doi.org/10.36721/PJPS.2021.34.1.SP.417-421.1

To assess the co-relation between corrected qt interval prolongation and abnormal scan during vasodilator nuclear stress test

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Abstract: In the detection of coronary heart diseases amongst the non-invasive techniques the role of myocardial perfusion imaging is indexed. The rationale of this study was to compare the different parameters and the association between the exercise MPI and vasodilator MPI in the detection of coronary artery disease (that is prolonged Qt interval with the size of perfusion defects). It was a cross-sectional prospective study with purposive non-probability sampling technique which was conducted in a tertiary care hospital from January 2020 to June 2020 for a period of 6 months. All patients regardless of gender were included in this study and age ranging from 30 to 80 years with comorbidities ranging from diabetes, hypertension and smokers were also included. A total of 100 patients were included in this study out of which 81% were male, 50% were diabetics, 69% were hypertensive, 39% had a history of coronary artery disease, 25% were smokers and 63% had hyperlipidemia. For statistical analysis SPSS 21 was applied and significant association was observed between DTS treadmill score and the perfusion defect in vasodilator MPI, corrected Qt interval and DTS tread mill score and between corrected Qt and size of the perfusion defect (P value < 0.001). It was thus seen that the different components of the noninvasive nuclear stress test tend to co-relate and thus aid in the detection of coronary artery disease increasing the accuracy of results.

Keywords: Coronary artery disease, nuclear stress test, QT interval, vasodilator.

INTRODUCTION

Coronary heart disease is a major cause of mortality and this health problem is reaching pandemic in both developed and developing countries. Today the utilization 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 (Chaturvedi *et al*., 2007). The interval of QT depicts the overall length of ventricular myocardial depolarization and re-polarization. Such a period is measured from the start of the QRS complex to the end of the Twave (Chaturvedi *et al*., 2007). Since the corrected QT interval has been affiliated with myocardial repolarization and electrical stability thus when prolonged it reflects electrical instability.

According to the ischemic cascade the prolongation of QT interval shows initial ischemia. The QT prolongation has been broadly detected in patients with the myocardial infarction and it has been proposed as one of the initial ECG abnormalities in transmural ischemia and a predictive indicator of arrhythmic events following AMI (Monitillo *et al*., 2016). In link with this observation, the ACTION trial revealed that, in patients with coronary artery disease, a QT interval extension of more than 430 milliseconds was a predictor of death comparable to 3-vessel disease (Stankovic *et al*., 2015) however; this study was implemented in patients with stable coronary artery disease. It has been revealed that the myocardial ischemia that occurs during balloon inflation in percutaneous transluminal coronary angioplasty directly produces variations in ventricular repolarization, comprising a major prolongation in the QT interval that continues for minutes, or even hours (Islam *et al*., 2020). The prolonged QT interval detected in patients with UA or AMI returned to normal values 48 hours after satisfactory myocardial revascularization and is a well identified marker that has remained merged into the factors tested for the calculation of ischemic risk in acute coronary syndrome (ACS) (Rodríguez-Jiménez *et al*., 2019).

Jensen (Jensen *et al*., 2015; Nowinski *et al*., 2000) revealed a QT decline after successful recanalization of the affected artery and George (George *et al*., 2015) noted a larger decrease of this electrocardiographic parameter following PCI as related to fibrinolysis. Eslami (Eslami *et al*., 2013) also revealed a major QT decline following PCI (5.8 ms mean related with 3.6 ms, p <0.001). These studies presented that as soon as the artery is effectively opened through primary coronary intervention the recommended treatment in international guidelines (Helmy *et al*., 2017; Nabati *et al*., 2018; Shawl *et al*., 1990) ventricular repolarization homogeneity is

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reconstructed between the affected myocardium's different zones. It has been postulated that the regulation of this interval in subjects who have gone through angioplasty is an indicator of satisfactory reperfusion (David *et al*., 2007). These outcomes suggest the probability of employing the QT interval prolongation as an initial sign of acute and transient myocardial ischemia. Objective of the current study was to evaluate the association of corrected QT interval prolongation with abnormal scan during vasodilator nuclear stress test.

MATERIALS AND METHODS

This cross-sectional observational study was carried out from January to June 2020, with purposive non-possibility grouping technique. The protocol of the study was permitted by the Ethical and Research Committee of the institute. The total number of patients was 100, who were referred to nuclear cardiology laboratory of Liaquat National Hospital for evaluation of chest pain.

Inclusion and exclusion criteria

Patients were excluded from the analysis if they had atrial fibrillation, bundle branch block, pacemakers or were treated with any drugs known to affect the QT interval. All included patients experienced a usual Bruce multi-stage maximal treadmill protocol.

Treadmill protocol

There were three electrocardiographic leads which were monitored closely and constantly. Blood pressure was monitored in interval of every 3 minutes. For the comparison of QT interval of rest and at peak of exercise, twelve lead electrocardiograms were used. Exercise testing was dismissed once patients touched an arbitrary percentage of the expected maximum heart rate or after well-renowned end points were met. Subjects who did not attain age-predicted heart rate were also involved in the study. All measurements were obtained by 2 sole observers. QT segments were measured by callipers through peak exercise and rest. When U waves were existent, the QT was measured to the nadir of the curve between the T and U waves. QT and RR intervals were measured in different leads to check for precision, and the mean was taken in cases of inconsistency in the 12-lead electrocardiogram. The QT interval was modified for heart rate by means of Bazett's formula. In conditions of T- and P-wave combination, the conclusion of the T wave was taken at the point where prolongation of the mark of greatest rapid descent transacted the baseline. Tracings wherever the configuration of the T wave was not perfect for understanding were omitted from the study.

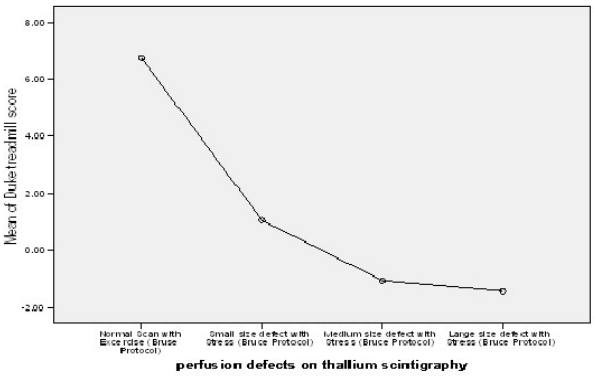
Gated SPECT-MPI data was recorded and analyzed for presence, extent and reversibility of myocardial perfusion defect. Stress induced left ventricular dilatation and increased lung uptake was also recorded (Pekdemir *et al*., 2006). The scans were explained by another nuclear radiologist's perspective of the QT analysis. Perfusion imaging data was stratified into Normal, low, intermediate and high risk groups according to severity of perfusion defect.

STATISTICAL ANALYSIS

For analysis of data all the variables were placed into the Statistical Package for Social Sciences software, version 21 (*SPSS Inc*). The data of descriptive statistics were calculated and presented as means and standard deviations, for continuous variables like age, exercise time (minutes), age predicted maximum heart rate, ST segment shift and DTS. Frequency and percentages were computed for gender, risk factors (hypertension, diabetes, smoking, dyslipidemia and family history of premature CAD), angina index, DTS and MPI categories. Chi-Square was applied for evaluation of demographic and clinical data whereas One-way ANOVA was applied to determine the correlation between corrected QT interval and MPI results. P value <0.05 was considered as significant.

RESULTS

A total of 100 patients were included in this study out of which 81% were male, 50% were diabetics, 69% were hypertensive, 39% had a history of coronary artery disease, 25% were smokers and 63% had hyperlipidemia (not shown in data).

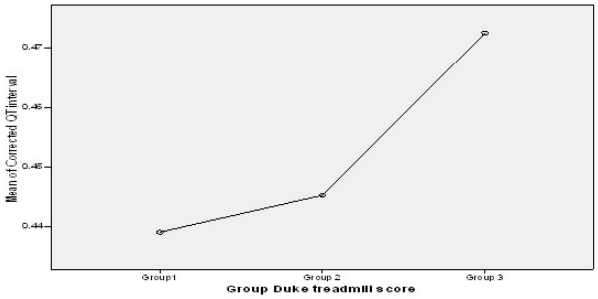


Using ANOVA test, there was a statistically significant relationship between DTS and perfusion defects (*p* value < 0.001)

Fig. 1: Relationship between DTS and Perfusion Defects

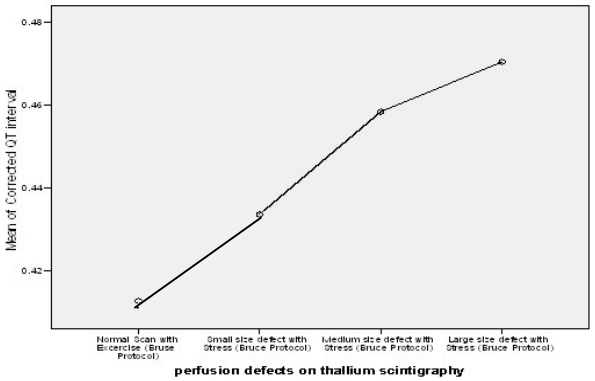
Table III shows the mean ages of patients who had normal, mild, moderate and large defects were 52.28, 60.6, 61.16 and 57.16 respectively and were statistically significant showing p value of ≤0.05. The percentage of male gender according to table I in the normal, mild, moderate and large defects groups were 64%, 92%, 92%, 76% and it was found to be statistically significant. Similarly the diabetics were found to be significant in the

different groups whereas the hypertensives showed insignificant difference on comparison. The percentage of patients with history of coronary artery diseases were 24%, 52%, 56% and 24% for normal, mild, moderate and large group defects with a significant p value. The smokers and the hyperlipidemic patients however showed insignificant p value in terms of comparison amongst different groups. The resting heart rate showed percentages of 73.4%, 69.5%, 64.4% and 77.3% for the normal, mild, moderate and large group defects respectively and was found to be significant. The resting systolic blood pressure with values of 132.56, 128, 129 and 138 for normal, mild, moderate and large defect was found to be insignificant when compared. However the parameters of corrected QT, BMI and DTS were found to have significant p values when compared amongst the different groups. Table 2 shows the drug administered was Dipyridamole for the test conduction along with the protocol followed.



Using ANOVA test, there was a statistically significant relationship between DTS and perfusion defects (p value < 0.001)

Fig. 2: Relationship between DTS and QT interval



Using ANOVA test, there was a statistically significant relationship between perfusion defects and QT interval (p value < 0.001).

Fig. 3: Relationship between Perfusion Defects and QT interval

Fig. 1 showed statistically significant relationship between the DTS and the perfusion defect with p value of <0.001 i.e., with low DTS score, the vasodilator scan shows almost normal result or mild and as the DTS score risk increases to high the perfusion defect also increases.

Table 1: DTS (Duke Treadmill Score Groups)

Groups Duke Treadmill Score	
Duke Treadmill Score 6 to 13	Group 1
Duke Treadmill Score -10 to 5	Group 2
Duke Treadmill Score -18 to -11	Group 3

Fig. 2 illustrated the different groups of DTS score which have been specified in the table I below when compared to the mean of corrected QT interval showed a statistical significance with p value of <0.001 i.e. from low to high risk DTS group there was an increase in the mean of corrected QT.

Table 2: Protocol for vasodilator nuclear stress test

Drug used	
Dipyridamole	Infused over a 4 minute period at 0.142mg/kg/minute.

Fig. 3 depicted the relation between the perfusion defects and the mean of corrected QT which was significant with p value <0.001. That is with an increase in the mean of corrected QT the defect size also increased from mild to large.

DISCUSSION

The first figure of the study showed a significant relationship between the DTS score and the defect size as noted on the nuclear stress test that as the DTS score steadily rises to be categorized in the range of high risk, the defect size also becomes large. To evaluate the suspected patients of CAD, the key method used is duke treadmill score (DTS) which gives diagnostic and prognostics evidence using factors like chest pain, exercise time and ST-segment depression (Günaydın *et al*., 2016). Shawl *et al* reported the gradual diagnostic value in DTS which used ROC analysis for the prediction of the substantial CAD present (75% stenosis) or the presence of severe CAD (50% left main disease or 3 vessel CAD). The results they have shown clearly revealed the cardiac events with high, moderate and low-risk grouping of DTS. The data revealed that yearly mortality were 7%, 2% and 0.6% respectively; those were near to the original DTS (Shawl *et al*., 1990). Earlier it was also reported by Hachamovitch *et al* that nuclear stress test also called as stress myocardial perfusion single –photon emission computed tomography (MPS) improved a gradual prognostic value in DTS for the evaluation and diagnosis of severe and major cardiac events (Hachamovitch *et al*., 2002).

The evaluation of this interesting association between stress MPS and high DTS was done by Shaikh *et al* in a minor group of population (N = 13) in the year 2011. They reported that all the patients with high DTS had high risk MPS (Shaikh *et al*., 2011).

Table 3: Demographic, clinical and electrocardiographic findings of the study population

Perfusion defects on thallium scintigraphy	Normal scan	Mild defect	Moderate defect	Large defect	p-value
Age (yrs)	52.28±10.23	60.60±9.46	61.16±11.10	57.16±8.44	0.007
Male gender	64.0%	92.0%	92.0%	76.0%	0.03
DM	56.0%	64.0%	24.0%	56.0%	0.03
Hypertension	72.0%	56.0%	68.0%	80.0%	0.32
H/O CAD	24.0%	52.0%	56.0%	24.0%	0.02
Smoker	8.0%	12.0%	20.0%	20.0%	0.21
Hyperlipidemia	64.0%	76.0%	60.0%	52.0%	0.36
Resting heart rate (beats/min)	73.44±13.80	69.52±9.49	64.60±12.37	77.36±13.37	0.003
Resting systolic blood pressure, *mm Hg*	132.56±19.89	128.00±18.26	129.00± 17.44	138.40±20.05	0.219
Corrected QT interval	.41±0.03	.43±0.04	.45±0.02	.47±0.03	<0.000
BMI	28.03±4.71	25.35±4.51	27.55±5.07	28.45±3.35	0.073
DTS	-9 to 12	-8 to 9	-18 to 13	-15 to -10	<0.000

Chi-Square was applied where $p \leq 0.05$ shows significant data

Whereas the second fig. of the study showed linear relationship between the DTS score and the corrected QT interval that as the corrected QT interval increased the patients DTS score also increased concomitantly. In the early stage of myocardial ischemia, many events occur simultaneously like diastolic dysfunction and systolic dysfunction represented by the ischemic cascade which interpret pathophysiological range further followed by changes in ECG and angina pectoris. The results of our study showed that ischemia induced QT interval prolongation is observed primarily during myocardial ischemia and proposed that prolongation of repolarization might symbol prominently in the ischemic cascade. The modification in the concept of ischemia cascade was represented by Ikonomidis *et al*. (2000) representing the 100% cases which were studied showed the prolongation of the QT interval and QT dispersion in ischemia. Previously it was indicated that QT dispersion showed contrarily during exercise in normal subjects compared to patients with coronary disease. It was also noted that the severity of coronary artery damage could also be identified by dispersion of corrected QT-interval. The values >59 ms have been related with myocardial viability (Ikonomidis *et al*., 2000). QT was also used as an indicator for other problems such as ventricular arrhythmias, CAD and myocardial viability. Nevertheless if test analyzation and subsequent patient management was based only on ECG values of ischemia, then the grouping and detection of endangered patients would be fewer than that attained with the DTS. Numerous prior reports have tried to compare the presence of exercise-induced ischemia with the presence and extent of significant coronary lesions (Morise *et al* 2000).

The third figure basically depicted the object of the study and showed the association of corrected QT with the defect size on the nuclear stress imaging which was shown as linear that is as the corrected QT increased, the defect size also increased.

One more study related to MESA (Multi-Ethnic Study of Atherosclerosis) has stated an autonomous affirmative relation between the baseline QT and cardiac and vascular events in middle-aged participants deprived of earlier CVD. The most significant thing about this study was that it was not specific to any sex and civilization (Helmy *et al*., 2017).

CONCLUSION

Thus, it is concluded that in the detection of coronary artery disease the different parameters of non-invasive testing tend to co-relate in terms of predicting the severity of coronary artery disease as depicted by our study.

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