The correlation between QRS dispersion and severity of coronary Artery Disease in Patients with non ST Elevation Myocardial Infraction

ABSTRACT:

Non ST elevation myocardial infarction (NSTEMI) has been the subject of numerous studies. Risk stratification is a fundamental element for the management of NSTEMI; therefore, several scores have been established in this direction, particularly prognostic markers derived from the ECG.
AIMS: The aim of our study is to correlate the dispersion of the QRS with the severity of coronary lesions assessed by the GENSINI score in patients admitted for NSTEMI at the University Hospital of Marrakech.
Methods: A retrospective study was conducted in the cardiology department of Mohammed VI university hospital of Marrakech from January 01, 2022 to March 31, 2022. Data was derived from the hospitalization register, including 30 patients (16 were women and 14 were men). Age ranged from 56 to 74 years with an average of 64.6 ± 9.3. Data was collected and analyzed by SPSS, the level of significance set at $p < 0.05$.
Results: In our study, we found a highly significant positive correlation between QRS dispersion (considered important if >20 ms) and admission heart rate ($p=0.003$) as well as the level of ultrasensitive troponins ($p=0.003$). There is also a very significant correlation between QRS dispersion and corrected QT interval ($p=0.005$), Moreover, we concluded that in patients admitted for NSTEMI, the greater the dispersion of the QRS, the higher the score of GENSINI ($p<0.0001$).
Conclusion: The dispersion of the QRS is a simple marker on the ECG that can have a predictive value in different clinical contexts, particularly in acute ischemic heart disease. Further studies are needed, however, to validate its usefulness in routine practice.

KEY WORDS: Cardiology, Coronary artery disease, myocardial infarction, prognostic markers

1. INTRODUCTION:

"Coronary artery disease (CAD) is the most common cause of mortality among adults in the in both developed, and developing countries" [1]. Therefore, all patients, especially with non-ST elevation myocardial infarction (NSTEMI), should undergo early risk stratification. This latter will impact decision making between an invasive treatment or non-invasive one.

"Various risk stratification scores have been developed. Prognostic markers derived from standard ECG in particularly have been interesting. Dispersion of surface ECG wave durations (P wave, QRS, QT interval, JT interval) has been studied in the quest of a simple non-invasive cardiac marker useful in predicting the risk of arrhythmias and sudden cardiac death. However, this last has intrinsic and methodological issues that question its utility". [2]

This paper presents data supporting the benefit of QRS dispersion as an easy accessible marker with potential value in the assessment of risk stratification in patients presenting with NSTEMI.

2. MATERIAL AND METHODS:

2.1 Study design and population:

Thirty patients presented with NSTEMI, were admitted to the Cardiology Care Unit for NSTEMI in university hospital of Marrakech, during the period between January 2022 and March 2022, they were 14 males and 16 females, their age ranged between 56 and 74 years with a mean of 64.6 ± 9.3.

The work has been done respecting The Code of Ethics of the World Medical Association for studied involving humans.

2.1.1 Inclusion criteria:

- Typical angina
- Non persistent ST segment elevation in limb leads or in precordial leads
- Positive high sensitive cardiac troponin test.

2.1.2 Exclusion criteria:

- History of myocardial infarction, or previous revascularization,
- History of congenital heart diseases,
- History of severe valvular heart disease,
- Paced rhythm, bundle branch blocks, AV blocks, Wolff–Parkinson–White Syndrome,
- Antiarrhythmic treatment,
- Electrolyte abnormalities,
- History of cerebrovascular disease,
- End stage kidney disease.

2.2 Patients Data:

2.2.1 cardio-vascular risk factors:

- Smoking: classified into four groups: never smoker, not current smokers, smokers (not daily) and current daily smokers.
- Diabetes mellitus: when HbA1C>6,5%.
- Dyslipidemia: when LDLc ≥ 130 mg/dl, HDLc < 40 mg/dl, total cholesterol ≥ 200 mg/dl, triglycerides ≥ 150 mg/dl.
- Hypertension: The definition of hypertension used was systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥ 90mmHg and/or self-reported treatment with antihypertensive medication.
- Obesity: BMI = 25–29.9 kg/m2 and ≥30 kg/m2 are used to define overweight and obesity, respectively.

2.2.2 Physical examination:

Heart rate (HR), systolic blood pressure (SBP), signs of left heart failure (Killip class).

2.2.3 QRS and QT measurements:

- QRS measurements: QRS duration is measured from the beginning of the Q wave to the end of the S wave. A normal range is from 40 to 100 milliseconds. 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 interval is measured from the beginning of the QRS complex to the end of the T-wave, and should be corrected for heart rate to enable comparison with reference values. The correction was done using Bazett's formula.

2.2.4 Laboratory tests:

- High Sensitive-Troponin T level on admission and 1 hour later to determine the peak level. A 20% or greater elevation of high-sensitive troponin level from the previous sample is considered positive.
- Serum creatinine.
- Electrolyte level

2.2.5 Trans–thoracic echocardiographic examination:

- A GE Vivid E9 machine was used to evaluate patients within 24 hours of admission. The following measurements were assessed:
- LV end-systolic and end-diastolic diameters and myocardial wall thickness were measured on a parasternal long-axis view using 2D recordings.
- Ejection fraction (%) was calculated from the apical four-chamber view using the modified Simpson's method.
- E wave: early diastole and A wave: atrial contraction peak velocities of the mitral valve, early (E') 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 >14, whereas an E/E' ratio <8 was considered to be normal.

2.2.6 Assessment of Coronary angiography/ GENSINI score:

The coronary angiography was performed for all enrolled individual, and the results were analyzed and calculated by at least two observers.

The calculation of Gensini score: "the degree of stenosis and the coronary artery lesion site were scored as follows: 1 point for ≤ 25% narrowing, 2 points for 26-50% narrowing, 4 points for 51-75% narrowing, 8 points for 76-90% narrowing, 16 points for 91-99% narrowing, and 32 points for total occlusion. Then, each lesion score is multiplied by a factor that takes into account the importance of the localization of the lesion in the coronary tree (5 for left main coronary artery, 2.5 for the proximal segment of the left anterior descending coronary artery, 2.5 for the proximal segment of the circumflex artery, 1.5 for the mid-segment of the left anterior descending coronary artery, 1.0 for the right coronary artery, the distal segment of the lest anterior descending coronary artery, the posterolateral artery, and the obtuse marginal artery, and 0.5 for the rest of the segments. Afterwards, and adjustment based on collaterals should be done: If a segment is totally occluded or 99% stenosis and receiving collaterals, a collateral adjustment factor is used, and the adjustment is reduced by the extent of disease in the vessel that is the source of collaterals (Fig. 1). The final GS is the sum of all the lesion scores". [3]

STEP 1 Calculation of the severity score for each lesion ≥ 25% and adjustment for total occlusions or 99% obstructive lesions receiving collaterals			
Degree of stenosis (%)	**Receiving collaterals**	**Adjustment for collaterals**	**Severity Score**
1-25	-	0	1
26-50	-	0	2
51-75	-	0	4
76-90	-	0	8
91-99	no	0	16
99	yes	-8	8
100	no	0	32
100	yes, and normal source vessel	-16	32-16=16
100	yes, and 25% stenosis source vessel	-12	32-12=20
100	yes, and 50% stenosis source vessel	-8	32-8=24
100	yes, and 75% stenosis source vessel	-4	32-4=28
100	yes, and 90% stenosis source vessel	-2	32-2=30
100	yes, and 99% stenosis source vessel	-1	32-1=31
STEP 2 A multiplying factor is applied to each lesion score based upon its location in the coronary tree			
Segment		**Right Dominance**	**Left Dominance**
RCA proximal		1	1
RCA mid		1	1
RCA distal		1	1
PDA		1	1
PLB		0.5	0.5
Left Main		5	5
LAD proximal		2.5	2.5
LAD mid		1.5	1.5
LAD apical		1	1
1st Diagonal		1	1
2nd Diagonal		0.5	0.5
LCx proximal		2.5	3.5
LCx mid		1	2
LCx distal		1	2
Obtuse Marginal		1	1
STEP 3 Sum of all the lesion severity scores			

Fig. 1. Step by step algorithm for the Gensini Score calculation.

Fig 1: step by step algorithm for the gensini score calculation

2.2.7 The GRACE risk Score:

The GRACE risk score predicts 6-month mortality after a patient has been discharged following hospital admission for ACS. It uses a predictive logistic model with eight prognostic variables to determine a patient's probability of death due to any cause during the first 6 months after discharge: Age, heart rate, systolic blood pressure, Killip class, creatinine, cardiac arrest at presentation, elevated troponin, St-segment deviation. To each variable, we can associate certain number of points. Patients can be classified into three categories of GRACE risk score: Low risk: 140 points, intermediate risk: 109 to 140 points, and high risk: >140 points.

2.3 Statistical analysis:

Based on the QRS dispersion, the enrolled patients were classified into 2 groups:

- Group (I): QRS dispersion ≤ 20 ms (n=18 patients)
- Group (II): QRS dispersion > 20 ms (n=12 patients)

Data were collected, tabulated on Microsoft Excel. All the analyses were performed using SPSS 16.0, for Windows statistical software. The significance level was set at $P < 0.05$.

3. RESULTS:

Table (1), showed the main characteristics of the population: 30 patients in total (14 males and 16 females) were included in the study, their age ranged between 56 and 74 years with a mean of 64.6 ± 9.3. the most common cardio-vascular risk factor was dyslipidemia (86%), then hypertension was second most common CV risk factor with a percentage of 80%, then diabetes mellitus and obesity in 3rd and 4th place with an incidence of 60% and 33% respectively.

Table (2), showed that there was a highly significant positive correlation between admission heart rate, maximum troponin level, OTc length and Gensini score, a significant positive correlation between age, QRS dispersion, Grace score and Gensini score and a significant negative correlation between LVEF and Gensini score was found.

Table (3), showed the clinical, biological and echocardiographic differences between subgroups. We noticed that SBP and HR were higher in the subgroup with QRS dispersion>20 ms, that LV diastolic and systolic dysfunction was correlated with higher QRS dispersion. It also showed that there was a significant difference between subgroups regarding maximum QRS dispersion QTc durations. subgroups **Table (4),** showed that regarding Initial troponin level and Grace score there was significant difference between subgroups.

Table 1: Main population characteristics

Population characteristics (n=30)		Percentage (100%)
Gender	Male	14 (46,6%)
	Female	16 (53,3%)
Smoking		8 (26,6%)
Diabetes mellitus		18 (60%)
Hypertension		24 (80%)
dyslipidemia		26 (86%)
Obesity		10 (33%)

Table 2: Analysis for significant Gensini score

		Gensini Score
Age (years)	P-value	0,014 (S)
HR (beats/min)	P-value	0,002 (HS)
QRS dispersion	P-value	0,015 (S)
QTc length	P-value	0,005 (HS)
LVEF (%)	P-value	-0,03 (S)
Initial troponin level	P-value	0,003 (HS)
Grace Score	P-value	0,016 (S)

Table 3: Clinical, biological and echocardiographic differences between subgroups

Variables		QRS dispersion>20 (n=12)	QRS dispersion <20 (n=18)	P value
Age		65,16 +/- 5,8	64,33 +/-9,6	0,115
Gender	F	4 (33,3%)	12 (77,7%)	0,295
	M	8 (66,6%)	6 (22,2%)	
Hypertension		8 (66,6%)	16 (88,8%)	0,227
smoking		4 (33,3%)	4 (22,2%)	0,448
Diabetes mellitus		4 (33,3%)	14 (77,7%)	0,365
HR	Mean	94,5 +/- 29,5	83,77+/- 17	0,003(HS)
	Median	92,5 (50-124)	82 (66-101)	
SBP	Mean	142,8 +/- 43,1	132,5 +/- 21,4	0,0001(HS)
	median	135,5 (130-186)	132 (118-150)	
WC	Mean	11156,6 +/-8133	10391,11+/-3608	0,083(S)
	Median	10515 (6230-19290)	11020 (5660-14000)	
K+	Mean	4,5 +/- 0,56	4,63+/-1,16	0,19
	Median	4,65 (3,9-5,1)	4,6 (3,7-5,8)	
Initial Troponin level	Mean	13271,6+/-52028	4633,11+/-9636,8	0,003(HS)
	Median	1885 (187-65300)	2636(220-14270)	
E/E'		7,97+/-5,02	7,84+/-4,15	0,24
LVEF	Mean	44,33+/-5,6	53,88+/-10,1	0,51
	Median	45,5(32-55)	58(37-64)	
Corrected QT	Mean	448+/-49	411+/-49,1	0,005(HS)
	Median	461(341-497)	410(371-461)	
GRACE score	Mean	150,83+/-11,16	97,7+/-30,2	0,065(S)
	Median	153(138-162)	113(17-128)	

Table 4: Comparison of subgroups regarding severity of ischemia

Variables (Mean+/- SD)	QRS dipersion≤20ms (60%)	QRS dispersion>20 ms (40%)	p-value
Initial troponin level	4633,11+/- 9636,8	13271,6+/-52028	0,003 (HS)
Gensini Score	29,6 +/- 18,3	54 +/- 30	<0,0001 (HS)

4. DISCUSSION:

"The optimal risk stratification of NSTEMI patients is a key priority in emergency medicine: It particularly improves the selection of higher-risk patients for invasive management. After evaluation of several risk predictors and risk scores, it was found that estimating risk based on clinical characteristics only is challenging and imprecise" [4]. "Although, prognostic markers derived from ECG have always been intriguing; As a matter of fact, dispersion of ECG wave durations or intervals like P wave, QRS, QT interval, JT interval have been previously studied in the search for non-invasive cardiac markers that can be used to assess the risk of atrial fibrillation, ventricular arrhythmia, and sudden cardiac death. Most studies refer to QT dispersion (QTd), but, after a brief success, the potential significance of QT dispersion slowly sank into obscurity, due to a number of fundamental and technical issues" [2]. Some authors have extended the same issues to P wave dispersion [5], but the question arises as to whether they also affect QRS dispersion.

Since it has been assumed that QT dispersion represents regional inhomogeneity of repolarization times, it is likely that QRS dispersion, as a result of a ventricular conduction deficit, represents regional inhomogeneity of depolarization times. "Pathophysiology of NSTEMI have shown that, regional intra-myocardial conduction delay can cause QRS prolongation and dispersion. However, up to this point, little data are available on the correlation between QRS duration/dispersion and CAD severity". [6]

Some few studies focused on the correlation between the QRS dispersion and the severity of myocardial infarction: Perkiömäki et al [7] studied a set of 100 patients: First group = normal group formed of 30 healthy patients with no myocardial infarction (MI), 40 patients with a history of MI, without ventricular arrhythmic events at electrophysiological study (EPS), and 30 patients with prior MI and history of cardiac arrest (12 patients) or ventricular tachycardia (VT) (18 patients) [8]. QRS dispersion was 28 ± 11 ms in the normal group, 46 ± 13 ms in the group with MI and no VT, and 48 ± 16 ms in the group with MI and VT ($p < 0.001$). The maximal QRS duration were also higher in patients with prior MI compared to healthy subjects ($p < 0.001$).

Mozos et al [8] studied "16 patients with history of MI. Patients with hypokalemia, hypocalcemia, or hypomagnesaemia and those not in sinus rhythm were excluded. The aim

of the study was to evaluate the link between signal-averaged late ventricular potentials (LVP) and QRS dispersion. The latter was measured manually using at least 8 leads for each patient. The QRS dispersion were compared in two groups of patients: with and without LVP (62.5% had LVP+). Results showed that QRS dispersion was significantly higher in the subgroup with LVP compared to the other subgroup (110.4 ms in LVP+ vs. 56.8 ms in LVP-, p= 0.05)".

In our study. We found that age was a significant forecaster of coronary lesions anatomy's complexity. Steg et al. [9] also found that "age is correlated with more complex and significant coronary lesions (left main or three vessel disease in NSTEMI). In general, the increased severity of CAD with the progression of age has been previously reported".

We also found highly significant positive correlation between admission high-sensitive troponin T level and Gensini score. Frey et al., [10] found "in the setting of NSTEMI, troponin elevations were a predictor of higher incidence of multi-vessel disease, complex lesions, and visible thrombus". Finally, Altun et al. [11] proved that "it was significantly correlated with SYNTAX score in NSTEMI and STEMI patients".

QRS dispersion > 20 ms showed significant positive correlation with high Gensini score and High Grace risk score. Higher troponin levels were encountered in patients with QRS dispersion > 20 ms. This was in agreement with the study of Frere et al. [12] who studied 96 patients with NSTE-ACS and found similar results.

The QRS dispersion might be a simple electrocardiographic marker, however it has a potential value in the assessment of patients in different clinical settings, including NSTEMI.

The determination of QRS dispersion in routine ECG at time of admission in NSTEMI patients, might be very helpful to the initial therapeutic plan: P2Y12 inhibitor loading, timing of percutaneous intervention, level of care. In patients with QRS dispersion > 20 ms, it is valid to delay P2Y12 inhibitor loading and to perform early coronary angiography. As well, justifies hospitalization in intensive care unit with continuous monitoring.

5. CONCLUSION:

This current study presents data supporting the utility of QRS dispersion in clinical practice to assess patients with higher ischemic risk: the correlation was highly significant between QRS dispersion>20 ms and higher admission troponin level and Gensini score.

Considering the small group of patients, the significance of the results to a larger scale remains unclear. More studies are needed to validate its clinical benefit in larger groups of patients.

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