# "ASSOCIATION OF QTc DISPERSION WITH CORONARY ANGIOGRAPHIC SEVERITY IN PATIENTS OF CHRONIC CORONARY SYNDROMES"

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#### **Introduction:**

Coronary artery disease (CAD) is a major health concern globally, with a particularly high burden in South Asian countries like Bangladesh. Patients with suspected or established chronic coronary syndromes (CCS) are: (i) patients with suspected CAD and 'stable' angina symptoms, and/or dyspnea; (ii) patients with new onset of heart failure (HF) or left ventricular (LV) dysfunction and suspected CAD; (iii) asymptomatic and symptomatic patients with stabilized symptoms < 1 year after an ACS or patients with recent revascularization (iv) asymptomatic and symptomatic patients with stabilized symptoms >1 year after initial diagnosis or revascularization; (v) patients with angina and suspected vasospastic or microvascular disease; and (vi) asymptomatic subjects in whom CAD is detected at screening[1]. The prevalence of chronic stable angina (CSA) in Bangladesh has been reported to be 25.9% [2]. However, Bangladesh is a small country with vast population and CAD is becoming a significant burden on health care services in Bangladesh as well with a high mortality [3]. The South Asian countries of India, Pakistan, Bangladesh, Sri Lanka and Nepal contribute the highest proportion of the burden of Cardiovascular Diseases (CVDs) compared to any other region globally [4-6].ECG has been widely used for cardiovascular risk assessment for long as one of the recent explanations for the development of life threatening ventricular arrhythmias. Determination of the QT dispersion by means of a standard ECG at rest is a marker of diagnosis of CAD [7]. The 12-lead electrocardiogram (ECG) is the most readily available noninvasive test for the detection of cardiac disease [8]. The inter-lead difference in QT intervals assessed from the standard ECG may provide a measure of ventricular repolarization inhomogeneity [9]. QT dispersion (QTD), defined as the difference between the longest and the shortest QT interval on the standard 12-lead electrocardiogram (ECG). This non-invasive marker of predisposition to life-threatening arrhythmias has been reported to have prognostic significance for predicting sudden death not only in postmyocardial infarction patients but in patients with other forms of coronary artery disease [10]. Myocardial regional ischemia may be associated with abnormalities of cardiac repolarization. QT interval dispersion (QTd) has emerged as a noninvasive

measurement for quantifying the degree of myocardial repolarization inhomogeneity. Inter-lead variations in QT interval reflect regional variations in ventricular repolarization and increased dispersion of ventricular recovery time provide a substrate that supports serious ventricular arrhythmias [11]. Corrected QT interval (QTc) is the duration of this parameter, adjusted for heart rate. The dispersion of corrected QT-interval (QTdc) measures severity of coronary artery damage. Higher QTdc is also related to complications such as malignant ventricular arrhythmias. QT dispersion and QTc dispersion is related to high mortality and poor functional outcomes in stroke patients also [12, 13]. The gold standard for the diagnosis and characterization of CAD is coronary angiography (CAG). CAG helps in diagnosis of heterogeneity of the composition, distribution, and location of atherosclerotic plaque within the coronary arteries and also help predict procedural outcome and complications of the disease [14]. Angiographic scoring systems were developed to assess the severity the coronary artery lesion, such as Gensini score. Gensini score is a widely used angiographic scoring system for quantifying the severity of CAD, and was first described in 1975 by Goffredo G. Gensini. The GS has been developed to characterize the complexity of CAD taking into consideration 3 main parameters for each coronary lesion: severity score, region multiplying factor and collateral adjustment factor. The severity score for each lesion may range from 1 to 32. Thus, it is a widely used and more meaningful measurement tool of the severity of CAD for the cardiologists [15]. Therefore, QTc dispersion can be used as a simple, accurate and inexpensive tool correlated with the angiographic severity of coronary artery disease. Chronic coronary syndromes related myocardial ischemia could change QT interval regionally in the area of ischemia and give rise to an increase in QTc dispersion in the 12-lead ECG, and these changes are related to extent and severity of coronary atherosclerosis, usually proven with coronary angiography [11]. In Bangladesh, there are little study available regarding the relation of QTc dispersion and coronary angiography. Therefore, this study was designed to assess the association of QTc dispersion with coronary angiographic severity in patients of chronic coronary syndromes.

Methodology

This study employed a cross-sectional analytical design to evaluate the association

between QTc dispersion and the severity of coronary artery disease (CAD) among

patients with chronic coronary syndromes (CCS) who underwent coronary

angiography at Sir Salimullah Medical College Mitford Hospital, Dhaka, from

November 2020 to October 2021.

**Study Population and Sampling** 

Study Population: All patients with CCS who underwent coronary angiography

during the study period were considered.

**Sampling:** A purposive sample of 92 patients meeting the inclusion criteria was

recruited.

**Inclusion and Exclusion Criteria** 

• **Inclusion criteria:** Patients aged >18 years with CCS undergoing coronary

angiography.

• Exclusion criteria: Acute coronary syndrome, congenital long QT syndrome,

atrial fibrillation, bundle-branch blocks, intra-ventricular conduction defects,

atrio-ventricular block, sinus node dysfunction, pacemaker, cardiomyopathy,

congestive heart failure, history of myocardial infarction, coronary artery

bypass surgery, coronary angioplasty, electrolyte imbalance, and use of QT

prolonging medications.

**Data Collection** 

After obtaining ethical approval, eligible patients provided written informed consent.

Demographic, clinical, ECG, and laboratory data were collected using a structured

questionnaire. A 12-lead ECG was obtained to calculate QTc dispersion. Coronary

angiography was performed to assess the presence and severity of CAD using the

Gensini score.

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#### **Variables**

• **Demographic:** Age, gender, family history of CAD

• Clinical: Risk factors for CAD (diabetes mellitus, hypertension, dyslipidemia, smoking)

• ECG: QTc dispersion

• Laboratory: Random blood sugar, serum creatinine, serum electrolytes, lipid profile

• Outcome: Presence and severity of CAD (angiographic evaluation and Gensini score)

#### **Data Analysis**

Data were analyzed using SPSS version 22.0. Descriptive statistics were used to summarize data. Student's t-test and chi-square test were employed for comparing continuous and categorical variables, respectively. Univariate and multivariate linear regression analysis determined the association between risk factors and QTc dispersion, and the severity of CAD. A p-value <0.05 was considered statistically significant.

**Ethical Considerations:** Ethical clearance was obtained, and strict confidentiality was maintained throughout the study.

#### **Results:**

In the study, 92 patients of chronic coronary syndromes were included among whom 46 patients with normal QT<sub>C</sub> dispersion (<50 ms) named as group A and rest 46 patients with increased QT<sub>C</sub> dispersion ( $\ge$ 50 ms) named as group B. Majority participants of chronic coronary syndromes were in 51-60 years of age (45.6%) followed by 41-50 years of age (30.4%). Mean age in group B was higher (55.22 $\pm$ 8.50 years) than group A (52.58 $\pm$ 10.05 years) patients (p=0.233). Majority participants in group B were male (87.0%) while female was predominant in group A (52.2%) patients. The study was statistically significant (p<0.001). Regarding risk factors, positive family history of CAD, dyslipidemia and smoking was significantly more among group B patients than group A (p<0.05). Regarding investigation profile,

mean values of total cholesterol, LDL and TG was significantly higher in group B patients (p<0.001)

**Table 1: Sample Characteristics: (n=92)** 

	Group A	Group B	Total	
Age group	(n=46)	(n=46)	(n=92)	p value
	frequency (%)	frequency (%)	frequency (%)	
≤40 years	5 (10.9%)	4 (8.7%)	9 (9.8%)	
41-50 years	18 (39.1%)	10 (21.7%)	28 (30.4%)	
51-60 years	16 (34.8%)	26 (56.5%)	42 (45.6%)	0.391*
61-70 years	5 (10.9%)	5 (10.9%)	10 (10.9%)	
>70 years	2 (4.3%)	1 (2.2%)	3 (3.3%)	
Mean±SD (years)	52.58±10.05	55.22±8.50	53.90±9.34	†0.233
Gender				
Male	47.8%	87%		
Female	52.2%	13%		
Risk Factors				
Family history of CAD	14 (30.4%)	31 (67.4%)	45 (48.9%)	0.002
Diabetes mellitus	14 (30.4%)	18 (39.1%)	32 (34.8%)	0.458
Hypertension	27 (58.7%)	33 (71.7%)	60 (65.2%)	0.216
Dyslipidemia	12 (26.0%)	29 (63.0%)	41 (44.6%)	0.002
Smoking	17 (36.9%)	33 (71.7%)	39 (54.2%)	0.002
investigation profile				

RBS, mmol/L	7.81±3.28	7.25±2.69	7.53±2.99	0.432
<b>Serum creatinine,</b> mg/dL	1.05±0.27	1.05±0.31	1.05±0.29	0.961
<b>Total Cholesterol,</b> mg/dL	156.94±30.41	202.72±37.01	179.83±40.77	<0.001
<b>LDL</b> , mg/dL	106.89±27.01	138.72±34.24	122.81±34.56	<0.001
<b>HDL</b> , mg/dL	36.83±1.88	38.97±10.41	37.90±7.50	0.229
TG, mg/dL	141.67±13.78	187.61±62.81	164.64±50.73	<0.001

<sup>\*</sup>p value measured by chi-square test,†p value measured by independent sample's t-test

Electrocardiographic results of the group A and B are shown in the above table. There were no significant differences in RR interval. QT maximum, QT<sub>C</sub> maximum were significantly higher in group B than group A (p<0.05). QT minimum and QT<sub>C</sub> minimum were higher in group A significantly (p<0.05). QT<sub>C</sub> dispersion were higher among group B patients which was highly significant (p<0.001).

**Table II: Electrocardiographic measurements of the study population (n=92)** 

	Group A	Group B	
Variables	(n=46)	(n=46)	p value*
	mean±SD	mean±SD	
RR interval (ms)	830.56±104.80	818.89±130.23	0.677
QT maximum (ms)	356.67±39.57	384.44±35.17	0.002
QT <sub>C</sub> maximum (ms)	394.28±43.38	427.81±41.25	0.001
QT minimum (ms)	323.06±36.63	300.83±30.08	0.006
QT <sub>C</sub> minimum (ms)	356.86±40.54	335.67±36.70	0.023

QT <sub>C</sub> dispersion (ms)	$37.42\pm10.31$	$92.28\pm20.78$	< 0.001

#### \*p value measured by independent student t test.

Patients in group B had significantly higher evidence of different extent of coronary artery stenosis. Double and triple vessel disease and left main stenosis were significantly more prevalent among group B patients (p<0.05).

Table III: Extent of vessel involvement among study population (n=92)

Vessel involvement	Group A	Group B	Total	
	(n=46)	(n=46)	(n=92)	p value*
	frequency (%)	frequency (%)	frequency (%)	
Normal	15 (32.6%)	3 (6.5%)	18 (19.6%)	0.003
SVD	31 (67.4%)	9 (19.6%)	40 (43.5%)	<0.001
DVD	0	13 (28.3%)	13 (14.1.9%)	0.001
TVD	0	19 (41.3%)	19 (20.6%)	<0.001
LMS	0	2 (4.3%)	2 (2.2%)	0.151

<sup>\*</sup>p value measured by chi-square test

**SVD:** Single vessel disease; **DVD:** Double vessel disease; **TVD:** Triple vessel disease; **LMS:** Left main stenosis **Group A:** Patients with normal QTc dispersion **Group B:** Patients with increased QTc dispersion.Mean Gensini score was significantly higher among group B  $(39.50\pm20.95)$  than group A  $(1.92\pm7.35)$  patients (p<0.001).

Table IV: Distribution of Gensini score among study population (n=92)

Gensini Score	Group A (n=46)	Group B (n=46)	p value*
Mean±SD	1.92±7.35	39.50±20.95	<0.001
Minimum	0	0	
Maximum	40	86	

<sup>\*</sup>p value measured by independent sample's t-test

Group A: Patients with normal QTc dispersion

Group B: Patients with increased QTc dispersion

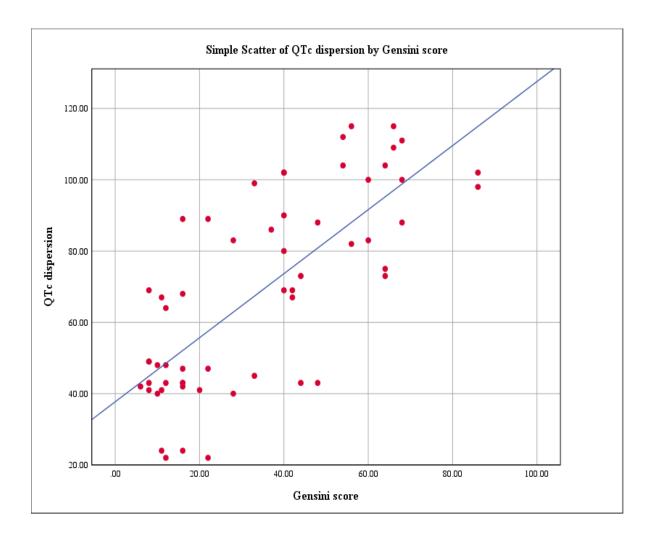


Figure 1: Scatter plots of correlation between QT<sub>C</sub> dispersion and Gensini score among study population (n=92)

Scatter plot of correlation between  $QT_C$  dispersion and Gensini score showed in above figure. In bivariate correlation it was found that  $QT_C$  dispersion was significantly correlated with Gensini score (r=0.709, p<0.001).

Male sex ( $\beta$ =0.407, p<0.001), family history ( $\beta$ =0.346, p=0.003), smoking ( $\beta$ =0.408, p<0.001) and QTc dispersion ( $\beta$ =0.664, p<0.001) were significantly correlated with Gensini score in univariate linear regression analysis.

Table V: Univariate analysis of the predictors of angiographic severity by Gensini score in patients of chronic coronary syndromes (n=92)

Variables	β	95% CI	p value*
Age	0.100	-0.361-0.885	0.405
Sex (male)	0.407	9.856-32.602	<0.001
Family history	0.346	5.963-27.753	0.003
DM	0.148	-4.503-19.613	0.216
HTN	0.123	-5.805-18.392	0.303
Dyslipidemia	0.202	-2.152-29.451	0.089
Smoking	0.408	10.930-35.882	<0.001
QT <sub>C</sub> dispersion	0.664	0.413-0.671	<0.001

β: Standardized Coefficients; CI: Confidence interval; DM: Diabetes mellitus;

HTN: Hypertension

<sup>\*</sup>Univariate linear regression done to measure significance.

In multivariate linear linear regression analysis, Gensini score had highly significant association with QTc dispersion ( $\beta$ =0.565, p<0.001).

Table VI: Multivariate analysis of the predictors of angiographic severity by Gensini score in patients of chronic coronary syndromes (n=92)

Variables	β	95% CI	p value
Sex (male)	0.099	-4.372-14.707	0.283
Family history	0.165	-0.137-16.244	0.054
Smoking	0.163	-0.941-19.644	0.074
QT <sub>C</sub> dispersion	0.565	0.289-0.575	<0.001

**β:** Standardized Coefficients; **CI:** Confidence interval;

#### **Discussion**

In the study, mean age of the patients was  $52.58\pm10.05$  years and  $55.22\pm8.50$  years in group A and group B respectively, which was almost similar between two groups. Overall maximum frequency was found in the age group of 51-60 years (45.6%). Almost similar mean age was observed by Islam et al.; Tikiz et al. and Yilmaz et al. which are comparable with the current study. [3,8,11] In this study it was observed that in group A patients, 24 (52.2%) were female and 22 (47.8%) were male while among group B patients, 40 (87.0%) were male and 6 (13.0%) were female with significance (p<0.001). As a whole 62 (67.4%) male and 30 (32.6%) female were found in the study with male female ratio 2.07:1. Similarly, Bampi et al., Da Luz et al. found that CAD was more common in male.[16,17] Female are less prone to developed IHD in premenopausal age due to protective role of estrogen, moreover smoking as a risk factor of IHD is less common in our country among female, which may explain male predominance of IHD[18].The common risk factors for coronary

<sup>\*</sup>Multivariate linear regression done to measure significance

artery disease in the present study showed that, hypertension (58.7%) was the highest among Group A patients followed by smoking (36.9%), family history of CAD (30.4%), diabetes mellitus (30.4%) and dyslipidemia (26.0%). In Group B, hypertension (71.7%) and smoking (69.5%) were the commonest followed by family history of CAD (67.4%), dyslipidemia (63.0%) and diabetes mellitus (39.1%). There was statistically significant of difference between the two groups in terms of family history of CAD, smoking and dyslipidemia. Smoking .habit was found 17 (36.9%) in group A and 32 (69.5%) patients in group B and statistically significant (p=0.002). In group A, 14 (30.4%) patients had family history of CAD and in group B, 31 (67.4%) patients and statistically insignificant (p=0.002). Dyslipidemia was found 12 (26.0%) and 29 (63.0%) patients with statistically significant (p=0.002) in group A and group B. Sharafat et al. found smoking as a highest prevalent risk factor, 56% in group A and 78% in group B [9]. This finding of the risk factors was similar regarding smoking habit & dyslipidemia with the study conducted by another study [8]. The electrocardiographic result showed mean values of RR interval, QT maximum, QT<sub>C</sub> maximum, QT minimum, QT<sub>C</sub> minimum, and QT<sub>C</sub> dispersion in group A were 830.56±104.80 ms, 356.67±39.57 ms, 394.28±43.38 ms, 323.06±36.63 ms, 356.86±40.54 ms, and 37.42±10.31 ms respectively. In group B, the values were  $818.89\pm130.23$  ms,  $384.44\pm35.17$  ms,  $427.81\pm41.25$  ms,  $300.83\pm30.08$  ms, 335.67±36.70 ms, and 92.28±20.78 ms respectively. QT maximum, QTc maximum were significantly higher in group B than group A (p<0.05). QT minimum and QTc minimum were higher in group A significantly (p<0.05). QT dispersion and QTc dispersion were higher among group B patients which was highly significant (p<0.001). That means the QT<sub>C</sub> dispersion in patients with significant CAD were higher than those with normal coronary angiogram. Double and triple vessel disease were significantly associated with group B patients with increased QT<sub>C</sub> dispersion. Severity of CAD was measured by Gensini score were higher in group B patients. In bivariate correlation it was found that QT<sub>C</sub> dispersion significantly associated with Gensini score (r=0.709, p<0.001). Previous study showed that, that QT<sub>C</sub> dispersion were significantly correlated with Gensini score which is similar to our findings [11]. Univariate and Multivariate linear regression analysis and Standardized Coefficients (95% CI) of explanatory variables was done for 92 patients with chronic coronary

syndromes considering Gensini score as dependent variable. According to univariate linear regression analysis it was observed that male sex ( $\beta$ =0.407, p<0.001), family history ( $\beta$ =0.346, p=0.003), smoking ( $\beta$ =0.408, p<0.001) and QTc dispersion ( $\beta$ =0.664, p<0.001) were significantly correlated with Gensini score. In multivariate linear regression analysis, Gensini score had highly significant association with QTc dispersion ( $\beta$ =0.565, p<0.001). Using SYNTAX score, another author similarly showed that, there was statistically significant moderate positive correlation between SYNTAX score and QT<sub>C</sub> dispersion (r=0.9, p<0.001) and heart rate (r= 0.45, p value <0.05) [19]. In present study, both univariate and multivariate linear regression analysis showed that prolonged QTc dispersion was a significant predictor for coronary artery stenosis which is routinely performed on hospital admission. Most important finding of the present study is that prolonged QTc dispersion is an independent predictor of severity of coronary artery disease in patients with chronic coronary syndromes.

#### Limitations

- All samples were collected from a single centre.
- Number of study population was limited.
- QT dispersion measurements were done manually using magnifying lens instead computer-assisted QT dispersion calculations.
- Angiography was evaluated by visual estimation, so there was chance of inter observer and intra observer variation of interpretation of the severity of the CAD.

#### **Conclusion**

This study observed a significant positive linear correlation between QTc dispersion and Gensini score. Moreover, both univariate and multivariate linear regression showed QTc dispersion as a significant marker of angiographic severity of coronary artery disease. As Electrocardiogram is a non- invasive diagnostic tool, which is widely available, easy to use and QTc dispersion could be used in predicting the severity of CAD. However, further extensive study is recommended before validating this finding.

**Conflict of interest:** None

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