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Expert Opinion Article

Correlation Of Corrected QT Interval With Quantitative Cardiac Troponin I Levels And Its Prognostic Role In Non ST Elevation Myocardial Infarction

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ABSTRACT

OBJECTIVES

Presence of different risk groups in non-ST-elevation acute coronary syndrome (NSTE-ACS), indicate the need for new tools to perform early diagnosis and prognostic stratification. In this sense, it has been shown that the corrected QT interval prolongation is an independent risk marker in NSTE-ACS with or without acute ischemic changes. of this study is to assess the correlation between prolongation of corrected QT interval and cardiac Troponin I in prognosis of patients with Non ST elevation Myocardial Infarction.

METHODS :

The study included 154 patients who presented to the Department of Cardiology, NEIGRIHMS, Shillong with NSTEMI . Non-STEMI myocardial infarction is characterized by abnormal cTnI ≥ 0.04 ng/ml. A 12-lead ECG was performed at admission in all cases and then at 6, 12, 18, 24 and 48 h post-admission. Blood samples were obtained after ≥ 6 hours since the beginning of the last episode of chest pain to assess cTnT . Major clinical events (MCE) observed up to 30 days post-discharge and considered as composite endpoint are: cardiac death, non-fatal myocardial and recurrent angina which led to cine coronary angiography, and according to the results, the ensuing urgent revascularization treatment within 30 days of admission. Patients were divided into two groups according to the presence (group A) or absence (group B) of MACE. QTc measurements were done on each patient and the highest QTc measured in the ECGs within 48 h post-admission is considered as the final value for analysis . Maximum QTc (QTc-max) is defined as the most prolonged value in each case, and QTc at admission and QTc-max were correlated with cTnI in each group. A ROC curve was generated to relate the QTc with major cardiovascular events Sensitivity, specificity and positive predictive value was estimated for QTc score in comparison to Troponin I levels for presence or absence of major cardiovascular events.

RESULTS The mean QTc of the study population was 466.60 ± 19.86. The mean QTc in patients who had MACE was 485.94 ± 25.95 while it was 465.81±11.89 in patients without MACE. While analysing the association between means of QTc in MACE present and MACE absent it was found to be statistically significant.(P≤0.001)

ROC curve analysis showed that the optimal QTc cut-off value for predicting was 463 ms, with Standard error = 0.056, 95% confidence interval= 0.682 to 0.851. QTc > 0.463 s. Sensitivity: 75.4%. Specificity: 65.8% (AUC = 0.856, 95% CI: 0.682 to 0.851)

The correlation between QTc-max and QTc at admission with cTnI in both groups resulted in a correlation coefficient of 0.593 between QTc-max and cTnI,(p < 0.001)

CONCLUSION : There is a significant correlation between prolongation of corrected QT interval and cardiac Troponin I in prognosis of patients with Non ST elevation Myocardial Infarction . QTc-max correlated with troponin levels and was an independent risk predictor. QTc can be considered as a useful and efficient tool for the prognostic stratification of NSTEMI, and its inclusion in future risk scales should therefore be given due consideration.

Introduction:

Presence of different risk groups in non-ST-elevation acute coronary syndrome (NSTE-ACS), indicate the need for new tools to perform early diagnosis and prognostic stratification. In this sense, it has been shown that the corrected QT interval prolongation is an independent risk marker in NSTE-ACS with or without acute ischemic changes.

However, there is scarce information about relationship of QTc with other variables of known prognostic value, such as cardiac troponins. This study will look for a bedside marker for early diagnosis and prognosis.

Study Hypothesis : Prolonged QT interval is positively correlated with troponin I levels in NSTE-ACS

Aims and objectives:
The purpose of this study is to assess the correlation between prolongation of corrected QT interval and cardiac Troponin I in prognosis of patients with Non ST elevation Myocardial Infarction.

METHOLOGY: An hospital based prospective observational study was carried out in the Department of Cardiology, NEIGRIHMS, Shillong in the period between .The project was approved by the Institutional scientific advisory committee as well as the Institutional Ethics committee. Consecutive recruiting was carried out after the research was duly explained and Informed consent duly signed.

Study Participants:
154 patients who presented to the Department of Cardiology, NEIGRIHMS, Shillong with NSTEMI were considered. All patients satisfying the inclusion and exclusion criteria and having given an informed consent to participate in the study were selected for the study.

Inclusion criteria:
1. Aged >18 years,
2. Admitted in hospital due to NSTE ACS, with or without acute ischemic ECG changes, classified as Braunwald´s subclass II-IIIB.

Exclusion criteria:
1. ST-segment-elevation AMI criteria.
2. Flat T wave (< 0.2 mV).
3. Wide QRS (≥ 0.12 s)
4. Serum potassium ≤ 3.5 mEq/l.
5. Severe ventricular hypertrophy.
6. Valve disease or severe cardiomyopathy.
7. Patients receiving antiarrhythmic or QT interval modi-fying drugs
8. Wolff-Parkinson-White, atrial fibrillation, atrial flutter or frequent/bigeminate extrasystoles

Sampling Technique : Consecutive sampling was done ; all patients fulfilling the criteria was enrolled in the study consecutively.

Study procedure Patients with unstable angina (UA) and non-Q wave myocardial infarction were included in the study. Unstable angina is defined as typical angina chest pain without elevation of biochemical markers, and with or without ECG changes. Non-STEMI myocardial infarction is characterized by abnormal cTnI ≥ 0.04 ng/ml. A 12-lead ECG was performed at admission in all cases and then at 6, 12, 18, 24 and 48 h post-admission. Blood samples were obtained after ≥ 6 hours since the beginning of the last episode of chest pain to assess cTnT. Demographic variables at admission such as age, gender, height, weight, arterial pressure, history of myocardial infarction, hypertension, diabetes mellitus, smoking, hypercholesterolemia, family history of coronary disease, cerebrovascular disease, and previous coronary revascularization were noted. All patients were classified at admission according to the TIMI score for NSTE-ACS.
After basal characterization, all patients were followed-up for 30 days after discharge.

Study endpoints
Major clinical events (MCE) observed up to 30 days post-discharge and considered as composite endpoint are: cardiac death, non-fatal myocardial infarction (defined by increased biochemical markers of myocardial injury, characteristic dynamic and evolving electrocardiographic changes and typical prolonged chest pain) and recurrent angina which led to cine coronary angiography, and according to the results, the ensuing urgent revascularization treatment within 30 days of admission. Patients were divided into two groups according to the presence (group A) or absence (group B) of MCE.

Measurement of corrected QT interval
QTc measurements were done on each patient and the highest QTc measured in the ECGs within 48 h post-admission is considered as the final value for analysis. Bazett´s formula is used to calculate QTc according to heart rate. QTc ≥ 0.450 s in men and ≥ 0.470 s in women are considered abnormally prolonged. Maximum QTc (QTc-max) is defined as the most prolonged value in each case, and QTc at admission and QTc-max were correlated with cTnI in each group.

Cardiac troponin I measurement
cTnI is measured in all cases, the sample is collected ≥ 6 h after the last angina episode. Concentrations ≥ 0.04 ng/ml are considered to be positive for myocardial injury. A second measurement is done in patients in whom the first determination was negative

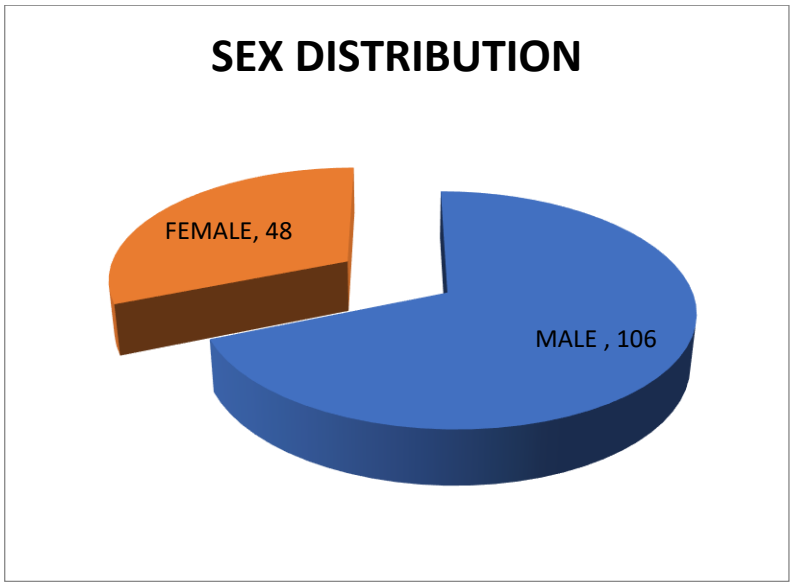
Statistical analysis:
Descriptive analysis was used to describe the socio - demographic characteristics of the study subjects. Continuous variables were expressed as mean

standard deviation and percentages were used for categorical behaviours.
Statistical significance was defined as a p value less than 0.05. Data entry and analysis was done on SSPS version 22.0

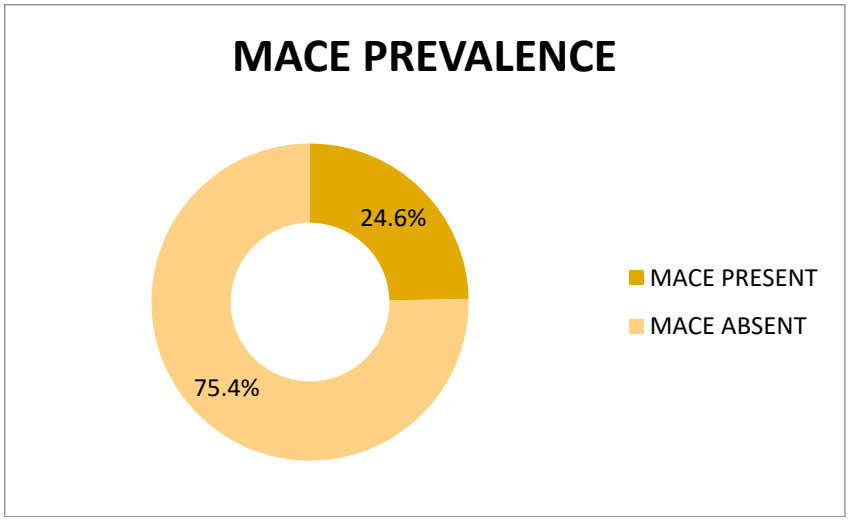
A ROC curve was generated to relate the QTc with major cardiovascular events Sensitivity, specificity and positive predictive value was estimated for QTc score in comparison to Troponin I levels for presence or absence of major cardiovascular events.

RESULTS
A total number of 154 patients presenting with NSTEMI and admitted in the Department of Cardiology , NEIGRIHMS during the 1 year study period were evaluated in this study.

Age and Sex Distribution of cases:-
The mean age of the patients enrolled in the study was 53.90 ±8.24 yrs. Most of the patients were in 5th , 6th and 7th decade of life .
106 (68.83 %) patients were male and 48 (31.14%) were female



ENDPOINT
30-day MACE occurred in 38/154 patients (24.6%). Out of these patients, 4/154 (4.6%) patients died within 30 days ; 12/154 (7.79 %) patients had suffered recurrent non fatal MI within 30 days; 22/154 (14.2%) patients suffered Unstable Angina requiring repeat revascularization within 30 days. Rest of the patients did not suffer MACE.



CLINICAL CHARACTERISTICS OF STUDY POPULATION ACCORDING TO OCCURRENCE OF MACE

	MACE PRESENT	MACE ABSENT	P VALUE
No. of Patients	38	116	
Age (Mean)	61.71 ± 9.31	51.34 ±6.02	P ≤ 0.01
Male gender	22	84	0.106
SMOKING	18	61	0.708
DM	20	38	0.0345
HYPERTENSION	24	60	0.261
H/O CAD	6	12	0.388
DYSLIPIDEMIA	25	65	0.345

The mean age of the patients having MACE was 61.71 ± 9.31 yrs while patients without MACE had a mean age of 51.34 ±6.02 yrs. The patients with MACE had a significantly higher age when compared to patients without MACE.(P ≤ 0.01)

The patients with MACE had a significantly higher incidence of Diabetes Mellitus [20(52.6%) vs 38(32.75%)] (p =0.0345)

No significant association was found between patients with MACE and without MACE in respect to gender , hypertension , history of CAD and dyslipidemia.

ASSOCIATION OF CLINICAL AND ECG CHARACTERISTICS WITH MACE

	MACE PRESENT	MACE ABSENT	P VALUE
HR (MEAN)	93.71 ± 13.70	90.27 ± 10.50	0.107
LVEF(MEAN)	45.52 ± 6.41	48.04 ± 5.85	0.025
SBP(MEAN)	123.94 ± 14.19	125.7 ± 10.06	0.402
QRS(MEAN)	80.36 ± 10.52	79.71 ± 7.83	0.685
ST DEV>0.5(N)	20	59	1.055
TIMI SCORE(MEAN)	3.76±0.75	2.24±0.84	≤0.001
TIMI SCORE>2(N)	33	51	≤0.001
KILLIP CLASS > 1, N	28	15	0.004
MULTIVESSEL CAD	18	39	0.175

TIMI SCORE AND MACE

The mean TIMI score in patients with MACE was 3.76±0.75 and was significantly higher in patients without MACE 2.24±0.84 (p≤0.001).

In 33 of the 38 patients with MACE the TIMI SCORE was more than 2 while 51 of the 116 patients without MACE had TIMI SCORE>2. The no patients with TIMI SCORE>2 had significantly higher rate of MACE . (p≤0.001).

KILLIP CLASS AND MACE

28 OF THE 38 patients with MACE had **KILLIP CLASS > 1 ; while 15 of 116 patients without MACE** had **KILLIP CLASS > 1.** The no patients with **KILLIP CLASS > 1**had significantly higher rate of MACE . (p=0.004).

HEART RATE AND SYSTOLIC BLOOD PRESSURE WITH MACE

The mean heart rate at admission in patients having MACE was 93.71 ± 13.70 while in patients without MACE was 90.27 ± 10.50. No statistical significance was noted. (p=0.107)

The mean systolic blood pressure at admission in patients having MACE 123.94 ± 14.19 while in patients without MACE was 125.7 ± 10.06. No statistical significance was noted. (p=0.402)

No significant association was found between patients with MACE and without MACE when mean QRS and mean LVEF were compared.

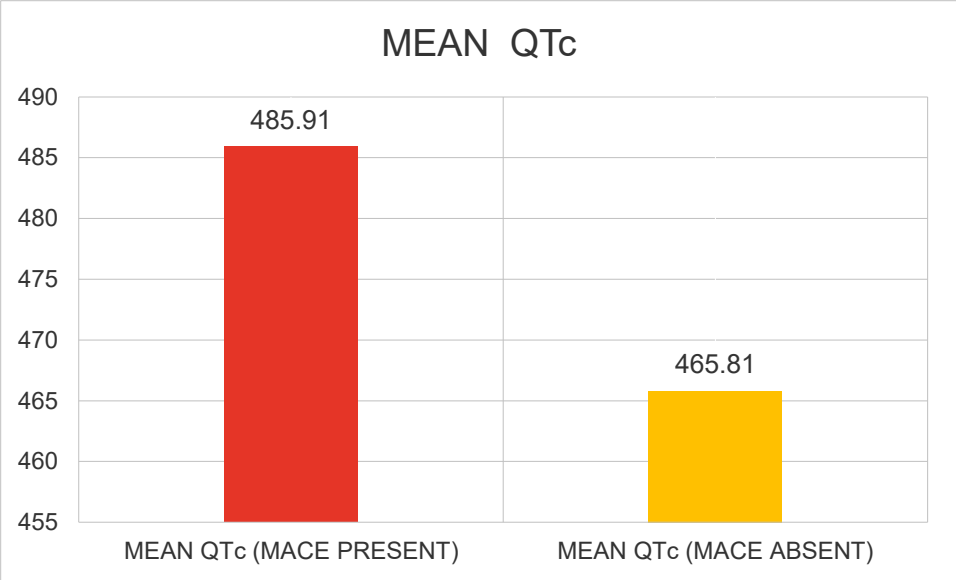
The number of patients with multivessel CAD was not significantly higher in patients having MACE than in without. (P = 0.175)

The number of patients with ST deviation more than 0.5mm in patients having MACE was not found to be significantly higher than those without MACE.

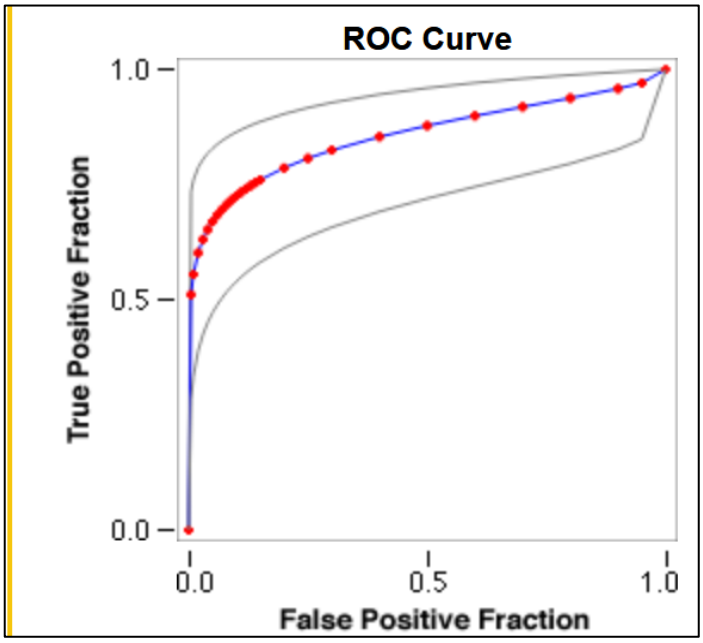
ASSOCIATION OF QTc with MACE IN NSTEMI

The mean QTc of the study population was 466.60 ± 19.86. The mean QTc in patients who had MACE was 485.94 ± 25.95 while it was 465.81±11.89 in patients without MACE.

While analysing the association between means of QTc in MACE present and MACE absent it was found to be statistically significant.(P≤0.001)



ROC curve analysis showed that the optimal QTc cut-off value for predicting was 463 ms, with Standard error = 0.056, 95% confidence interval= 0.682 to 0.851. QTc > 0.463 s. Sensitivity: 75.4%. Specificity: 65.8% (AUC = 0.856, 95% CI: 0.682 to 0.851)



Summary Statistics:

Total Cases: 154

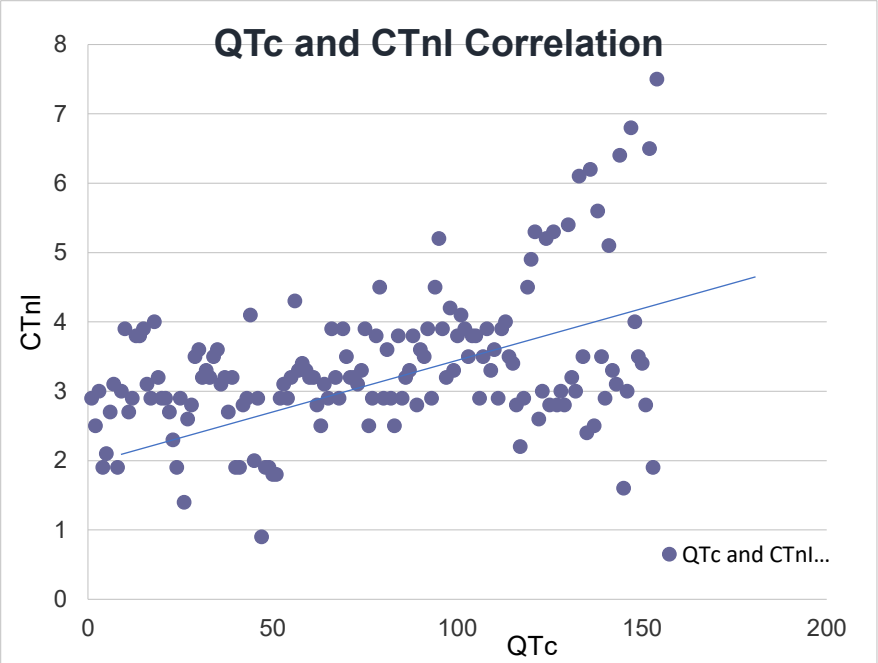
Positive Cases: 38

Negative Cases: 116

Fitted ROC Area: 0.856

CORRELATION BETWEEN CARDIC TROPONIN I (CTnI) AND QTc

The correlation between QTc-max and QTc at admission with cTnI in both groups resulted in a correlation coefficient of 0.593 between QTc-max and cTnI,($p < 0.001$)



DISCUSSION

The 12 lead ECG is the first tool in evaluation of patient presenting with symptoms suggestive of ACS**.** Several studies have been published showing the prolonged corrected QT interval (QTc) as an independent risk marker in NSTE-ACS with or without acute ischemic changes, both at 30-day post-discharge or long-term follow–up. (1 - 3).

This study was done with an aim to assess the correlation between prolongation of corrected QT interval and cardiac Troponin I in prognosis of patients with Non ST elevation Myocardial Infarction.

A total number of 154 patients presenting with NSTEMI and admitted in the Department of Cardiology , NEIGRIHMS during the 1 year study period were evaluated in this study.

The mean age of the patients enrolled in the study was 53.90 ±8.24 yrs. Most of the patients were in 5th , 6th and 7th decade of life .

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ENDPOINT

The endpoint of 30-day MACE occurred in 38/154 patients (24.6%). Out of these patients, 4/154 (4.6%) patients died within 30 days ; 12/154 (7.79 %) patients had suffered recurrent non fatal MI within 30 days; 22/154 (14.2%) patients suffered Unstable Angina requiring repeat revascularization within 30 days. Rest of the patients did not suffer MACE.

The patients with MACE had a significantly higher incidence of Diabetes Mellitus [20(52.6%) vs 38(32.75%)] (p =0.0345)

No significant association was found between patients with MACE and without MACE in respect to gender , hypertension , history of CAD and dyslipidemia.

TIMI SCORE AND MACE

The mean TIMI score in patients with MACE was 3.76±0.75 and was significantly higher in patients without MACE 2.24±0.84 (p≤0.001).

The no patients with TIMI SCORE>2 had significantly higher rate of MACE . (p≤0.001).

The no patients with **KILLIP CLASS > 1** had significantly higher rate of MACE . (p=0.004). 28 OF THE 38 patients with MACE had **KILLIP CLASS > 1 ; while 15 of 116 patients without MACE** had **KILLIP CLASS > 1.**

ASSOCIATION OF QTc with MACE IN NSTEMI

QT c was found to be significantly higher in patients with MACE than in patients without MACE .(P≤0.001) The mean QTc in patients who had MACE was 485.94 ± 25.95 while it was 465.81 ± 11.89 in patients without MACE.

ROC curve analysis showed that the optimal QTc cut-off value for predicting was 463 ms, with Standard error = 0.056, 95% confidence interval= 0.682 to 0.851. QTc > 0.463 s. Sensitivity: 75.4%. Specificity: 65.8% (AUC = 0.856, 95% CI: 0.682 to 0.851)

CORRELATION BETWEEN CARDIC TROPONIN I (CTnI) AND QTc

The correlation between QTc-max and QTc at admission with cTnI in both groups resulted in a correlation coefficient of 0.593 between QTc-max and cTnI,(p < 0.001)

There are a very similar studies studying the relation of QTc with prognosis in NSTEMI.

Our study was in sync with most of the previous studies .

In 2000, Döven et al correlated QT dispersión (QTd) with cTnT levels in NSTE-ACS patients. They found that QTd was greater in cases with elevated cTnT and postulated QTd as a non-invasive marker of myocardial injury and a useful variable to select high risk patients. (4)

Rushkin et al observed the highest transient QTc prolongation in non-Q wave AMI compared to UA patients, and concluded that the analysis of this variable could help to the early differentiation of UA from non-Q wave AMI, suggesting that QTc prolongation would not only be related to ischemia but also with the degree of necrosis(5)

In 2003, Gadaleta et al published the results of 102 patients with UA and acute ischemic changes. They reported that a QTc ≥ 0.460 s in the admission ECG was an independent risk marker for clinical events such as cardiac death, non-fatal myocardial infarction and need for urgent revascularization at 30 day follow-up (6)

Kenigsberg et al showed for the first time that QTc prolongation is the earliest electrocardiographic sign of early transmural ischemia, which was present in 100% of the studied cases. (7)

Rajvanshi S et al found that QTc-max interval has a strong positive linear correlation with cTnI level. Prolonged QTc has utility as an independent high risk predictor in NSTEMI population (8)

Llois SC et al reported that the correlation between QTc-max with cardiac troponin T resulted in a correlation coefficient of 0.38 (p< 0.001). On multivariate analysis, QTc > 0.458 sec was an independent predictor of MACE risk in NSTEACS population (OR = 4.1, p=0.002) (9)

Jimenez-Candil et al reported that risk of MACE was higher when prolonged QTc (> 450 ms) was present in patients with Troponin I > 0.1 ug/l (72% vs 35%; OR 4.8; p<0.001) vs. negative troponin release (70% vs 15%; OR 13; p<0.001). (10)

Apart from Rajvanshi S et al all other studies included both NSTEMI and UA. But our study included exclusively cases of NSTEMI and found significant association of QTc with MACE and had significant positive correlation with Cardiac troponin I in patients of NSTEMI.

CONCLUSION

There is a significant correlation between prolongation of corrected QT interval and cardiac Troponin I in prognosis of patients with Non ST elevation Myocardial Infarction . QT c was found to be significantly higher in patients with MACE than in patients without MACE .(P≤0.001) . The mean QTc in patients who had MACE was 485.94 ± 25.95 while it was 465.81±11.89 in patients without MACE. ROC curve analysis showed that the optimal QTc cut-off value for predicting was 463 ms, with Standard error = 0.056, 95% confidence interval= 0.682 to 0.851. QTc > 0.463 s. Sensitivity: 75.4%. Specificity: 65.8% (AUC = 0.856, 95% CI: 0.682 to 0.851) QTc-max correlated with troponin levels and was an independent risk predictor. QTc can be considered as a useful and efficient tool for the prognostic stratification of NSTEMI, and its inclusion in future risk scales should therefore be given due consideration.

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