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To Study the Utility of QTc Dispersion in Diabetic Autonomic Neuropathy using Ewing's Parameters

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ABSTRACT

Diabetic autonomic neuropathy (DAN) is the least recognized and understood complications of diabetes despite its significant negative impact on survival and quality of life in people with diabetes. QT dispersion in a routine Electrocardiogram (ECG) is a useful marker to identify Type 2 diabetes mellitus (T2DM) patients with a high mortality risk. Therefore this study was undertaken to assess the prevalence of DAN and the utility of QTc dispersion in the ECG in diabetes patients using Ewing's tests. Two hundred **(**200) diabetic subjects aged between 40 to 70 years were taken for this study. After explaining the purpose and technique of the test they were subjected to a battery of non-invasive autonomic function tests recommended by Ewing. QT interval is measured using Bazett's formula. Early QTcd changes were observed in 56% of the subjects. Gender based results showed significant earlier QTcd changes in both genders. ($p<0.001$) Among the intergroup Normal QTcd changes versus definite changes were more significant in males, whereas early versus definite was more significant in females. Autonomic neuropathy changes were seen indicating strong Corelation between diabetic duration and QTcd. ($p<0.001$) QTc dispersion based on Ewing's test parameters has prognostic importance in T2DM patients with autonomic dysfunction.

Keywords: QTc dispersion, Ewing's tests, Diabetic autonomic neuropathy

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INTRODUCTION

Diabetic autonomic neuropathy (DAN) was defined as an alteration in at least one of the three bedside clinical tests evaluating parasympathetic innervations to the heart, as proposed by Ewing [1]. DAN typically occurs as a system-wide disorder affecting all parts of the autonomic nervous system [2]. Facets of ventricular repolarization, including the length of the QT interval on surface resting electrocardiogram (ECG), are a matter of growing interest because of their potential prognostic significance [3]. There are a large number of physiological factors influencing the duration of the QT interval, including age, sex [4] and, most importantly, heart rate and autonomic nervous system activity [5].

Earlier consensus statements indicate that testing for the prolongation of Bazett's heart rate-corrected QTc interval is easy and specific for diabetic autonomic failure [6]. A lengthening of the QT interval and alteration of the QT dispersion have been reported in patients with diabetic autonomic neuropathy and appear also to have prognostic significance [7]. The relation between a prolonged QT interval and an increased risk of sudden death has been extensively explored in familial long QT syndrome, sudden infant death, and ischemic heart disease, as well as in adults with diabetes mellitus [8, 9] QTc dispersion (QTcd) is not the only diagnostic test, but because of its easy availability and cost effectiveness, as ECG is routinely done we could henceforth make an early diagnosis in these patients who are prone for sudden death. This study was undertaken to evaluate the utility of QTc dispersion in the ECG in T2DM subjects using Ewing's tests.

METHODOLOGY

The study was conducted on Type 2 diabetic mellitus (T2DM) patients at Vijayanagara Institute of Medical Sciences, Bellary attending the Medicine out Patient Department. Two hundred subjects (100 males and 100 females) were taken for this study. Institutional ethical clearance was taken. Diagnosed cases of T2DM aged between 40 to 70 years and free from symptoms of autonomic neuropathy (like Syncope, diarrhea, constipation, abnormal sweating, heat intolerance, urinary disturbances and others) were included in the study group. Patients taking medications/cardiovascular diseases that could influence autonomic nervous function and QT interval were excluded from the study[10]. Purpose and technique of the test was explained to the patients and the following cardiac autonomic function tests were performed after taking written informed consent. They were subjected to a battery of non-invasive autonomic function tests as recommended by Ewing [1].

Ewing's tests

Test	Normal (<60 milliseconds)	Early (60 milliseconds)	Definite (>60 milliseconds)
Resting heart rate	60 - 90 beats/min	90- 100 beats/min	>100 beats/min
Sinus arrhythmia	>= 15 beats/min	11- 14 beats/min	<10 beats/min
Valsalva ratio	>= 1.21	1.11- 1.20	<1.10
QTc dispersion (QTcd)	<60 ms	-	>60 ms

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The patient is asked to rest in supine position for 15 minutes and then 12-lead ECG (CARDIART 108T/MK) recorded QT interval is measured from the onset of the QRS complex to the end of the T wave and corrected to the heart rate using Bazett's formula QTc= QT / (RR interval)$^{1/2}$. QTc dispersion is the difference between the maximum and the minimum QTc in the 12 lead ECG[11].

STATISTICAL ANALYSIS

Fisher's Exact Test used to study the catagorial analysis. T test was used for group wise comparison. Pearson's correlation used to study the relationship between QTcd and variables of Ewing's tests & diabetic duration.

RESULTS

We have studied the QTc dispersion based on Ewing's test parameters in T2DM patients. Total numbers of study subjects were 200 (males-100 and females-100). The Mean age of males and females was 56.16 ± 9.13 and 56.66± 9.767 respectively. The QTcd changes were classified as Normal (<60ms), Early (60ms) and Definitive (>60ms).

Table-1: In 33 subjects QTcd changes were normal. In 112 subjects, early QTcd changes were observed, out of which 98 subjects QTcd < 60 ms and 14 subjects show >60ms which was significant. 55 subjects showed definitive QTcd changes. Results of all three categories were significant. (p<0.001)

Table 1: Distribution of diabetics based on Ewing's test parameters and QTc dispersion

Categories based on Ewing's test (number and % of total diabetics)	QTc dispersion		p-value
	<60 (n=166)	≥60 (n=34)	
Normal (n=33, 16.5%)	33 (19.87%)	00 (0.00%)	<0.001
Early (n=112, 56%)	98 (59.03%)	14 (41.17%)	
Definite (n=55, 27.5%)	35(21.08%)	20 (58.83%)	

Fisher's Exact Test

Table-2 showed gender based distribution of Ewing's tests and QTc dispersion. Results showed varied results in males and females. Earlier QTcd changes were significant in both genders. (p<0.001) Normal and definitive QTcd changes were not significant in both males and females.

Table 2: Gender based distribution of Ewing's test categories and QTc dispersion

Categories based on Ewing's test		QTc dispersion		p-value
		<60	≥60	
Normal	Males (n=13)	13 (100%)	00 (00%)	1.00
	Females (n=20)	20 (100%)	00 (00%)	
Early	Males (n=62)	48 (77.41%)	14 (22.59%)	<0.001
	Females (n=50)	50 (100%)	00 (00%)	
Definite	Males (n=25)	11 (44%)	14 (56%)	0.01
	Females (n=30)	24 (80%)	06 (20%)	

Fisher's Exact Test

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Table-3 shows intergroup comparison of Ewing's tests by't'test. Among the intergroups normal QTcd changes versus definite changes were more significant in males, whereas early versus definite was more significant in females.

Table 3: Comparison of QTc dispersion values between various categories of Ewing's test

	Groups			p-value		
	Normal	Early	Definite	Normal v/s Early	Normal v/s Definite	Early v/s Definite
Males	52.5±4.96	53.29±17.96	67.2±14.9	0.78	<0.001	0.001
Females	49.1±7.44	45.60±7.83	53.77±7.96	0.10	0.04	<0.001

T test

Table-4 shows autonomic neuropathy changes with respect to duration of diabetes. When QTcd was correlated with Ewings parameters and diabetic duration we observed significant correlation between QTcd and sinus arrhythmia. Correlation between diabetic duration and QTcd was highly significant. ($p<0.001$)

Table 4: Pearson's correlation between QTc dispersion and various parameters of Ewing's test & Diabetic duration

Relationship between	r - Values	p – Value	Significance
QTc Vs Resting Heart Rate	-0.099	0.1631	NS
QTc Vs Sinus arrhythmia	-0.16	0.0236	S
QTc Vs Valsalva ratio	-0.1	0.1589	NS
QTc Vs Diabetic duration	0.375	<0.001	HS

r = Pearson's correlation co-efficient.
HS – Highly significant ($p<0.001$)
S – Significant ($p<0.05$)
NS – Not significant ($p>0.05$)

DISCUSSION

Autonomic function tests can detect cardiovascular complications at the early stages of involvement in asymptomatic T2DM patients [2]. Age is associated with myocardial fibrosis and with biochemical changes in the myocardium, resulting in disturbances of repolarisation and prolongation of the QT interval and QTd [12]. In our study subjects were above 50 years showing QTcd changes.

Acute hyperglycaemia produces significant increments of QTc and QTc dispersion in normal subjects Psallas M et al[13]. in their study have shown that T2DM patients have a greater prolongation of the QT interval and greater QTd than do those with T1DM resulting in disturbances of repolarisation and prolongationof the QT interval and QTcd. Our study results were similar. Wei K[14] and his collegues showed that in adult diabetic patients with autonomic dysfunction have increased QTc dispersion suggesting ventricular refractoriness, which may be one of the factors sudden death. Our study result show definitive QTcd changes who may prone for sudden death.

Sex is one of the physiological factor influencing the duration of the QT interval [4]. The mechanism for the steeper QT interval-rate adaptation in women is unclear. The QT

interval is dependent on the summation of several depolarizing and repolarizing ionic currents that contribute to the action potential duration (APD). The amplitude of these ionic currents is influenced by heart rate [15]. In our study definitive QTcd changes were seen in both males and females.

In long-term follow-up by Sawicki [16] and his collegues showed that QT dispersion in a routine ECG is a useful marker to identify T2DM indicating strong correlation between diabetic and QTcd, which was similar to our study.

To conclude, QTcd is one among the diagnostic test in T2DM patients with autonomic dysfunction, as ECG is routinely done investigation which is easy available and cost effective. Therefore an early diagnosis helps in these patients who are prone for sudden death. So further evaluation can to be done by Heart rate variability.(HRV)

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