ORIGINAL ARTICLE

EFFECT OF SEVERITY OF ISCHEMIA ON QT DISPERSION IN PATIENTS WITH CORONARY ARTERY DISEASE

Sadia Mubarak, Sidra Hamid*, Bushra Riaz, Mamoona Shafiq***, Zubia Razzaq†**

Department of Physiology, Islamabad Medical and Dental College, Islamabad, *Rawalpindi Medical University, Rawalpindi, **Pak International Medical College, Peshawar, ***Islam Medical College, Sialkot, †HITEC-Institute of Medical Sciences, Taxila, Pakistan

Background: Coronary artery disease (CAD) is the most prevalent cause of death due to myocardial ischemia. QT dispersion is a marker of increased risk for myocardial ischemia events. The objective of this study was to find out the effect of severity of ischemia on ventricular repolarization heterogeneity by measuring and comparing QT dispersion in single, double and triple coronary artery disease patients. **Methods:** This cross-sectional comparative study was conducted in the Department of Physiology, Army Medical College (AMC) in collaboration with Electrophysiology Department, Armed Forces Institute of Cardiology (AFIC). Forty patients aged 55±8 Years with CAD were included in the study. Holter monitors were used to attain ECG recordings digitally with ten electrodes. For exploration of digital QT dispersion data CardioScan Luxury version was used. **Results:** Out of 40 patients 18 (45%) had single, 16 (40%) double, and 6 (15%) had triple vessel disease. A significant difference was noted on comparison across mean values of QT dispersion in three groups with single, double and triple vessels coronary artery disease (p=0.01). There was also a remarkable difference of QT dispersion between single and triple vessel disease patients (p=0.007). **Conclusion:** Ventricular repolarization heterogeneity increases with the ischemia. Patients with triple vessel disease are more prone to risk of developing life threatening arrhythmias.

Keywords: QT dispersion, Ischemia, Holter monitoring, Coronary artery disease

Pak J Physiol 2022;18(4):11–3

INTRODUCTION

Ischemic heart disease (IHD) is the foremost root of sudden cardiac death.[1] Coronary ischemia is caused by coronary artery occlusion which can lead to ischemia related changes in duration of repolarization.[2] This altered duration of repolarization period between adjoining myocardial cells may directly incite development of early after depolarizations (EAD).[3] These ischemic changes can modify the pathway of action potential and can build re-entrant circuits which enables development of a polymorphic ventricular tachycardia termed 'torsade's de pointes'. Re-entrant circuits can result in sudden cardiac arrest.[4] Myocardial ischemia causes reduction of ATP and intracellular creatinine phosphate along with accretion of lactic acid and K^+ in interstitial fluid. Depletion of ATP causes diminished sodium potassium pump ATPase activity which results in elevated K^+ ions in extracellular fluid.[5]

QT dispersion (QTD) is an electrophysiological tool for measuring repolarization heterogeneity by measuring difference between minimum and maximum interval in a 12-lead ECG. Altered electrical potentials can increase 3-D dispersal of repolarization that can cause decrease of refractory period giving a tendency for re-entry of arrhythmias.[6] Arrhythmias in long QT syndrome are believed to be due to the generation of early or delayed after depolarizations as a result of triggered activity.[7] Reopening of 'L type' calcium channels plays an important role in developing early after depolarizations whereas enhanced calcium release from sarcoplasmic reticulum is the basis of delayed after repolarizations. Apart from 'triggered activity', re-entry circuits are established due to slow and fragmented repolarization process which provide a substrate for fatal ventricular arrhythmias.[8]

QT dispersion has been measured in many research ventures in the field of cardiac electrophysiology. It has been assessed as a good prognostic tool for cardiac death due to arrhythmias. Increased QT dispersion has been linked with augmented chances of fatal ventricular arrhythmias. Studies have shown that QT dispersion increases in various cardiac ailments like myocardial infarction, ventricular hypertrophies, heart failure, long QT syndrome and cardiomyopathies.[9]

In patients with myocardial ischemia QT dispersion decreases significantly after successful thrombolysis. Although the impact of exercise seems to worsen the ventricular repolarization heterogeneity due to residual ischemia.[10] The severity of ischemia increases with augmented number of occluded vessels. Positive correlation between the severity of ischemia and scattering of QTD has been reported in triple coronary vessel disease patients.[11] QTD decreases with effective regain in perfusion with percutaneous transluminal coronary angioplasty (PTCA) and re-stenosis can cause more dispersal of QTD. QT dispersion is significantly higher during the anginal episodes as matched with painless ischemic disorders.[11]

QT dispersion in CAD patients correlates with the extent and severity of ischemia and tends to be normal when ischemia is reduced after angioplasty. The

objective of this study was to see the possible correlation of QT dispersion with ischemic burden in terms of number of vessels involved, and to detect pair-wise comparison of QT dispersion between different groups of single, double and triple coronary vessels disease.

PATIENTS AND METHODS

This cross-sectional comparative study was carried out at Department of Physiology, Army Medical College in collaboration with Clinical Cardiac Electrophysiology Department of Armed Forces Institute of Cardiology from 2015 to 2019 after approval by Ethical Review Board of Army Medical College. Properly conversant and written consent from the patients were taken. Fifty-three diagnosed patients of coronary artery disease by cardiologists (defined as minimum one coronary artery vessels disease with more than 70% of occlusion) were included in the study with non-probability convenience sampling technique. Digital holters with diagnostic monitoring software technology were used to perform 12 lead ECG recording in CAD patients. Data of 13 patients were discarded due to uninterpretable recording. The final data comprised of total 40 patients labelled as 18 single, 16 double and 6 triple vessels patients. Data were analysed with Lux version of Cardio Scan.

The interval between Q and T in three consecutive beats were marked and measured with toggling of vertical parameters. QTD is the difference between the maximum and minimum intervals among 3 consecutive normal beats.

The data were analysed using SPSS-24. The numerical variables like age and QT dispersion were calculated as Mean±SD, whereas frequency and percentage were calculated for categorical variables like groups of patients having single, double or triple vessel disease. As the frequency of patients in different groups was small and did not follow the normal distribution, non-parametric, Kruskal Wallis test was used for comparison of means across the three groups. Pair-wise post hoc analysis was performed using Dunn-Bonferroni method. Value of alpha was adjusted at 0.05 with 95% confidence level.

RESULTS

Forty patients were recruited with mean age of 55±8 years (range 34–68 years). Frequency and percentage of patients with single, double and triple vessel disease are shown in Table-1. Mean value of QT dispersion was 41.30±7.22 mSec with a range of 30 to 56 mSec. Mean values of QT dispersion in three groups of patients with single, double and triple vessel disease are shown in Table-2. Calculated on nonparametric Kruskal Wallis test across the three groups, p was 0.01 (Table-2).

Table-3 shows the pair-wise comparison of QT dispersion between different groups. Also shown are unadjusted and Bonferroni adjusted p illustrating significant difference of QT dispersion between single and triple vessel disease groups (p=0.007).

Table-1: Frequency and percentage of patients with single, double and triple vessel disease

Coronary artery disease	Frequency	Percentage
Single vessel disease	18	45
Double vessel disease	16	40
Triple vessel disease	6	15

Table-2: Comparison of QT dispersion across the three groups of single, double and triple disease

Coronary artery disease	QTD (mSec)	*p*
Single vessel disease	38.44±6.14	0.01*
Double vessel disease	41.75±7.47	
Triple vessel disease	48.67±3.93	

*Significant

Table-3: Post hoc pair-wise comparison of QT dispersion between different groups

Group pairs	Unadjusted	Bonferroni adjusted
	p	
SVCAD-DVCAD	0.21	0.64
SVCAD-TVCAD	0.002	0.007*
DVCAD-TVCAD	0.03	0.11

*Significant

DISCUSSION

There is important increase in QT dispersal in CAD patients which is increased significantly with the number of vessels involved. Prolonged QT dispersion is ascribed to the changes due to ischemic injury. The conduction of electrical impulse alters in the regions with ischemia which can lead to decreased impulse transmission and longer action potential duration. Both may lead to heterogeneous repolarization patterns and ionic imbalances provoking development of re-entry circuits leading to fatal arrhythmias.

Almyahi *et al*[12] carried out a study to compare QT dispersion in patients with single, double and triple vessel disease. They compared QTD in 184 patients and 30 normal controls. They had 56 Single, 66 Double, 30 Triple and 32 left main stem coronary artery disease patients. They found that QT dispersion clearly increased with the Gensini scoring. Left ventricular dysfunction and history of myocardial infarction were associated with elevation of dispersal according to their multiple regression analysis.[12] Our findings are affirmative with their results that there is increase in dispersal of QT points in all 12 leads. This transient ischemia or chronic hypo-perfusion may lead to increased production of oxygen free radicals causing impairment of sarcolemma and ATPase activity leading to calcium overload which may trigger enzyme activities resulting in fatal arrhythmias.[13]

Recently, Al Alwany *et al*[14] concluded the same results. Their study compared 55 SVD, 39 DVD and 16 TVD patients. There was a significant difference in QTD between groups. QT dispersion was constantly increasing with vessels involvement but it also decreased with successful percutaneous transluminal coronary

angioplasty which caused restoration of normal blood flow to the ischemic tissues. After successful angioplasty effect of arrhythmias decreased significantly.[14]

Various studies support the view that QTD can be directly correlated with underlying extent of ischemia.[15] After successful coronary angioplasty there is a decrease in QTD, and it increases in cases of restenosis.[16] It has also been reported that changes in QT dispersion associate with the degree of ischemia related with amount of coronary vessels involved.[17] In our study QTD was analysed in attempt to evaluate the effect of severity of ischemia by the involvement of number of coronary arteries like single, double or triple vessels. The amount of QTD was significantly increased in triple vessel diseased patients which shows a simple method for evaluation of amount of myocardial risk and it seems to provide a good prognostic tool as a predictor of outcome in patients with coronary artery disease.

Our results are comparable with Helmy *et al*[9], who observed QT dispersion in non-Q wave myocardial infarction patents and correlated it with severity of underlying ischemia on the basis of number of vessels involved. They found that single vessel disease patients had significantly shortened QT dispersion (p=0.01) and corrected QT dispersion (p<0.001). Our results are comparable with their findings. Underlying CAD agonizes frequent prolonged episodes of silent ischemia that may subside QT dispersion.

CONCLUSION

Coronary artery disease is a major cause of sudden cardiac death especially with prevalence of two or more diseased vessels. The results of our study provide an insight into the factors affecting ventricular repolarization heterogeneity in relation to number of vessels involved. QT dispersion value provides a practical and non-invasive marker for recognizing patients at higher risk.

STUDY LIMITATIONS

The study was short duration and used convenience sampling. Consequently, our sample size was trivial and also the male to female ratio was not maintained.

REFERENCES

1. Ralapanawa U, Sivakanesan R. Epidemiology and the magnitude of coronary artery disease and acute coronary syndrome: A narrative review. J Epidemiol Glob Health 2021;11(2):169–77.
2. Tsvetkova AS, Azarov JE, Bernikova OG, Ovechkin AO, Vaykshnorayte MA, Demidova MM, *et al*. Contribution of depolarization and repolarization changes to J-wave generation and ventricular fibrillation in ischemia. Front Physiol 2020;11:568021.
3. Grune J, Lewis AJM, Yamazoe M, Hulsmans M, Rohde D, Xiao L, *et al*. Neutrophils incite and macrophages avert electrical storm after myocardial infarction. Nat Cardiovasc Res 2022;1(7):649–64.
4. Bhar-Amato J, Davies W, Agarwal S. Ventricular arrhythmia after acute myocardial infarction:'The Perfect Storm'. Arrhythm Electrophysiol Rev 2017;6(3):134–9.
5. AlAsmari A. Myocardial Ischemia/Reperfusion Injury and Cardioprotection: Novel Roles of Frataxin and Uridine Triphosphate. PhD Dissertation, Auburn University, Auburn, Alabama; 2017. Available at: http://hdl.handle.net/10415/5683
6. Zagkli F, Georgakopoulou A, Chiladakis J. Effects of transcutaneous cardiac pacing on ventricular repolarization and comparison with transvenous pacing. Pacing Clin Electrophysiol 2020;43(9):1004–11.
7. El-Sherif N, Turitto G, Boutjdir M. Acquired long QT syndrome and electrophysiology of torsade de pointes. In: El-Sherif, N. (Ed) Cardiac Repolarization. Springer, Cham; 2020.p. 201–16.
8. Hawash AA. Persistent inward currents play a role in muscle dysfunction seen in myotonia congenita. PhD Dissertation, Wright State University. New York; 2017. Available at: https://corescholar.libraries.wright.edu/cgi/viewcontent.cgi?article=2940&context=etd_all
9. Helmy H, Abdel-Galeel A, Kishk Kishk Y, Mohammed Sleem K. Correlation of corrected QT dispersion with the severity of coronary artery disease detected by SYNTAX score in non-diabetic patients with STEMI. Egypt Heart J 2017;69(2):111–7.
10. Amoni M, Dries E, Ingelaere S, Vermoortele D, Roderick HL, Claus P, *et al*. Ventricular arrhythmias in ischemic cardiomyopathy—New avenues for mechanism-guided treatment. Cells 2021;10(10):2629.
11. Ozturk U, Ozturk O. Relation between index of cardioelectrophysiological balance and stroke severity in patients with acute ischemic stroke. Niger J Clin Pract 2020;23:768–74.
12. Almyahi M, Alkinani TA, Majdi K, Azzawi FS, Basheer A. Relationship between QT interval dispersion and degree of coronary artery disease. Indian J Forensic Med Toxicol 2020;14(2):1321–7.
13. Johnson DM, Antoons G. Arrhythmogenic mechanisms in heart failure: linking β-adrenergic stimulation, stretch, and calcium. Front Physiol 2018;9:1453.
14. Al Alwany AA. Effect and benefit of percutaneous coronary intervention in chronic total occlusion on ventricular repolarization: QT correction and dispersion. J Med Life 2022;15(8):1025–30.
15. Kosmopoulos M, Roukoz H, Sebastian P, Kalra R, Goslar T, Bartos JA, *et al*. Increased QT dispersion is linked to worse outcomes in patients hospitalized for out-of-hospital cardiac arrest. J Am Heart Assoc 2020;9(16):e016485.
16. Islam MS, Mondal SK, Jahan J, Arefin M, Ahmed N, Das PR, *et al*. Effect of PCI on QTC dispersion in patients with angina. Univ Heart J 2020;16(1):33–9.
17. Suleimani HF, Eshraghi A, Daloee MH, Hoseini S, Nakhaee N. Effect of nicorandil on QT dispersion in patients with stable angina pectoris undergoing elective angioplasty. Electronic Physician 2017;9(8):4934–41.

Address for Correspondence:

Dr. Sadia Mubarak, Department of Physiology, Islamabad Medical and Dental College, Islamabad, Pakistan.
Cell: +92-332-5020560
Email: sadia.smcian@gmail.com

Received: 9 Dec 2021 **Reviewed:** 27 Dec 2022 **Accepted:** 29 Dec 2022

Contribution of Authors:

SM: Acquisition and data collection **BR:** Drafting and interpretation of results **ZR:** Contribution in concept and review
SH: Drafting and contribution in concept **MS:** Redrafting and analysis of data

Funding: None **Conflict of interest:** None