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ORIGINAL ARTICLE

Correlation between QRS Dispersion and Severity of Coronary Artery Disease Detected by GENSINI score in Patients with non ST Elevation Myocardial Infraction

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ABSTRACT

Background: The aim of the present study is to correlate QRS dispersion with the severity of coronary artery lesion in patients with NSTEMI detected by GENSINI score (short term outcome). **Methods**: The whole study group consisted of 96 (63 males and 33 females) patients presented with NSTEMI . Age ranged from 46 and 75 years with a mean of 57.4 ± 6.8. Table (7) summarizes baseline clinical and laboratory data of the study population. **Results**: We included 96 consecutive patients who were admitted to our Cardiology Care Unit for NSTEMI in the period between Marsh to September 2018. All patients were given the necessary information about the study. Zagazig University, Faculty of Medicine ethics committee approved our study, and a written informed consent was obtained from patients (patients included 63 males and 33 females patients with their age ranged from 46 and 75 years with a mean of 57.4 ± 6.8) . **Conclusion**: In the current study, we found highly significant positive correlation between admission heart rate and maximum high-sensitive troponin T level and Gensini score > 20 in the setting of NSTEMI. A significant positive correlation between age, male gender, QRS measurements, QTc dispersion, LVESD and Grace score and Gensini score > 20 was found in the setting of NSTEMI. A significant negative correlation between LVEF and Gensini score > 20 was found.

Keywords; QRS Dispersion, Severity, Coronary Artery Disease, GENSINI score, NSTEMI

INTRODUCTION

Coronary artery disease (CAD) is a major cause of mortality and this health problem is reaching pandemic in both developed, and developing countries. Every effort is done to risk stratify coronary artery disease patients and various risk stratification scores have been developed. Moreover, the assessment of severity of coronary artery lesion has gained major concern **[1]**.

Non-ST-elevation myocardial infarction (NSTEMI) is lower on the severity spectrum of acute coronary syndromes than is myocardial infarction (MI), resulting from complete occlusion of a major coronary artery. As the name implies, it is a syndrome that does not exhibit the dramatic ST elevation observed in the standard 12-lead ECG in chest pain patients with confirmed acute MI. The important clinical significance of NSTEMI is that delay in diagnosis can lead to increased morbidity, risk of arrhythmia, and death **[2]**.

Dispersion of surface ECG wave durations or intervals (P wave, QRS, QT interval, JT interval) has been studied in the search for non-invasive cardiac markers useful in predicting the risk of atrial fibrillation, ventricular arrhythmia, and sudden cardiac death, and also as nonspecific prognosis

markers. The largest body of data refers to QT dispersion (QTd), but, after an initial of positive results, the potential significance of QT dispersion slowly entered into obscurity, due to a number of fundamental issues **[3]**.

Donoiu et al. [4] concluded that, the QRS dispersion is a simple electrocardiographic marker with potential value in the assessment of patients in different clinical settings: ischemic heart disease, heart failure, and cardiomyopathies. More studies are needed to validate its clinical utility for predicting the risk for ventricular arrhythmias and sudden cardiac death, and for the evaluation of the response to cardiac resynchronization therapy.

METHODS

Patients

This study included 96 consecutive patients presented with NSTEMI, who were admitted to the Cardiology Care Unit for NSTEMI in Faculty of Medicine, Zagazig University, during the period between Marsh 2018 to September 2018, they were 63 males and 33 females, their age ranged between 46 and 75 years with a mean of 57.4 ± 6.8).

Written informed consent was obtained from all subjectss and the study was carried according to the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studied involving humans.

Patients were divided into 2 groups:

Group (A): QRS dispersion ≤ 20 ms (N0. 68 patients)

Group (B): QRS dispersion > 20 ms (N0. 28 patients)

Inclusion criteria (diagnosis of NSTEMI)

- Typical ischemic chest pain
- Absent ST segment elevation 1 mV in limb leads or 2 mV in precordial leads
- Positive high sensitive-troponin.

Exclusion criteria (known confounders of QRS prolongation)

- Previous myocardial infarction,
- History of previous revascularization,
- Patients with previous diagnosis of cardiomyopathy, congenital heart diseases or significant valvular heart diseases,
- Patients with paced rhythm, bundle branch blocks, AV blocks, Wolff–Parkinson–White Syndrome,
- Patients taking medications that could affect QRS interval such as amiodarone and digitalis,
- Patients with electrolyte disturbances,
- Patients with cerebrovascular disease or significant renal impairment

Patients Data

- **Full history taking**: with emphasis on cardiac risk factors including cigarette smoking, diabetes mellitus, hypercholesterolemia and hypertension. A patient was assigned to be a current smoker (when he or she smoked any cigarettes on a regular basis within 3 weeks before the index event), ex-smoker (if they admit cessation for more than 3 weeks before the index event) or non-smoker. Diabetes mellitus was identified when dietary treatment and/or medical therapy were required to control blood glucose levels or when HbA1c levels exceed 6.5%. Dyslipidemia was defined as serum total cholesterol levels of 200 mg/dl or more, low density cholesterol more than 130 mg/dl, HDL less than 40 and triglycerides equal or more than 150 mg/dl or use of statin medication . Hypertension is defined as office systolic BP value ≥140 mmHg and/or diastolic BP value ≥90 mmHg or use of antihypertensive medication.
- **Thorough clinical examination:** with special emphasis on heart rate (HR), systolic blood pressure (SBP), signs of heart failure (Killip class) and pulmonary oedema.
- **Resting 12-lead surface electrocardiography (ECG) at admission:**
- **Heart rate** was calculated from the ECG strip.
- **QRS measurements:**

Since the correlation between the manually and the computer-measured QRS duration is excellent (r=0.96), all measurements were done manually using magnifying lens. QRS duration was measured as the time, expressed in ms, elapsed between the initiation of the Q or R waves until the end of the R or S waves. QRS dispersion was calculated as the difference between the maximum QRS

duration and the minimum QRS duration of the 12 lead ECG.

- **QT measurements:**

QT duration was measured as the time, expressed in ms, elapsed from the beginning of the QRS until the end of the T wave, defined as the T wave return point to the isoelectric line, or the nadir between the T and U waves when the latter is present. QTc (corrected QT duration) was done using Bazett's formula (QTC = QT/$\sqrt{RR}$**)**. QTc dispersion was measured as the difference between the maximum QTc and the minimum QTc of the 12 lead ECG.

Laboratory Workup

- **High sensitive-Troponin T** level on admission and serially every 24hours to determine the peak level. A 20% or greater elevation of high-sensitive troponin level from the previous sample is considered reinfarction when associated with chest pain with or without dynamic ECG changes. Normal reference values were obtained from a multicenter reference study, and the 99th percentile value was determined at 14 ng/L.
- Serum creatinine
- Electrolyte (serum Na and K) level
- **Trans–thoracic echocardiographic examination:** was done using GE, Vivid E9 machine equipped with a 4 MHz transducer. Images were taken while patient is supine or in left lateral position. Every patient was examined within 24 hours of admission. All measurements were taken according to the recommendations of the American Society of Echocardiography. A simultaneous electrocardiogram was recorded in all subjects. The following measurements were obtained:

2-D echocardiography:

- LV end-systolic (LVESD) and end-diastolic (LVEDD) dimensions and myocardial wall thickness were measured from the left parasternal long-axis view using 2D guided M-mode recordings with the cursor positioned at the tips of the mitral valve leaflets and perpendicular to the posterior wall. LV volumes and ejection fraction were calculated from the apical four-chamber view using the modified Simpson's method.
- **Conventional and tissue-Doppler imaging** included early (E) and atrial (A) peak velocities of the mitral valve, myocardial systolic velocity (S') and early (E') and atrial (A') myocardial diastolic velocities obtained from the lateral mitral annulus. The ratio of trans-mitral E peak velocity to E' peak velocity of lateral mitral annulus (E/E' ratio) was determined as an index of LV end diastolic pressure (LVEDP). Increased LVEDP was defined as an E/E' ratio >15, whereas an E/E' ratio <8 was considered to be normal.

Coronary angiography (CAG):

- All patients underwent coronary angiography within one month after NSTEMI (the timing was left to the discretion of the attending physician). CAG was performed using the femoral approach with standard Judkin's technique. All of the angiograms were recorded to compact discs in DICOM format and evaluated 'off-line' later. Gensini score is equal to the sum of all segment scores (each segment score equals segment weighting factor multiplied by a severity score). Segment weighting factors are between 0.5 and 5.0. Severity scores reflecting the specific percentage luminal diameter reduction of the coronary artery segment are 32, 16, 8, 4, 2, and 1, respectively, for 100%, 99%, 90%, 75%, 50%, and 25%. Calculation was done by two experienced cardiologists who were blinded to the current study. In case of disagreement, opinion was obtained from a third cardiologist, and the final calculation was made by consensus. Gensini score > 20 was considered high.

Statistical analysis

Data were collected, tabulated and analyzed by SPSS 20, software for Windows. The significance level was set at $P < 0.05$.

RESULTS

Table (1), showed that there was a highly significant positive correlation between admission heart rate and maximum troponin level and Ginsini score > 20, a significant positive correlation between age, male gender, QRS dispersion, QTc dispersion, LVESD and Grace score and Gensini score > 20 and a significant negative correlation between LVEF and Gensini score > 20 was found. **Table (2),** showed that

according to multivariate logistic regression, male gender, high heart rate and QRS dispersion were independent predictors of high Ginsini score > 20. **Table (3),** showed that according to ROC analysis, a HR> 80 beat/minute and QRS dispersion > 20 ms showed the highest accuracy for predicting Gensini score >20. **Table (4),** showed that the clinical and echocardiographic differences between both groups demonstrating higher incidence of clinical heart failure as well as LV diastolic and systolic dysfunction. **Table (5),** showed that there was a significant difference between subgroups regarding maximum QRS duration and minimum and maximum QTc durations and No significant difference in QTc dispersion between subgroups. Regarding QRS duration there was significant difference between subgroups regarding maximum QRS duration, there was no significant difference between subgroups regarding minimum QRS duration, regarding QT interval there was a significant difference between subgroups regarding maximum QT interval and regarding QTc dispersion there was no significant difference between subgroups. **Table (6),** showed that regarding Initial troponin level there was significant difference between subgroups. Regarding Maximum troponin level there was significant difference between subgroups. Regarding Initial CK-MB level there was no significant difference between subgroups. Regarding Maximum CK-MB level there was significant difference between subgroups. Regarding Gensini score there was significant difference between subgroups. **Table (7),** showed that regarding in-hospital outcome there was significant difference between subgroups as regard to ≥ 2 angina episodes. Regarding Reinfarction. Regarding Ventricular arrhythmia there was significant difference between subgroups and regarding there was a highly significant difference between subgroups. A regard to major bleeding and Sudden cardiac death there was no significant difference between subgroups .

Table 1. Univariate analysis for Gensini score > 20

		Gensini score
Age (years)	R-value	0.262
	P-value	**0.015 (S)**
Male gender	R-value	0.286
	P-value	**0.005 (S)**
HR (beat/min)	R-value	0.541
	P-value	**<0.001 (HS)**
Maximum QRS duration (ms)	R-value	0.341
	P-value	**0.001 (S)**
Minimum QRS duration (ms)	R-value	0.302
	P-value	**0.003 (S)**
QRS dispersion (ms)	R-value	0.248
	P-value	**0.015 (S)**
QTc dispersion (ms)	R-value	0.289
	P-value	**0.01 (S)**
LVEDD (mm)	R-value	0.088
	P-value	0.393
LVESD (mm)	R-value	0.252
	P-value	**0.013 (S)**
LVEF (%)	R-value	-0.304
	P-value	**0.003 (S)**
Serum creatinine (mg/dL)	R-value	-0.003
	P-value	0.980
Maximum high sensitive troponin level	R-value	0.523
	P-value	**<0.001 (HS)**
Grace score	R-value	0.247
	P-value	**0.015 (S)**

S= significant, HS= Highly significant

Table 2. Multivariate regression analysis for Gensini score > 20

Gensini score >20 (odds ratio)	Coefficient	Stand ad error	Wald	Degree of freedom	P value	Odds ratio	95% C.I for odds ratio	
							Lower	Upper
Male gender	1.618	.575	7.912	1	0.005 (s)	5.042	1.633	15.567
HR (beat/min)	.085	.031	7.355	1	0.007 (S)	1.088	1.024	1.157
QRS dispersion (ms)	.020	.008	5.576	1	0.018 (NS)	1.020	1.003	1.037

NS= non significant, S= significant

Table 3. Cut-off values for predicting Gensini score > 20.

Cut-off values	SN % (95% CI)	SP % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	AUROC (95% CI)	p-value
HR >80 (beat/min)	75 % (60.4 – 86.4)	75 % (60.4 – 86.4)	75 % (60.4 – 86.4)	75 % (60.4 – 86.4)	0.736 (0.513 – 0.715)	**<0.001 (HS)**
QRS dispersion >20 ms	45.8 % (31.4 – 60.8)	87.5 % (74.8 – 95.3)	78.6 % (59.0 – 91.7)	61.8 % (49.2 – 73.3)	0.658 (0.554 – 0.752)	**0.0029 (S)**

AUROC: Area Under Receiver Operating Characteristic curve., **SN:** Sensitivity, **SP:** Specificity, **PPV:** Positive Predictive Value, **NPV:** Negative Predictive Value. **95%CI:** 95% Confidence Interval. p< 0.05 is significant

Table 4. Clinical and echocardiographic differences between subgroups

Variables		QRS dispersion ≤20 68 (70.8%)	QRS dispersion >20 28 (29.2%)	p-value (Sig.)
Age (years)	Mean ± SD	57.7 ± 7.1	56.5 ± 5.9	0.662 (NS)
	Median (Range)	60 (46 – 75)	55.5 (46 – 65)	
Gender	Male	43 (63.2%)	19 (67.9%)	0.24 (NS)
	Female	25 (36.8%)	9 (32.1%)	
Hypertension		30 (44.1%)	14 (50%)	0.559 (NS)
Diabetes Mellitus		16 (23.5%)	8 (28.6%)	0.604 (NS)
Dyslipidemia		14 (20.6%)	6 (21.4%)	0.512 (NS)
Smoking		27 (39.7%)	13 (46.4%)	0.544 (NS)
Heart rate (beat/min)	Mean ± SD	77.4 ± 9.6	80.2 ± 19.9	0.952 (NS)
	Median (Range)	75 (65 – 91)	72.5 (65 – 140)	
SBP (mmHg)	Mean ± SD	158.3 ± 12.3	153.8 ± 29.3	0.720 (NS)
	Median (Range)	160 (140 – 180)	150 (75 – 190)	
Killip class	Class I	44 (64.7%)	16 (57.1%)	**<0.01 (HS)**
	Class II	13 (19.1%)	5 (17.9%)	
	Class III	11 (16.2%)	7 (25%)	

Variables		QRS dispersion ≤20 68 (70.8%)	QRS dispersion >20 28 (29.2%)	p-value (Sig.)
Creatinine (mg/dL)	Mean ± SD	1.14 ± 0.39	1.15 ± 0.37	1.00 (NS)
	Median (Range)	1.15 (0.6 – 1.9)	1.1 (0.62 – 1.8)	
WBCs (*10^3/mm^3)	Mean ± SD	8.5 ± 2.6	9.4 ± 1.2	0.078 (NS)
	Median (Range)	8.85 (2.2 – 12.8)	10 (7.1 – 11)	
Na level (mmol/L)	Mean ± SD	139.4 ± 1.9	139.1 ± 3.9	0.685 (NS)
	Median (Range)	140 (135 – 142)	140 (130 –145)	
K level (mmol/L)	Mean ± SD	3.6 ± 0.28	3.7 ± 0.36	0.05 (NS)
	Median (Range)	3.5 (3.0 –4.2)	3.5 (3.0 –4.5)	
E/E' >15		21 (31%)	15 (54%)	**0.03 (S)**
LVEDD (mm)	Mean ± SD	51.1 ± 8.6	55.3 ± 10.3	**0.029 (S)**
	Median (Range)	51.5 (33 – 66)	54 (44 – 76)	
LVESD (mm)	Mean ± SD	34.3 ± 8.8	38.4 ± 11.5	0.318 (NS)
	Median (Range)	32.5 (17 – 51)	33.5 (27 – 65)	
LVEF (%)	Mean ± SD	62.3 ± 9.4	55.3 ± 12.8	**0.025 (S)**
	Median (Range)	63 (45 – 80)	60 (30 – 68)	

Table 5. Comparison between subgroups regarding QRS and QTc measurements

Variables (Mean ± SD)	QRS dispersion ≤20 68 (70.8%)	QRS dispersion >20 28 (29.2%)	p-value (Sig.)
Maximum QRS duration (ms)	72.1 ± 34.7	93.8 ± 42.8	**0.047 (S)**
Minimum QRS duration (ms)	64.6 ± 18.5	72.7 ± 15.6	0.050 (NS)
Maximum QTc interval (ms)	297.3 ± 27.8	336.7 ± 45.1	**0.005 (S)**
Minimum QTc interval (ms)	265.8 ± 32.4	290.0 ± 58.3	**0.004 (S)**
QTc dispersion (ms)	17.5 ± 43.3	36.7 ± 55.6	0.263 (NS)

NS= non significant, S= significant

Table 6. Comparison between subgroups regarding severity of ischemia

Variables (Mean ± SD)	QRS dispersion ≤20 68 (70.8%)	QRS dispersion >20 28 (29.2%)	p-value (Sig.)
Initial troponin level	190.5 ± 65.4	245.0 ± 115.8	**0.03 (S)**
Maximum troponin level	802.3 ± 238.5	1368.5 ± 391.0	**0.02 (S)**
Initial CK-MB level	82.1 ± 64.8	106.8 ± 66.5	0.177 (NS)
Maximum CK-MB level	110.1 ± 87.1	209.6 ± 95.2	**0.04 (S)**
Gensini score (points)	23.7 ± 36.9	47.0 ± 38.3	**0.001 (S)**

NS= non significant, S= significant, HS= highly significant

Table 7. Comparison between subgroups regarding in-hospital outcome

≥ 2 angina episodes		**16 (23.5 %)**	**17 (60.7 %)**	**0.003 (S)**
Reinfarction		**1 (1.5 %)**	**1 (3.6 %)**	**0.01(S)**
Ventricular arrhythmia		**2 (2.9 %)**	**3 (10.7 %)**	**0.01(S)**
Major bleeding		**3 (4.4 %)**	**1 (3.6 %)**	**0.275 (NS)**
Sudden cardiac death		**2 (2.9 %)**	**1 (3.6 %)**	**0.063 (NS)**
Grace score (points)	**Mean ± SD**	**87.7 ± 10.8**	**117.5 ± 9.4**	**<0.001(HS)**
	Median (Range)	**88 (65 – 103)**	**121 (104 – 130)**	

NS= non significant, S= significant, HS= Highly significant

DISCUSSION

NSTEMI patients appear to be undertreated in terms of coronary reperfusion when compared to patients with STEMI, although they have higher risk profile. Numerous studies have clearly demonstrated that more intensive, even aggressive, management of these patients results in significantly better outcomes, in terms of reduction of major adverse cardiac events**[5]**.

QRS dispersion is a simple electrocardiographic marker with potential values in the assessment of patients in different clinical settings: ischemic heart disease, heart failure, and cardiomyopathies. In NSTEMI, regional intra-myocardial conduction delay is expected with resulting QRS prolongation and dispersion. So far, little data are available on the correlation between QRS duration and dispersion and in-hospital outcome and CAD severity in NSTEMI patients. Being simple and reproducible, QRS measurement can help rapid risk stratification and proper management in these patients**[6]**.

In our study, we found highly significant positive correlation between ***maximum high-sensitive troponin T level*** and Gensini score. **Frey et al., [7]** found in the setting of NSTEMI, troponin I elevations were associated with a higher incidence of multi-vessel disease, complex lesions, and visible thrombus. In the era of high-sensitive troponin T, **Altun et al. [8]** found that it was significantly correlated with SYNTAX score in NSTEMI and STEMI patients. **Cardoso et al. [9]** found similar results with much stronger correlation.

In our study on NSTEMI patients, we found that ***age*** was a significant predictor of complex coronary anatomy. Similarly, **Steg et al. [10]** found that age is correlated with left main or three vessel disease in NSTEMI. In general, the increased severity of CAD with the progression of age has been previously reported. The rate of this increase was, however, more prominent in men between 30 and 49 years of age, whereas a steady increase by age was encountered in women**.**

In our study, we found significant positive correlation between ***QTc dispersion*** and Gensini score. Using the same scoring system, **Yilmaz et al. [11]** reported the same finding. **Yunus et al. [12]** found that QTc dispersion decrease after successful coronary revascularization and increase with restenosis.

In our study, we found that QRS measurements (maximum and minimum durations as well as dispersion) showed significant positive correlation with high Gensini score. Significantly higher troponin levels were encountered in patients with QRS dispersion > 20 ms. This was in agreement with the study of **Rencuzogullari et al. [13] who** studied 176 patients with NSTE-ACS and found that patients with higher SYNTAX score were associated with longer QRS duration as well as longer R wave peak time (ventricular activation time or intrinsicoid deflection); the latter being an independent predictor of SYNTAX score > 22. this results were in agreement with the study of **Yilmaz**

et al. [14] found that resting heart rate > 77 was an independent predictor of SYNTAX score > 22 in stable CAD.

In our study, reinfarction occurred significantly more common in patients with QRS dispersion > 20 ms, while **Jiménez-Candil et al. [15]** found that QRS duration > 100 ms was associated with higher incidence of reinfarction in NSTEMI patients.

In our study, we found that the group with QRS dispersion > 20 ms had higher GRACE score with very significant statistical power and was in agreement with the study of Yamada **et al. [16]**.

To the best of our knowledge, we didn't find any study specifically addresses the correlation between QRS duration and dispersion to GRACE score in NSTEMI patients. GRACE risk score was higher in patients with fragmented QRS in patients with NSTEMI. Taking into consideration the proved highly significant association between QRS dispersion and GRACE score, we recommend using this simple ECG sign for rapid triage of NSTEMI patients; even much more rapid than GRACE score parameters are available. Of course, larger sample size and multi-center design are still needed for verification **[17]**.

We recommend measuring QRS dispersion at time of admission in NSTEMI patients. This helps gauging therapeutic plans e.g. clopidogrel loading, timing of intervention, level of care (intensive versus intermediate care unit). In patients with QRS dispersion > 20 ms, it is justifiable to delay clopidogrel loading and to perform early coronary angiography. As well, these patients are recommended to receive intensive level of care with continuous arrhythmia monitoring.

CONCLUSION

In the current study, we found highly significant positive correlation between admission heart rate and maximum high-sensitive troponin T level and Gensini score > 20 in the setting of NSTEMI. A significant positive correlation between age, male gender, QRS measurements, QTc dispersion, LVESD and Grace score and Gensini score > 20 was found in the setting of NSTEMI. A significant negative correlation between LVEF and Gensini score > 20 was found. Male gender, admission heart rate and QRS dispersion were independent predictors of severe CAD (Gensini score > 20). Cut-off values of admission heart rate > 80 and QRS dispersion > 20 ms are independent predictors of severe CAD. Patients with QRS dispersion > 20 ms had higher incidence of clinical heart failure as well as LV systolic and diastolic dysfunction. Patients with QRS dispersion > 20 ms had significantly higher incidence of in-hospital recurrent angina episodes, reinfarction and ventricular arrhythmias.

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