Relation of Corrected QT Interval Dispersion with Severity of Coronary Artery Disease in patients with Non ST elevation Myocardial Infarction

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Abstract: Objective: Our aim is to study the relation between corrected QT dispersion and severity of coronary artery disease in patients with non ST elevation myocardial infarction. **Patients and methods:** This study was conducted on 60 patients attended at Cardiology department of Al-Azhar University Hospital at the period from January 2017 and august 2017. They were diagnosed as non ST elevation myocardial infarction. And the QT intervals is measured manually in all leads, and heart rate is corrected (QTc) using the Bazett's formula it is square root method obtained by dividing the actual QT interval by the square root of the RR interval (QTc = QT/square root of R-R interval in seconds) then QTc dispersion was assessed from a 12-lead electrocardiogram (ECG) as the difference between the longest and shortest QTc intervals. Then they were subjected to coronary angiography within 72 hours after admission then Syntax Score was calculated by syntax calculator it is a new tool to grade the complexity of coronary artery disease and we do Correlation between QTc dispersion and syntax Score. **Results**: The study included 60 patients. The total number of males in the study was 40(66.67%), and the total number of females was 20 (33.33%). The age has ranged from 47 to 66 years and the mean age was (55.4±4.7) years. The mean of QTc dispersion was (59.65±5.81) m sec. There is significant positive correlation between syntax score and QTc dispersion, p=0.0001. **Conclusion:** QTc dispersion can be used as a simple, accurate and inexpensive tool correlated with the severity of coronary artery disease in patients with acute coronary syndrome. **Recommendation:** Further large scale studies should be carried out to confirm the relationship between QTc dispersion and severity of coronary artery disease. Measurement of QTc dispersion should be done routinely for all patients admitted with acute coronary syndrome.

[Mansour Mohamed Mostafa, Mohammad Moanes Mohammed, Tarek Ahmed Dabash, and Mohamed Hussien Mousa Ahmed. **Relation of Corrected QT Interval Dispersion with Severity of Coronary Artery Disease in patients with Non ST elevation Myocardial Infarction.** *Researcher* 2018;10(7):1-8]. ISSN 1553-9865 (print); ISSN 2163-8950 (online). http://www.sciencepub.net/researcher. 1. doi:10.7537/marsrsj100718.01.

Keywords: Relation; QT; Interval Dispersion; Coronary; Artery Disease; patient; Myocardial Infarction

1. Introduction

ECG remains a highly valuable tool for heart disease management, an ever-increasing number of individuals are being treated for non-ST-elevation acute coronary syndrome. The clinical profile of these patients is highly heterogeneous, and the incidence of events varies widely **(Anderson et al., 1995).**

The QT interval is determined in the electrocardiogram from the beginning of the QRS complex whether it starts with a Q wave or an R wave to the point at which the T wave or the U wave if present returns to the isoelectric line. Thus it includes the duration of ventricular depolarization and repolarization, and corresponds to the action potential duration **(Jimenez-Candil et al., 2008).**

In 34% to 54% of the patients with non-ST-elevation acute coronary syndrome the ST segment shows no evidence of changes upon their arrival at the hospital and the subsequent course is highly variable.This explains the interest in the study of other ECG parameters that could provide additional information that would complement the ST segment analysis such as QRS complex duration, T wave abnormalities or duration of the corrected QT interval **(Jimenez-Candil et al., 2007).**

In a number of epidemiological studies involving theoretically healthy individuals, the ventricular repolarization abnormalities in the Electrocardiogram not only the ST segment deviations but changes in T wave morphology and QT interval prolongation as well have been associated with an increased risk of cardiac death probably because they could be markers of ventricular hypertrophy, left ventricular dysfunction or myocardial ischemia **(Straus et al., 2006).**

Nowinski et al., (2000) explained that the myocardial ischemia occurring during balloon inflation in percutaneous transluminal coronary angioplasty immediately produced changes in ventricular repolarization including a significant prolongation in the QT interval that persisted for

minutes or even hours. These findings suggest the possibility of employing the QT interval as an early marker of acute and transient myocardial ischemia.

Several mechanisms have been proposed to be involved in the prolongation of the QT interval secondary to acute myocardial ischemia changes in the myocardial response to catecholamines or to cholinergic stimulation, perturbation of calcium or potassium ion channels or induction of changes in the intracellular hydrogen concentration **(Cinca et al., 1981).**

Beyond the basic mechanisms clinical interest in this causal relationship is long-standing, and the observation that acute transmural myocardial ischemia prolonged the QT interval and that this increase in the QT interval following Q wave acute myocardial infarction was associated with a significantly higher risk for sudden death **(Straus et al.,2006).**

Values of QTc dispersion vary widely, ranging from 10 to 60 msec in normal subjects. In a review of 8455 healthy control subjects of various ages including healthy children the mean QT dispersion values ranged from 10 to 60 msec **(Malik & Batchvarov 2000).**

One study of 273 patients found that the presence of QT dispersion ≥60 msec immediately after exercise could detect the presence of a significant coronary stenosis with a sensitivity and specificity of 77 and 88 percent in patients who also have significant ST segment depression and 72 and 86 percent in those without ST segment depression **(Koide et al., 2000).**

Various angiographic scoring systems were developed to assess the severity of the coronary artery lesion. Recently SYNTAX has been introduced. The SYNTAX score has been designed to better anticipate the risks of percutaneous or surgical revascularization, taking into account the functional impact of the coronary circulation with all its anatomic components including the presence of bifurcations, total occlusions, thrombus, calcification, and small vessels, by SYNTAX score based on the well-known SYNTAX trial the first to relate QTc dispersion to the severity of coronary artery disease as assessed by SYNTAX score. The main finding of this study was that there is strong positive correlation QTc dispersion and severity of coronary artery disease detected by SYNTAX score **(Sianos et al.,2005).**

Sharafat et al., (2013) who studied the relationship between extent of coronary vessel involvement in acute ST elevated myocardial infarction (STEMI) patients with QT dispersion. They used three different coronary angiographic scores: vessel score, Friesinger score and Leaman score to assess coronary angiographic severity. There was a strong positive correlation between the QT dispersion and vessel, and Friesinger and Leaman coronary angiographic severity scores ($r = 0.75$, $p < 0.001$, $r = 0.79$, $p< 0.001$ and $r = 0.71$, $p < 0.001$ respectively).

Aim of the study:

Our aim was to study the relation between corrected QT dispersion and severity of coronary artery disease in patients with non ST elevation myocardial infarction.

2. Patients and Methods:

This study was conducted on 60 patients attended at Cardiology department of Al-Azhar University Hospital. They were presented by cardiac symptoms (chest pain, dyspnea, etc., acute coronary syndrome). They were subjected to coronary angiography within72 hours after cardiac consultant and ECG findings suggestive acute coronary syndrome. The coronary interventions were done at cardiac catheter unit of Al-Azhar University Hospitals by experienced interventional cardiologist at the period from january 2017 and august 2017.

Inclusion criteria:

• Patients with non -STEMI (positive troponin & ckmb, ST segment depression, chest pain).

Exclusion criteria:

• Patients with significant arrhythmias.
• Patients with bundle branch block.
• Patients with heart failure and myocardial disease.
• Patients with history of perior MI.
• Patients with more than mild valvular heart disease.
• Patients with renal failure or hepatic failure.
•Patients taking drugs known to prolong the QT interval (quinidine, Procainamide, disopyramide, ibutilide, dofetilide, sotalol and amiodaron).

Methods:

All patients were subjected to the following:

(A) Acquisition of written consent of agreement of participation.

(B) Personal data collection, demographic and risk factors assay.

• Hypertension (systolic pressure >140 mm Hg or diastolic pressure >90 mm Hg) **(Andrews et al., 2000).**
• Obesity (body mass index >30kg/m2) **(Antoniucci et al., 2003).**
• Diabetes Mellitus is a general term for heterogeneous disturbances of metabolism for which the main finding is chronic hyperglycaemia (HbA1c ≥ 6.5 % or Fasting plasma glucose ≥ 126 mg/dl) **(Kerner and Brücke., 2014).**

(C) Electrocardiography:

The standard 12-lead electrocardiogram (ECG) is routinely recorded at a paper speed of 25 mm/s and standardization of 10mm/1mv ECG tracings of good quality, then by using magnifying lens the QT

intervals is measured manually in all leads, and heart rate is corrected (QTc) using the Bazett's formula it is square root method obtained by dividing the actual QT interval by the square root of the RR interval (QTc = QT/square root of R-R interval in seconds) **(Draft.,2002).**

The QTcdispersion is measured as the difference between longest and shortest QTc intervals in any of the 12 ECG leads So QTc dispersion = QTc maximum - QTc minimum **(Panicker et al.,2014).**

Values of QTc dispersion vary widely, ranging from 10 to 60 msec in normal subjects **(Malik & Batchvarov 2000).**

(D) Laboratory assessment:

- Cardiac enzyme: (Troponin I, CK MB).
- Kidney and Liver functions.

(E) Echocardiography:

LVESD defined as the frame after aortic valve closure or the frame in whichthe cardiac dimension or volume is smallest **(Lang., et al 2005).**

LVEDD defined as the first frame after mitral valve closure or the frame in the cardiac cycle in which the respective LVdimension or volume measurement is the largest **(Lang., et al 2006).**

LV systolic function should be routinely assessed using 2DE or 3DE by calculating EF from EDV and ESV. LV EFs of <52% for men and <54% for women are suggestive of abnormal LV systolic function EF is calculated from EDV and ESV estimates, using the following formula: EF = (EDV –ESV)/EDV **(Kocabay., et al 2014).**

(f) Cardiac Catheterization:

Coronary angiograms is assessed by an experienced interventional cardiologist and each major coronary artery is inspected for significant lesions. Significant coronary artery disease is defined as ≥70 % diameter stenosis in any coronary artery. It's important to always obtain at least to perpendicular views of each coronary artery lesion. Severity of a lesion is based on percent diameter stenosis compared with a normal reference segment. Lesions are generally classified as sever if 70% or more in the LAD, LCX and RCA or 50% in the left main artery **(Levine., et al 2011).**

(g) SYNTAX Score:

Syntax Score was calculated by syntax calculator. Various angiographic scoring systems were developed to assess the severity of the coronary artery lesion. Recently SYNTAX has been introduced. The SYNTAX score has been designed to better anticipate the risks of percutaneous or surgical revascularization, taking into account the functional impact of the coronary circulation with all its anatomic components including the presence of bifurcations, total occlusions, thrombus, calcification, and small vessels According to SYNTAX score, Low score (0–22), Intermediate score (23–32), and High score (≥33). Then a correlation between QTc dispersion and SYNTAX score was done **(Sianos., et al 2005).**

3. Results:

The study was conducted in Al-Azhar University, from january 2017 to august 2017. The study included 60 patients who underwent to coronary angiography with in 72 hour and after cardiac consultant and ECG findings suggestive acute coronary syndrome.

Age distribution:

The age has ranged from 47 to 66 years and the mean age was (55.4±4.7) years.

Gender distribution:

The total number of males in the study was 40(66.67%), and the total number of female was 20(33.33%).

Table (1) Demography of studied population:

Variable	Mean	SD	Median
Age	55.4	4.724	55
		N	%
Sex	Female	20	33.33
	Male	40	66.67

Co-morbidities:

The majority of patients had 2 comorbidity together (53.3%), while 25% and 20% of patients had 3 and 1 comorbidity respectively, finally only one patients had no comorbidity. 65% was diabetic, 88.3% with hypertension and 48.3% was obese.

Table (2) Classification of Patients according to Co-morbidities:

Comorbidity		N=60	%
DM	Negative	21	35
	Positive	39	65
HTN	Negative	7	11.67
	Positive	53	88.33
Obesity	Negative	31	51.67
	Positive	29	48.33
No. of comorbidity	0	1	1.67
	1	12	20
	2	32	53.33
	3	15	25

Echo finding:

The mean EF% was 64% with SD about 2%, the mean LVEDD and LVESD was (4.37±0.55) and (2.83±0.39) cm respectively.

Table (3) Echo finding:

Variable	Mean	SD	Median
E F%	0.64	0.02	0.65

LVEDD	**4.37**	**0.55**	**4.5**
LVESD	**2.83**	**0.39**	**3**

ECG Finding:

The mean of long QTc, short QTc and QTc dispersion was (431.53±11.73), (371.98±8.76) and (59.65±5.81) m sec respectively, with normal HR 72.3 beat/min.

Table (4) ECG Finding:

Variable	Mean	SD	Median
Long QTc	**431.53**	**11.73**	**430**
Short QTc	**371.98**	**8.76**	**373.5**
QTcdisp	**59.65**	**5.81**	**60**
H R	**72.32**	**9.62**	**70**

Coronary angiography finding:

1- The minimum lesion of coronary blood vessels was one and the maximum was 3 with median 1.

2- The majority of patients had LAD obstruction (68.3%), followed by LCX obstruction (53.3%), the lowest percent for PL (10%), RCA (6.6%) and PDA (5%).

Table (5) Minimum lesion and Maximum lesion:

Vessels No.	Median	Minimum	Maximum
	1	**1**	**3**

Table (6) Vessels affected:

Vessels affected	N/60 total	%
RCA	**4**	**6.67**
PL	**6**	**10**
PDA	**3**	**5**
LCX	**32**	**53.33**
LAD	**41**	**68.33**

3- The obstructed division in RCA, PL and PDA was the proximal segments, while LCX obstruction happened in promimal, distal and obtuse margine 1 and LAD; obstruction happened in proximal, Mid and distal segments.

Table (7) Site of vessels affected:

Site of vessels affected		N	%
RCA	**Non sig.**	**2**	**3.33**
	Proximal	**2**	**3.33**
PL	**Proximal**	**6**	**10**
PDA	**Proximal**	**3**	**5**
LCX	**Non sig.**	**3**	**5.26**
	Proximal	**15**	**26.31**
	Distal	**3**	**5.26**
	O M 1	**11**	**19.3**
LAD	**Non sig.**	**12**	**20**
	Proximal	**19**	**31.67**
	Distal	**2**	**3.33**
	Mid	**8**	**13.33**

4- The degree of obstruction varies from non sig. (30%) up to 80% in certain tributaries

Table (8) Degree of obstruction:

Degree of obstruction		N	%
RCA	**50%**	**2**	**3.33**
	70%	**2**	**3.33**
PL	**70%**	**5**	**8.33**
	80%	**1**	**1.67**
PDA	**70%**	**2**	**3.33**
	80%	**1**	**1.67**
LCX	**30%**	**3**	**5**
	70%	**18**	**30**
	80%	**11**	**18.33**
LAD	**30%**	**12**	**20**
	70%	**19**	**31.67**
	80%	**10**	**16.67**

Effect of gender on QTc dispersion:

No significant statistical difference between male and female group as regarding QTc dispersion; p=0.5

Table (9) Effect of gender on QTc dispersion:

QTcdisp		N	Mean	SD	F	P
Sex	Female	20	58.9	6.4	0.5	0.5
	Male	40	60.02	5.5		

Effect of co morbidity on QTc dispersion;

There were no effect of comorbidity in QTc dispersion whatever the number of co morbidity was, or type of co morbidity (DM, HTN and obesity), p=0.4, 0.6, 0.9 and 0.6 respectively.

Table (10) Effect of co morbidity on QTc dispersion:

QTcdisp		N	Mean	SD	F	P
No. of co- morbidity	0	1	66	*	0.9	0.4
	1	12	59	6.1		
	2	32	58.9	6.1		
	3	15	61.2	4.8		
DM	Negative	21	59.2	6.3	0.2	0.6
	Positive	39	59.8	5.5		
HTN	Negative	7	59.8	5.5	0.01	0.9
	Positive	53	59.6	5.8		
Obesity	Negative	31	59.3	6.1	0.2	0.6
	Positive	29	60	5.5		

Correlation between QTc dispersion and Echo finding:

There was a significant negative relationship between EF% and QTc dispersion, while no significant correlation between QTc and other echo parameters (LVEDD and LVESD), p= 0.02, 0.3 and 0.9 respectively.

Table (11) Correlation between QTc dispersion and Echo finding:

Echo. Finding	QTc disp.	
EF%	r	-0.29
	p	0.02
LVEDD	r	-0.13
	p	0.3
LVESD	r	-0.009
	p	0.94

Correlation between QTc dispersion and SYNTAX Score

Significant positive correlation between syntax score and QTc dispersion, p=0.0001.

Table (12) Correlation between QTc dispersion and syntax score:

	QTc dispersion	
syntax score	r	0.896
	p	0.0001

4. Discussion:

ECG remains a highly valuable tool for heart disease management. Corrected QT interval dispersion is a useful ECG parameter to assess prognosis in ischemic heart disease and specifically acute coronary syndrome. Understanding QT interval physiopathology helps assess importance of QT measurement in this context. Dispersion of the QT interval is defined as the difference between the longest and the shortest QT interval in all electrocardiographic leads, which may be possibly measured. That parameter electrocardiographically, translates the asynchrony of repolarization of ventricular myocardial rows **(Antzelevitch et al., 1996).**

The present study was conducted at Al-Azhar University, from January 2017 to august 2017. The study included 60 patients who underwent coronary angiography within 72 hour from onset of acute coronary syndrome who was admitted to the Cardiac care unit of Al-Azhar University Hospitals in Cairo. The aim of this study was to determine the prognostic value of prolongation of the corrected QT (CTc) interval in patients with acute coronary syndrome.

In our study There was a significant negative relationship between EF% and QTc dispersion, while no significant correlation between QTc and other echo parameters (LVEDD and LVESD), p= 0.02, 0.3 and 0.9 respectively.

There were significant statistical difference between the patients with single, duple and triple vessels disease as regarding QTc dispersion, p<0.0001. ther was a Strong positive correlation between the number of vessels affected and the QTc dispersion, p<0.0001

Our results coincides with the result of a Study published in Egyptian heart journal by Hatem et al. in January, 2017. They were the first to relate QTc dispersion to the severity of coronary artery disease as assessed by SYNTAX score. The main finding of that study was that there is strong positive correlation between QTc dispersion and severity of coronary artery disease detected by SYNTAX score. They chose to use 60 ms as a cut off value to divide their study population into two groups. They didn't state that 60 ms is the cut off for prolonged QTc rather being an arbitrary value to subdivide their study population into two groups for statistical purpose. This value was derived from previous studies such as Yunus et al. 5 and Sharafat et al. **(Hatem et al.,2017).**

Moreover, in correlation studies, they used QTc as a continuous variable. The present study was concordant with Sharafat et al. who studied the relationship between extent of coronary vessel involvement in acute myocardial infarction patients with QT dispersion. They used three different coronary angiographic scores: vessel score, Friesinger score and Leaman score to assess coronary angiographic severity. There was a strong positive correlation between the QT dispersion and vessel, and Friesinger and Leaman coronary angiographic severity scores ($r = 0.75$, $p< 0.001$, $r =0.79$, $p< 0.001$ and $r =0.71$, $p <0.001$ respectively). **(Sharafat et al., 2013).**

The present study was also concordant with Choi et al. who studied the change of QT dispersion after percutaneous transluminal coronary angioplasty (PTCA) in angina patients, in which they investigated the short-term effect of PTCA on QT dispersion in patients with coronary artery disease and no history of previous myocardial infarction. They found that QT dispersion decreases in patients with no history of myocardial infarction at 1 month following successful PTCA. This suggests that PTCA facilitates a favorable recovery from inhomogeneous repolarization due to myocardial ischemia **(Choi et al., 1998).**

Tikiz, et al., (2001) studied QT dispersion in single coronary artery disease and the relation between QT dispersion and diseased coronary artery or lesion localization. They observed that patients with single vessel disease had wider QT dispersion at baseline, which further increased significantly with exercise. This finding supported the idea that severity of localized ischemia rather than extent of coronary artery disease would be expected to have a greater effect on inducible QT dispersion.

On the other hand among patients with three vessel coronary artery disease, Stierle, studied the relation between QT dispersion and the extent of myocardial ischemia. They found a relationship between QT dispersion and the extent of myocardial ischemia in patients with three vessel coronary artery diseases. They stated that in patients with coronary artery disease, QT dispersion increased during peak ischemic stress, while it remains almost unchanged in patients with normal coronary arteries **(Stierle et al., 1998).**

Yilmaz et al. (2006) reported that by using Gensini score, an association of QT dispersion and QT dispersion ratio with extent and severity of coronary artery disease. In their study the more extent and severe coronary artery disease was related to higher QT dispersion.

Yunus et al. (1997) found that QT interval dispersion decreases after successful coronary artery revascularization and increases with restenosis. Therefore, QT interval dispersion may be a marker of recurrent ischemia due to restenosis after PTCA.

Moreover, QTc dispersion was correlated with ST segment resolution after coronary revascularization. It was stated that myocardial reperfusion improves electrical stability and reduces repolarization heterogeneity. Recovery of myocardial electrical homogeneity is not immediate and begins 24 h after revascularization as assessed by QTc and QT dispersion. **(Hamza et al., 2014).**

Polychronis., (1999) studied the effects of ischemia on QT dispersion during spontaneous anginal episodes. He found that QT dispersion is significantly increased during spontaneous angina in patients with documented coronary artery disease and history of previous myocardial infarction. Also QT dispersion was significantly higher during the anginal episode compared to the painless conditions.

Conclusion:

QTc dispersion can be used as a simple, accurate and inexpensive tool correlated with the severity of coronary artery disease in patients with acute coronary syndrome.

Recommendation:

Further large scale studies should be carried out to confirm the relationship between QTc dispersion and severity of coronary artery disease. Measurement of QTc dispersion should be done routinely for all patients admitted with acute coronary syndrome.

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7/3/2018