] Although it is now well recognized that the syndrome of HF with preserved EF is heterogeneous and can result from factors other than diastolic dysfunction.[18-20] The presence of diastolic dysfunction helps distinguish the HF syndrome from other processes, such as pulmonary diseases resulting in dyspnea.[21]

A previous study of patients with hypertension and LV hypertrophy also found a modest correlation between the traditional Doppler parameters of diastolic dysfunction, supporting the association between diastolic dysfunction and QTc.[14] Although none of the patients in this study had a diagnosis of congenital long QT syndrome, a recent study of patients with long QT syndrome found that the tissue Doppler E' was lower in patients with long QT syndrome than in healthy controls. Other studies have also found a link between long QT syndrome and mechanical abnormalities in cardiac contraction and relaxation.[22]

The differentiation between QRS and QTc as electrocardiographic parameters associated with DD merits further discussion. When the QRS duration is prolonged, the association between QTc and E' might be dominated by factors other than prolonged electrical repolarization (e.g., LV intraventricular and interventricular dyssynchrony) causing abnormal LV relaxation and DD. When the QRS is narrow, the association between QTc and E' appears to be a function of prolonged repolarization.

These results should not be taken to indicate that the electrocardiographic QT interval can screen for/or replace comprehensive echocardiography in the evaluation of patients with suspected HF; but the high specificity of the electrocardiographic QTc interval can assist in ruling out diastolic dysfunction in patients of suspected heart failure with a normal ejection fraction, especially when echocardiography is not available. In addition, when interpreting the results of this study, the following limitation should be considered. This study did not include more sophisticated QT-related electrocardiographic measures such as QT dispersion. Nevertheless, the QT interval (as opposed to the QT dispersion) is an electrocardiographic parameter that is readily available and, therefore, more routinely applicable on a clinical basis.

CONCLUSION

With high sensitivity and specificity values, prolonged electrocardiographic QTc interval is a useful diagnostic test in predicting diastolic dysfunction in patients with suspected heart failure.

REFERENCES

1. Lombardo G, D'Amico F. Diastolic heart failure in elderly patients. *J Hypertens* 2010; **28**:e 55.
2. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr* 2009; **22**:107-33.
3. Mogelvang R, Sogaard P, Pedersen SA, Olsen NT, Marott JL, Schnohr P, *et al.* Cardiac dysfunction assessed by echocardiographic tissue Doppler imaging is an independent predictor of mortality in the general population. *Circulation* 2009; **119**: 2679-85.
4. Ho CY. Echocardiographic assesement of diastolic function. In: Solomon SD, editor. Essential echocardiography. New Jersey: *Humana Press*; 2007.p.119-32.
5. Arteaga RB, Hreybe H, Patel D, Landolfo C. Derivation and validation of a diagnostic model for the evaluation of left ventricular filling pressures and diastolic function using mitral annulus tissue Doppler imaging. *Am Heart J* 2008; **155**:924-9.
6. Nishimura RA, Jaber W. Understanding diastolic heart failure: the tip of the iceberg. *J Am Coll Cardiol* 2007; **49**:695-7.
7. Loehr LR, Rosamond WD, Chang PP, Folsom AR, Chambless LE. Heart failure incidence and survival (from the atherosclerosis risk in communities study). *Am J Cardiol* 2008:1016-22.
8. Jolobe O. Evaluation of jugular venous pressure in suspected heart failure: does it matter in 2012. *Br J Hosp Med (Lond)* 2012; **73**:114.
9. Surawicz B, Childers R, Deal BJ, Gettes LS, Bailey JJ, Gorgels A, *et al.* AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. *Circulation* 2009; **119**:e235-40.
10. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, *et al.* Focused update of the ACC/AHA 2005 guidelines for the diagnosis and management of heart failure in adults. *Circulation* 2009; **119**:e391- e479.
11. Haugaa KH, Edvardsen T, Leren TP, Gran JM, Smiseth OA, Amlie JP. Left ventricular mechanical dispersion by tissue Doppler imaging: a novel approach for identifying high-risk individuals with long QT syndrome. *Eur Heart J* 2009; **30**:330-7.
12. Baloch DM , Rasheed SZ, Rajput IA, Samad A. Prevalence of left ventricular diastolic dysfunction in patients with left ventricular hypertrophy. *Pak Heart J* 2010; **43**:20-6.
13. Kane GC, Karon BL, Mahoney DW, Redfield MM, Roger VL, Burnett JC Jr, *et al.* Progression of left ventricular diastolic dysfunction and risk of heart failure. *JAMA* 2011; **306**:856-63.
14. Zareba KM, Shenkham HJ, Bisognano DJ. Comparison of acute electrocardiographic presentations in patients with diastolic vs. systolic heart failure. *Congest Heart Fail* 2009; **15**:165-9.
15. Wilcox JE, Rosenberg J, Vallakati A, Gheorghiade M, Shah SJ. Usefulness of electrocardiographic QT interval to predict left ventricular diastolic dysfunction. *Am J Cardiol* 2011; **108**:1760-6.
16. Redfield MM, Jacobsen SJ, Burnett JC Jr, Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. *JAMA* 2003; **289**: 194-202.
17. Persson H, Lonn E, Edner M, Baruch L, Lang CC, Morton JJ, *et al.* Investigators of the CHARM Echocardiographic Substudy-CHARMES. Diastolic dysfunction in heart failure with preserved systolic function: need for objective evidence: results from the CHARM Echocardiographic Substudy-CH'ARMES. *J Am Coll Cardiol* 2007; **49**:687-94.
18. Bench T, Burkhoff D, O' Connell JB, Costanzo MR, Abraham WT, St John Sutton M, *et al.* Heart failure with normal ejection fraction: consideration of mechanisms other than diastolic dysfunction. *Curr Heart Fail Rep* 2009; **6**:57-64.
19. Sanderson JE, Yip GW. Heart failure with a normal ejection fraction. *BMJ* 2009; **338**:b52.
20. Vrtovec B, Delgado R, Zewail A, Thomas CD, Richartz BM, Radovancevic B. Prolonged QTc interval and high B-type natriuretic peptide levels together predict mortality in patients with advanced heart failure. *Circulation* 2003; **107**:1764-9.
21. Paulus WJ, Carsten TP, Sanderson JE3, Rusconi C, Flachskampf FA, Rademakers FE, *et al.* How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the heart failure and echocardiography associations of the European Society of Cardiology. *Eur Heart J* 2007; **28**: 2539-50.
22. Haugaa KH, Edvardsen T, Leren TP, Gran JM, Smiseth OA, Amlie JP. Left ventricular mechanical dispersion by tissue Doppler imaging: a novel approach for identifying high-risk individuals with long QT syndrome. *Eur Heart J* 2009; **30**: 330-7.