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ORIGINAL ARTICLE

Correlation of corrected QT dispersion with the severity of coronary artery disease detected by SYNTAX score in non-diabetic patients with STEMI

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KEYWORDS

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Abstract *Introduction:* Determination of the QT interval dispersion by means of a standard ECG at rest has been widely used for cardiovascular risk assessment during the last 15 years as one of the recent explanations for the development of life threatening ventricular arrhythmias. However, little is known about the relation between QT dispersion and the severity of coronary artery atherosclerosis as defined by SYNTAX score.

Aim of work: The present study was done to assess the correlation between QTc dispersion and the severity of coronary artery disease in acute ST elevation myocardial infarction (STEMI) detected by SYNTAX score.

Patients and methods: It included 50 patients who were non-diabetic, non-hypertensive and diagnosed as acute STEMI within 6 months undergoing coronary angiography in the cath. lab. of Assiut University Hospital. QT dispersion was calculated as the difference between the longest (QT max) and the shortest QT (QTmin) interval recorded by standard 12 lead ECG. The QT interval was corrected by using Bazett's formula (QTc = QT/square root of R-R interval in seconds). Corrected QT dispersion (QTcd) was defined as the difference between the maximum and minimum QTc for a given heart rate. The SYNTAX score is calculated by syntax calculator, a new tool to grade the complexity of coronary artery disease.

Results: Out of 50 participating patients, there were 43 (86%) males with mean age 53.9 ± 12.1 years. The mean QTc dispersion was 83.1 ± 20.3 ms, while mean SYNTAX score was 11.6 ± 6.1. There is a strong positive correlation between QTc dispersion and SYNTAX score.

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This was not related to age, gender, risk factors or family history of ischemic heart disease. Of note, there was a relationship between QTc dispersion and serum creatinine.

Conclusions: Our study concluded that there is a significant positive correlation between corrected QT dispersion and severity of coronary artery disease as assessed by SYNTAX score.

1. Introduction

Coronary heart disease 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] Today the utility of the ECG has been overshadowed by the ability of the echocardiography and interventional cardiology to evaluate the possible site and extent of lesion of coronary artery after myocardial infarction.[2]

Determination of the QT dispersion by means of a standard ECG at rest has been widely used for cardiovascular risk assessment during the last 15 years as one of the recent explanations for the development of life threatening ventricular arrhythmias. It is based on the prolongation and dispersion of repolarization between neighboring regions of myocardium.[2]

The inter-lead variation of QT interval provides an index of the heterogeneity of ventricular repolarization. The most commonly used index to calculate QT dispersion has been off difference between the longest and shortest QT intervals on the twelve-lead electrocardiography (ECG), which is often adjusted for heart rate.[3]

Some studies showed that patients with single vessel CAD had wider resting QT dispersion when compared to control group, which further increased significantly with exercise.[3] Other studies showed a relation between QT dispersion and the extent of myocardial ischemia in patients with three vessel coronary artery disease.[4]

QT interval dispersion had been found to decrease after successful coronary artery revascularization and increase with restenosis. Therefore, QT interval dispersion may be a marker of recurrent ischemia due to restenosis after percutaneous coronary angioplasty.[5] It had been also shown that QT dispersion is significantly increased during spontaneous angina in patients with documented coronary artery disease and history of previous myocardial infarction. QT dispersion was significantly higher during the anginal episode compared to the painless conditions.[6] However, little, if any, was reported about the relation of QTc dispersion and severity of coronary artery lesion as detected by SYNTAX score.

Various angiographic scoring systems were developed to assess the severity 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.[7]

2. Aim of the study

The aim of the present study was to discover the relationship between QT dispersion and severity of coronary atherosclerotic disease as detected by SYNTAX score in stable non-diabetic patients who suffered acute STEMI.

3. Patients and methods

3.1. Study patients

The study is a prospective, single center study carried out in Assiut University Hospitals during the period between 1st March and 30th November 2015. It enrolled 50 patients who were diagnosed to have acute STEMI according to WHO criteria:

- Typical chest pain.
- ST segment elevation 1 mV in limb leads and 2 mV in chest leads.
- Positive cardiac enzymes (Ck, Ck-MB, Troponin).

All study population were managed medically using thrombolytic therapy.

The study protocol was approved by ethical committee of Assiut Faculty of Medicine and written consent was taken for every participant.

Exclusion criteria include diabetes mellitus, hypertension, patients with paced rhythm, old myocardial infarction (more than 6 months), atrial fibrillation, bundle branch blocks, intraventricular conduction delays, AV block, sinus node dysfunction, Wolff–Parkinson–White Syndrome, patients taking medications that could affect QT interval such as amiodarone and digitalis, electrolyte imbalance, post CABG status, post PCI status, cerebrovascular disease, renal impairment (serum creatinine >2.0 mg/dL), cardiomyopathy, congenital heart diseases and valvular heart disease.

All patients were subjected to

(1) Full clinical evaluation: This includes detailed history and thorough general and cardiac clinical examination. History of angina, heart failure and currently used medications was reported. Dyslipidemia is reported when the patient has recent lipogram with at least one disturbed serum lipid value.

(2) Laboratory investigations include lipogram, random blood sugar, serum electrolytes; sodium, magnesium and potassium, renal function (serum urea and creatinine).

(3) Detailed echocardiography:

To evaluate the cardiac condition segmental wall motion abnormalities suggestive of coronary artery disease, cardiac dimensions, and left ventricular function are included and cardiomyopathy, congenital and/or valvular heart disease are excluded.

(4) Twelve lead ECG.

The analyzed ECG was conducted within the first week after the acute myocardial infarction. Firstly, heart rate was calculated from the ECG strip. Using magnifying lens, QT dispersion was calculated for all patients as the difference between the longest (QT max.) and the shortest QT (QT min.) interval recorded by standard 12 lead ECG.[8] The QT interval was corrected by using Bazett's formula (QTc = QT/square root of R-R interval in seconds). Corrected QT dispersion was defined as the difference between the maximum and minimum QTc for a given heart rate. So QTc dispersion = QTc maximum - QTc minimum. Based on the previous literature, the patients have been divided into two groups based on QTc dispersion value;[9]

Group I: QTc dispersion <60 ms (msec) (16 patients)

Group II: QTc dispersion $\geqslant 60$ ms (msec) (34 patients)

(5) Coronary angiography:

All patients underwent conventional invasive coronary angiography using standard techniques within one month after STEMI. Images were acquired in optimal projection angles, at 25 frames per second. From the baseline diagnostic angiogram, each coronary lesion producing $\geqslant 50\%$ diameter stenosis in vessels $\geqslant 1.5$ mm was scored separately and added together to provide the overall SYNTAX score, which was calculated using the SYNATX score algorithm.[7]

All angiographic variables pertinent to SYNTAX score calculation were computed by two experienced cardiologists who were blinded to the current study on angiograms. In case of disagreement, opinion was obtained from the third cardiologist, and the final decision was made by consensus.

(6) Statistical analysis:

Data were analyzed by statistical package for the social sciences (SPSS, version 16). The following statistics were carried out.

Descriptive statistics: The ranges, means, and standard deviations were calculated for interval and ordinal variables and the frequencies and percentages for categorical variables. Normal and continuous variables were compared using Student's t-test, paired t-test, or ANOVA as appropriate. Categorical variables are compared by Chi-square test. The level of significance was set at $p < 0.05$.

Correlation

- QTc dispersion was correlated with age, heart rate, ejection fraction, serum electrolytes and kidney function (serum urea and creatinine).
- SYNTAX score was correlated with age, heart rate, ejection fraction, serum electrolytes and kidney function (serum urea and creatinine).
- Then a correlation between QTc dispersion and SYNTAX score was done.

4. Results

I. Study population (Table 1):

Table 1 summarizes the demographic data, risk factors, used medications, laboratory analysis, ECG findings, echo results and SYNTAX score of the study population.

II. Analysis of QTc dispersion:

Table 2 compares group I (QTc dispersion <60 ms, 16 patients, 32%) and group II (QTc dispersion $\geqslant 60$ ms, 34 patients, 68%) in order to assess different parameters that could be associated with prolonged QTc dispersion. The range of QTc dispersion was 45–121 ms. There was no age or gender difference between both groups. Both groups were also comparable regarding smoking history, dyslipidemia, and family history of ischemic heart disease. Heart failure was shown to have statistically significant relationship with prolonged QTc dispersion (p value < 0.05). There was no difference in other clinical, Echo and laboratory data except serum creatinine that was significantly higher among those with prolonged QTc dispersion (p value < 0.05). Using Student's t test; SYNTAX score was significantly high among group II (p value < 0.001), Table 2 and Fig. 1.

III. Analysis of SYNTAX score:

According to SYNTAX score, our study population were divided into

(a) Low score (0–22): 38 patients (76%) had low scores.
(b) Intermediate score (23–32): 9 patients (18%) had intermediate scores.
(c) High score ($\geqslant 33$): 3 patients (6%) had high score.

Using ANOVA test, there was a statistically significant relationship between SYNTAX score and QTc dispersion (p value < 0.001, Fig. 2).

IV. Correlations:

(A) QTc dispersion and SYNTAX score

There was statistically significant strong positive correlation between SYNTAX score and QTc dispersion ($r = 0.9$, p value < 0.001, Fig. 3).

(B) QTc dispersion and clinical, echo and laboratory findings:

There was statistically significant weak positive correlation between QTc dispersion and serum creatinine level ($r = 0.3$, p value < 0.05). Also there was statistically moderate positive

Table 1 Demographic, clinical, laboratory, electrocardiographic and SYNTAX score of the study population.

Parameter	$n = 50$
Age (mean ± SD) in years	53.9 ± 12.1
Male gender (%)	43 (86)
Smoking (%)	37 (74)
Dyslipidemia (%)	39 (78)
Family history of ischemic heart disease (%)	32 (64)
Angina (%)	16 (32)
Heart failure (%)	11 (22)
Beta blocker therapy (%)	37 (74)
ACE-inhibitors (%)	40 (80)
Diuretics (%)	11 (22)
Statin Therapy (%)	50 (100)
Serum urea (mean ± SD) in mg/dL	31.8 ± 6.1
Serum creatinine (mean ± SD) in mg/dL	0.95 ± 0.11
Random blood sugar (mean ± SD) in mg/dL	130.1 ± 23.5
Serum Na^+ (mean ± SD) in mmol/L	140.0 ± 3.4
Serum K^+ (mean ± SD) in mmol/L	4.4 ± 0.4
Serum Mg^{++} (mean ± SD) in mEq/L	1.8 ± 0.2
Heart rate (mean ± SD) in beats/min	78.3 ± 9.7
QT dispersion (mean ± SD) in msec.	72.4 ± 16.1
QT corrected dispersion (mean ± SD) in msec.	83.1 ± 20.3
Ejection fraction (mean ± SD) in%	59.4 ± 4.6
SYNTAX score (mean ± SD)	11.6 ± 6.1

Table 2 Analysis of QTc dispersion.

Parameter	Group I	Group II	*p* value
	QTc dispersion <60 ms ($n = 16$)	QTc dispersion $\geqslant 60$ ms ($n = 34$)	
Age (mean ± SD) in years	53.7 ± 14.5	53.9 ± 12	0.9
Male gender (%)	13 (81.3)	30 (88.2)	0.8
Smoking (%)	13 (81.3)	24 (70.6)	0.6
Dyslipidemia (%)	12 (75)	27 (79.4)	0.7
Family history of ischemic heart disease (%)	10 (62.5)	22 (64.7)	0.9
Angina (%)	5 (31.3)	11 (32.4)	0.8
Heart failure (%)	2 (12.5)	9 (26.5)	0.004*
Beta blocker therapy (%)	11 (68.8)	26 (76.5)	0.09
ACE-inhibitors (%)	12 (75)	28 (82.4)	0.6
Diuretics (%)	4 (25)	7 (20.6)	0.1
Statin Therapy (%)	16 (100)	34 (100)	0.3
Serum urea (mean ± SD) in mg/dL	31.1 ± 5.6	32.2 ± 6.4	0.6
Serum creatinine (mean ± SD) in mg/dL	0.90 ± 0.10	0.97 ± 0.11	0.03*
Random blood sugar (mean ± SD) in mg/dL	129.1 ± 22.3	134.5 ± 32.2	0.5
Serum Na^+ (mean ± SD) in mmol/L	142.0 ± 4.1	139.4 ± 3.2	0.08
Serum K^+ (mean ± SD) in mmol/L	4.7 ± 0.6	4.4 ± 0.5	0.2
Serum Mg^{++} (mean ± SD) in mmol/L	1.9 ± 0.1	1.8 ± 0.2	0.5
Heart rate (mean ± SD) in beats/min	67.7 ± 1.9	79.8 ± 9.4	0.003*
Ejection fraction (mean ± SD) in%	60.1 ± 4.7	59.1 ± 4.1	0.4
SYNTAX score (mean ± SD)	3.8 ± 1.7	12.7 ± 5.7	0.0001*

* Statistically significant.

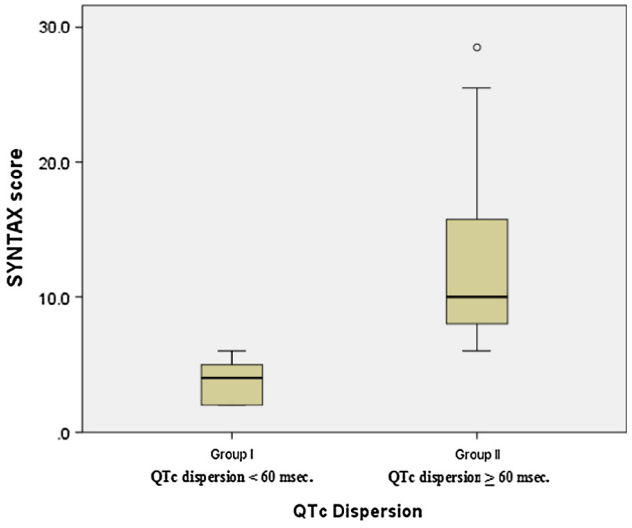

Figure 1 Relationship between QTc dispersion and SYNTAX score, Student *t* test, *p* value < 0.001.

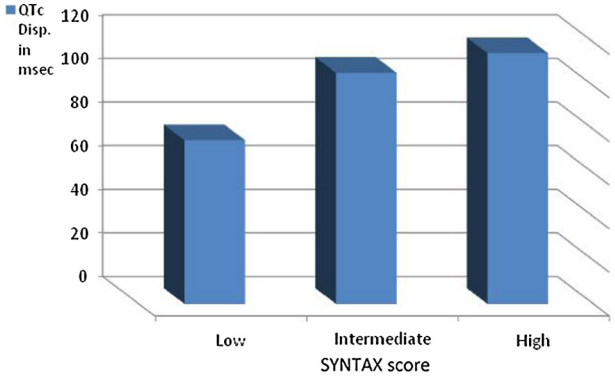

Figure 2 Relationship between QTc dispersion and SYNTAX score, ANOVA test, *p* value < 0.001.

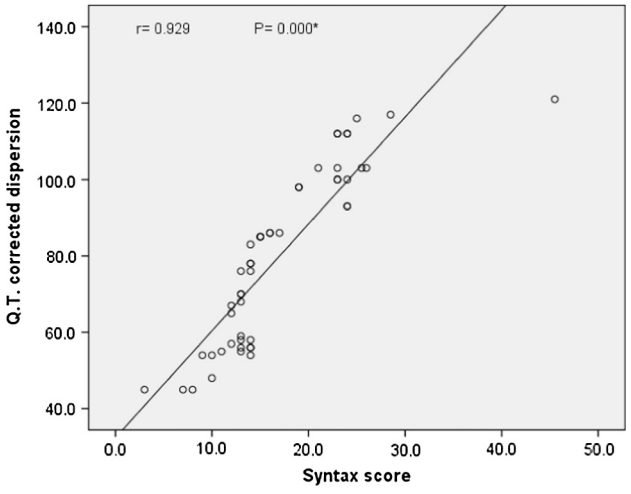

Figure 3 Scatterplot of the relationship between QTc dispersion and SYNTAX score.

correlation between QTc dispersion and heart rate ($r = 0.5$, *p* value < 0.05), Table 3.

(C) SYNTAX score and clinical, echo and laboratory findings:

There was statistically significant moderate positive correlation between SYNTAX score and heart rate ($r = 0.45$, *p* value < 0.05). On the other hand, SYNTAX score failed to show correlation with any other clinical or laboratory data, Table 4.

5. Discussion

Dispersion of the QT interval is defined as the difference between the longest and the shortest QT interval in all

Table 3 Correlation between QTc dispersion and clinical, echo, laboratory and SYNTAX score parameters.

	r value	*p* value
Age	0.14	0.3
Serum urea	0.08	0.6
Serum creatinine	0.32	0.02*
Random blood sugar	−0.12	0.5
Serum Na^+	−0.08	0.5
Serum K^+	−0.12	0.4
Serum Mg^{++}	0.06	0.7
Heart rate	0.53	0.001*
Ejection fraction	−0.2	0.09
SYNTAX score	0.9	0.001*

* Statistically significant.

Table 4 Correlation between SYNTAX score and clinical, echo and laboratory and QTc dispersion findings.

	r value	*p* value
Age	0.22	0.1
Serum urea	0.12	0.4
Serum creatinine	0.21	0.1
Random blood sugar	−0.23	0.1
Serum Na^+	−0.13	0.4
Serum K^+	−0.20	0.2
Serum Mg^{++}	0.05	0.8
Heart rate	0.45	0.001*
Ejection fraction	−0.31	0.1
QTc dispersion	0.9	0.001*

* Statistically significant.

electrocardiographic leads, which may be possibly measured. That parameter electrocardiographically translates the asynchrony of repolarization of ventricular myocardial rows.[10]

Over the last several years, QT duration and QT dispersion (measured in surface ECG recordings) have been explored as a potential noninvasive measure of non-uniform recovery of ventricular excitability in myocardium. QT interval dispersion is abnormally increased in patients with acute myocardial infarction, acute coronary ischemia, heart failure, idiopathic long QT syndrome, dilated cardiomyopathy and hypertrophic cardiomyopathy.[11]

Kenigsberg et al. have modified the classical concept in ischemic cascade, demonstrating, in 100% of the cases studied, that the earliest event to take place in ischemia is the prolongation of the QTc interval and QTc dispersion.[12]

MESA (Multi-Ethnic Study of Atherosclerosis) study has reported an independent positive association between the baseline QTc and cardiac and vascular events in middle-aged participants without prior CVD. Importantly this association was not limited to a specific sex or ethnicity.[13]

Several studies documented the relationship between severity of coronary artery disease and QTc dispersion.[9,12,13] However, these studies used different scoring systems to assess severity of coronary artery disease such as vessel score, Friesinger score and Leaman score in Sharafat et al. [14], and vessel score, diffuse score and Gensini score in Yilmaz et al. [4]. However, in 2005, a rather recent score was introduced as SYNTAX score based on the well-known SYNTAX trial.[7] So we are the first to relate QTc dispersion to the severity of coronary artery disease as assessed by SYNTAX score. The main finding of the present study was that there is strong positive correlation QTc dispersion and severity of coronary artery disease detected by SYNTAX score.

We chose to use 60 ms as a cutoff value to divide our study population into two groups. We didn't state that 60 ms is the cutoff for prolonged QTc rather being an arbitrary value to subdivide our 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. [14]. Moreover, in correlation studies, we 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 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).[14]

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.[15]

Tikiz, et al. 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.[16]

On the other hand among patients with three vessel coronary artery disease, Stierle, et al. 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.[3]

Using Gensini score, Yilmaz et al. reported 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.[4]

Yunus et al. 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.[5] 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.[17] Polychronis 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.[6]

Our study reported a positive correlation between QTc dispersion and serum creatinine. Murat Celik et al. investigated QT dispersion in relation to glomerular filtration rate in patients with coronary artery disease and found that QT dispersion increases with low glomerular filtration rate. QT dispersion tends to be higher in patients with poor renal function independent of angiographic severity of coronary artery disease. QT dispersion may be a potentially useful non-invasive test in the management of patients with poor renal function, especially those with coronary artery disease. Deterioration of renal function has a negative effect on cardiovascular biology and physiology and can lead to deterioration of ventricular repolarization and myocardial homogeneity.[18] In patients with renal failure, prolonged QT dispersion may occur due to several mechanisms.[19] Ventricular dilation,[20] myocardial fibrosis,[21] myocardial calcification, myocyte hypertrophy, increased collagen interstitial matrix,[20] uremic autonomic neuropathy,[22] impaired metabolism of potassium, calcium, and phosphate have been suggested as potential mechanisms for QT dispersion prolongation in patients with chronic renal failure.[19,23,24]

5.1. Limitations

The study group involved a relatively small number of patients; however, we overcome this problem by using the appropriate statistical tests. We measured QT dispersion manually using magnifying lens instead computer-assisted QT dispersion calculations. However, our method has been described in previous studies. Moreover, inter- and intraobserver variability was not done for this technique with high variability.

6. Conclusions

QTc dispersion can be used as a simple, accurate and inexpensive tool correlated with the severity of coronary artery disease in patients with acute ST elevation myocardial infarction. For the first time we managed to correlate QTc dispersion with the severity of coronary artery lesion as assessed by a novel scoring system, the SYNTAX score.

Conflict of interest

No conflict of interest.

Recommendations

Further large scale studies should be carried out to confirm the relationship between QTc dispersion and SYNTAX score. Measurement of QTc dispersion should be done routinely for all patients admitted with acute myocardial infarction.

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