# QT Dispersion

I. LÕRINCZ
1st Department of Medicine, University Medical School of Debrecen, Hungary

**Summary**

*Invasive studies have demonstrated that regional differences in the ventricular recovery time reflected as differences in the QT intervals corresponded to different regions of the myocardium. This non-homogeneity is called QT dispersion (QTd). It was proposed by Campbell's group as a non-invasive marker to assess ventricular repolarization inhomogeneity. Increased QT interval dispersion decreases the threshold for ventricular tachycardias (VT) and is associated with a risk of VT and sudden cardiac death (SCD). This simple, inexpensive, bed-side method has become very popular in the last nine years for risk stratification in patients with acute myocardial infarction (AMI), congestive heart failure, as well as dilated and hypertrophic cardiomyopathy, or for monitoring drug effects on ventricular repolarization, etc. Controversial questions on the value of this popular method arise because of: a) a lack of adequate standardization, b) an exact measurement of T-wave end, c) a manual or automatic computerized measurement, d) reproducibility, e) the large standard deviation of QT dispersion in some patients, f) the fact that the sensitivity and specificity is often low, g) and because most published papers on this subject have been based on retrospective studies. Despite technical and methodological limitations of measuring the QTd may be useful and relevant in the future.*

**Key Words**

QT dispersion, repolarization, arrhythmia, risk assessment

## Introduction

The interval between the onset of the Q wave and the end of the T-wave of the standard surface electrogram (ECG) is considered to represent the time between the cell depolarization and the electrical recovery or repolarization. The routine evaluation of the ventricular repolarization is based on measurements of the QT interval in lead II or a lead with the largest T-wave, as well as the calculation of a mean QT interval from particular subset of leads [1].

Mirvis reported a significant spatial variation in QT intervals in normal individuals and patients with AMI [2]. Day et al. and later others suggested that the measurement of the inter-lead variability in the duration of the QT interval and the assessment of the so-called QTd, defined as the greatest QT interval (QTmax) minus the least QT interval (QTmin), was a more sensitive marker of enhanced ventricular vulnerability than the QT prolongation itself [3-5]. Recent clinical studies refer to the fact that QTd accurately reflects spatiotemporal heterogeneity of ventricular recovery times, and that a QTd of 70-120 ms can be indicative of increased arrhythmia risk. Furthermore, one may assume that an increase in QTd predicts the proarrhythmic effect of antiarrhythmic agents influencing cardiac repolarization and refractoriness [4][6-8].

## Pathophysiological basis of an abnormal QT dispersion

The pathophysiology underlying increased QTd is not fully understood, but is likely to be multifactoral. Arrhythmogeneity depends partly on modulations of ion currents, partly on an abnormal ventricular structure and partly on the metabolism [9]. Increased dispersion of the refractoriness may be due to regional differences in ventricular wall stress (mechano-electric or contraction-excitation feedback), caused by ventricular dilatation and fibrosis. This hypothesis is

supported by the findings of increased QTd in patients with acquired long QT interval [10], AMI [11,12], hypertrophic cardiomyopathy [13,14], hypertension and left ventricular hypertrophy [15], as well as in diabetic patients with autonomic neuropathy [16], uremic neuropathy, and during hemodialysis [17]. QTds are associated with an increased risk of VT and SCD in patients with chronic heart failure [5], mitral valve prolapse [18], AMI [19] as well as long QT syndrome [3], and with an increased risk of cardiac mortality in patients with peripheral arterial disease [20].

The cellular basis for QTd recorded on the body surface is not completely understood. The heterogeneity of the repolarization is due to regional differences in the action potential duration, and the activation time. Very recently, it has been demonstrated that the dispersion in repolarization may arise from differences in the action-potential duration between cell groups originating from different layers of the ventricular myocardium. It was demonstrated that the presence of M-cells (in the mid-myocardial layer) is characterized by a prolonged repolarization in comparison to endocardiac or epicardiac cell layers. The peak of the T-wave in the body-surface ECG was found to reflect the end of the action potential of the epicardiac layer, and the T-wave offset represented the termination of the repolarization in the mid-myocardial layer (containing M-cells). From this point of view, the time difference between the T-wave peak (Tp) and the end of the T-wave (Te) reflects the transmural dispersion of repolarization [21].

## Difficulties occurred during the measurement of QT, JT, TpTe intervals and dispersions

Twelve-lead ECGs are recorded by means of a 12-channel ECG recorder at a paper speed of 25-50 mm/s and 10 mm/mV gain. The intervals for each lead can be measured manually with calipers, a ruler or the (semi-) automatic method. This method poses certain difficulties:

1) The QT interval in the surface ECG is slightly shorter than the ventricular recovery time.
2) The onset of the QRS complex and the T-wave end may be very difficult to define, thus very short or long leads may have to be excluded from the measurements.
3) The U wave may be hidden behind the T-wave or T- and U-wave may be clearly separated.
4) The QTd is not only influenced by the number of measured leads. If, in clinical practice, there are difficulties in determining the end of the T-wave, there are two possibilities: either the T-wave peak or the point where the maximal slope of the descending part of the T-wave cuts the isoelectric line [22-24].

## Heartrate correction, QTc

The most often used formula for heart-rate correction is the Bazett formula. There are also several other correction formulas in use (Fridericia, Kawataki, Sagie, Funck-Brenato, Karajalninen, Hodges, etc.) [25]. In this context, Malik et al. suggested that QTd should be preferred to QTc dispersion [26].

## Reproducibility of measurements and computer-assisted semiautomatic and automatic system for the measurement of the QT dispersion

When a single QT interval is measured by different observers, significant differences - up to 20 ms - can occur. However, the reproducibility of the mean QT interval is generally considered as good. Conversely, the reproducibility of the manually measured QTd is poor, with a relative error between 25% and 35% [22,23,27]. There are major methodological problems in measuring the QTd, resulting in low reproducibility of results from the same investigator. These problems are mainly related to difficulties in defining the end of the T-wave. Yet, the paper speed also affects the reproducibility. The interobserver variability of visual QT interval measurements is 30%. The interobserver bias in the T-interval amounts to 20 ms [22]. Dabar et al. found that in patients with vascular desease the QTd appears to have a sensitivity of 92% and a specificity of 43% in predicting cardiac death. In the same study the borderline value of 80 ms had a 67% sensitivity and 89% specificity [20].

The automatic computerized methods for measuring QTd can help to perform large studies and can exclude the interobserver and/or intraobserver variability. Glancy et al. found a 100% repeatability for their automatic system [23,28]. The automatic QT interval measurements are more stable and reproducible than manual measurements, but the discrepancy between manual and automatic measurement suggests that the

clinical experience gained with manual assessment cannot be applied blindly to data obtained from automatic systems [28-30].

**The QT dispersion in patients with varying cardiac diseases**

The normal range for QTd is 40-50 ms with a maximum of 65 ms. If the QTd values are greater than 65 ms, the patients risk serious ventricular arrhythmia or SCD. Patients with structural heart disease and at risk of VT have QTd values from 66 to 115 ms [3,21], while values over 130 ms would be found almost exclusively in patients with a congenital long QT interval, who failed to respond to beta-adrenergic blocking agents [31]. The long QT syndrome dramatically demonstrates increased QTd. Probably, this variable is related to SCD and VT. There are studies which show no differences in the degree of dispersion between long QT syndrome groups with frequent or infrequent clinical symptoms [3,10].

During AMI, QTd is increased and successful thrombolysis is associated with less QTd in postinfarction patients [12]. The increased QTd is independent of the degree of left ventricular dysfunction or clinical characteristics of patients [32]. The dynamics of QTd gradually increased from day 1, reaching a maximum on day 3, and falling gradually at discharge. During coronary angioplasty, no changes in QTd were found [33]. Other studies have shown that coronary angioplasty significantly decreases QT dispersion [34]. The early coronary reperfusion may reduce the electrophysiological instability by lowering QTd in the recovery phase after AMI [35]. QTd is decreased after successful coronary artery revascularization and increased with restenosis [36]. Patients with vasospastic angina exhibit an increased QTc dispersion compared to patients with atypical chest pain [37]. The QTd of the resting ECG one month after an anterior-wall AMI is unrelated to the estimated infarct size and the degree of left ventricular dysfunction [38]. Myocardial ischaemia induced by incremental atrial pacing in patients with coronary artery disease (CAD) caused an acute increase in QTd. Such "inducible" QTd may prove to be more useful than resting QTd in assessing the individual risk of arrhythmic events [39]. In a retrospective case control study, QTd in postinfarction patients who died during the follow-up was compared with matching survivors. At day 3, the increased QTd did not show any risk of SCD, but as the QTd had not decreased 4 weeks after the infarction, this was associated with a higher mortality risk [23]. Other studies could neither find the risk marker of QTd and TpTe dispersion in postinfarction patients. A very recently published paper showed that QTd measurements were significantly increased in those patients who died and that QTd resulted in an independent predictor of all-cause mortality on multivariate analysis in postinfarction patients. These patients all suffered from heart failure [19]. Barr's study group showed that QTd taken from standard ECG predicted SCD in 44 patients with chronic heart failure secondary to ischaemic heart disease. Patients with SCD had a significantly higher QTd compared to the survivors [5]. The ACE inhibitor, ramipiril, therapy after AMI complicated by heart failure, is associated with a significant reduction of QTd after seven weeks [19]. Enalapril reduces QTc dispersion in mild congestive heart failure secondary to CAD [40]. It was demonstrated that, in patients with CAD, who had non-sustained VT, inducibility of monomorphic VT was associated with an increase in QTd [41]. Increased QTd was linked to an increased incidence of fatal and non-fatal myocardial infarction in the 6,595 middle aged men included in the West of Scotland Coronary Prevention study [42], and to an increased incidence of cardiac death in the 5,812 patients of the Rotterdam Study of the Elderly [43].

A prospective study demonstrated that QTd has no predictive value for arrhythmias and SCD, although the QTd was higher in patients with idiopathic dilated cardiomyopathy and arrhythmias at the 13 ± 7 -month follow-up [44]. The study of Fei et al. suggests that QTd does not predict death in idiopathic cardiomyopathy [45]. Others showed that JT dispersion was a better predictor for SCD [46]. Another study showed that QTd was significantly greater in patients with dilated cardiomyopathy and SCD [47]. In a retrospective study, QTd measured by Holter was higher in SCD patients than in healthy subjects and matched control patients during the entire day. QTd has a clear circadian variation in normal subjects, whereas this variation is blunted in SCD patients [30].

The QTd is significantly increased in patients with hypertrophic cardiomyopathy compared with normal subjects; it was also shown that QTd is significantly increased in patients with serious VT or SCD [14]. Tielman showed that QTd was greater in patients with mitral-valve prolapse and ventricular arrhythmia [18].

There was a significant correlation between complex premature ventricular complexes and QTd in patients with mitral-valve prolapse [48]. Conti et al. demonstrated that, after catheter ablation of AV junction, an increase in QTd was associated with episodes of polymorphic VT in their patients and with significant higher risk of rhythm disturbance, especially in patients with severely depressed left ventricular function [49]. The increased QTd in patients with aortic stenosis requiring valve replacement was reduced after valve replacement [50]. There is a strong link between QTc dispersion and cardiac death in patients with peripheral vascular disease [20]. Increased QTd was shown in hypertension with increased left ventricular mass [15], while abnormalities in QTd could not be found in persons with athletic left-ventricular hypertrophy [47]. Ramipiril, felodipine and enalapril reduced the QTd in patients with hypertension [51].

**QT dispersion and antiarrhythmic treatment**

Priori et al. reported that β-blocking agents reduce QTd and improve the survival rate of patients with a congenital long QT syndrome, responsive to such a pharmacotherapy [31]. There are also data with respect to β-blocking agent-induced reduction of QTd in patients with chronic heart failure [52]. Some observations suggest that β-blockers may diminish QT/QTc dispersion, which is for example the case with atenolol in patients suffering from cardiac X-syndrome, a special condition characterized by enhanced sympathetic drive [53]. A retrospective study demonstrated that both selective and nonselective β-blockade had equivalent effect on reducing QTc dispersion. Prospective studies of QTc dispersion - within large β-blocker mortality studies using both selective and nonselective agents - with a longer follow-up period are necessary to confirm the clinical relevance of these findings. These trials, including the ongoing head-to-head trial of a selective and nonselective agent (Carvedilol or METoprolol [COMET] trial), will hopefully elucidate whether different effects on SCD and all-cause mortality do exist [54].

Increased QTd during Class I/A antiarrhythmic drug therapy is occasionally associated with the development of “torsade de pointes” VT. A consistent reduction in QT and QTc dispersions was found only with amiodarone, an agent claimed to be also safe in patients who had previous episodes of sotalol and/or Class I/A drug-induced “torsades de pointes” [3,4,7,55,56]. The chronic amiodarone therapy increases the QT interval and causes a homogenous prolongation of the repolarization, manifested in a reduction of QTd [4]. Amiodarone reduces the transmural heterogeneity of ventricular repolarization both in canine and human hearts [57-59]. More specifically, amiodarone displays greater prolongation of action-potential duration (APD) in the epicardiac and endocardiac cells with less increase - or even a diminution - of the repolarization of the mid-myocardial M cells with intrinsically long APD [58,59]. In patients with postinfarction ventricular arrhythmias, amiodarone decreases QTd significantly [7]. In patients with d,l-sotalol-induced “torsade de pointes” ventricular arrhythmias, amiodarone reduces QTd and does not evoke proarrhythmia [8]. Additionally, amiodarone administration is able to halt the amplification of QTd in patients treated with Class I/A antiarrhythmic drugs [4,55]. Moreover, amiodarone was found to lengthen the QT interval and decrease QTd in patients with hypertrophic cardiomyopathy [13].

There is evidence that d,l-sotalol prolongs the QT interval and diminishes QTd [11]. In postinfarction arrhythmic patients, d,l-sotalol, sematilide, and a novel selective IKr-blocking Class III agent, modestly decreased QTd, while amiodarone caused a significant reduction of this variable [7]. In a placebo-controlled study, d,l-sotalol administration was associated with an increased maximal QTc interval and a decreased QTc dispersion in patients 6 months after AMI [60]. D,l-sotalol prolongs homogeneously the QT interval in patients with structurally normal hearts, i.e., with a concomitant decrease of QTd. Other recent studies also suggest that the regional dispersion of ventricular repolarization may decrease during d,l-sotalol therapy [60].

**Conclusion**

The diagnostic and prognostic value of prolonged QTd continues to be disputed. It is still an open question whether the standard 12-lead surface ECG is a useful tool to assess the risk. There is controversy about the value of this method because of:

a) a lack of adequate standardization,
b) an exact measurability of the T-wave end,
c) the discrepancy of manual or automatic measurement,

d) reproducibility, and
e) the fact that most published papers have been retrospective studies so far.

The available data suggest that it is a marker of mortality after AMI associated with heart failure. It is not clear if it adds much information in relation to other prognostic markers and, more importantly, its sensitivity for predicting future adverse events is very low. The most published studies dealt with multivariate analysis. Prospective studies are needed to avoid making false decisions on the basis of false results. Studies with statistically large samples (Rotterdam, West Scotland) had positive results, but their value for the individual patient is still questionable.

## References


[1] Surawicz B, Knoebel SB. Long QT. Good, bad, or indifferent? J Am Coll Cardiol. 1984; 4: 398-413.

[2] Mirvis DM. Spatial variation of QT intervals in normal persons and patients with acute myocardial infarction. J Am Coll Cardiol. 1985; 5: 625-631.

[3] Day CP, McComb JM, Campbell RWF. QT dispersion: an indication of arrhythmia risk in patients with long QT intervals. Br Heart J. 1990; 63: 342-344.

[4] Hii TY, Wyse DG, Gillis AM, et al. Precordial QT interval dispersion as a marker of torsade de pointes. Disparate effects of class Ia antiarrhythmic drugs and amiodarone. Circulation. 1992; 86: 1376-1382.

[5] Barr CS, Naas A, Freeman M, et al. QT dispersion and sudden unexpected death in chronic heart failure. Lancet. 1994; 343: 327-329.

[6] Zabel M, Portonoy S, Franz M R. Electrocardiographic indexes of dispersion of ventricular repolarization: an isolated heart validation study. J Am Coll Cardiol. 1995; 25: 746-752.

[7] Cui G, Sen L, Sager P, et al. Effects of amiodarone, sematilide, and sotalol on QT dispersion. Am J Cardiol. 1994; 79: 896-900.

[8] van de Loo A, Klingenheben T, Hohnloser SH. Amiodarone therapy after sotalol-induced torsade de pointes: prolonged QT interval and dispersion in differentiation of pro-arrhythmic effects. Z Kardiol. 1994; 83: 887-890.

[9] Choy AM, Lang CC, Chomsky DM, et al. Normalization of aquired QT prolongation in humans by intravenous potassium. Circulation 1997; 96: 2149-2154.

[10] Linker NJ, Colonna P, Kekwick CA, et al. Assessment of QT dispersion in symptomatic patients with congenital long QT syndromes. Am J Cardiol. 1992; 69: 634-638.

[11] Day CP, McComb, JM, Matthews J, et al. Reduction in QT dispersion by sotalol following myocardial infarction. Eur Heart J. 1991; 12: 423-427.

[12] Moreno FL, Villanueva T, Karagounis LA, et al. Reduction in QT interval dispersion by successful thrombolytic therapy in acute myocardial infarction. TEAM-2 Study Investigators. Circulation. 1994; 90: 94-100.

[13] Dristas A, Abaroumi E, Gilligan D, et al. QT interval abnormalities in hypertophic cardiomyopathy. Clin Cardiol. 1992; 15: 739-742.

[14] Buja G, Miorelli M, Turrini P, et al. Comparison of QT dispersion in hypertrophic cardiomyopathy between patients with and without ventricular arrhythmias and sudden death. Am J Cardiol. 1993; 72: 973-976.

[15] Clarkson PB, Naas AA, McMahon A, et al. QT dispersion in essential hypertension. QJM. 1995; 88: 327-332

[16] Wei K, Dorian P, Newman D, et al. Association between QT dispersion and autonomic dysfunction in patients with diabetes mellitus. J Am Coll Cardiol. 1995; 26: 859-863.

[17] Lõrincz I, Zilahi Z, Kun C, et al. ECG abnormalities in hemodialysis. Am Heart J. 1997; 134: 1138-1140.

[18] Tieleman RG, Crijns HJ, Wiesfeld AC, et al. Increased dispersion of refractoriness in the absence of QT prolongation in patients with mitral valve prolapse and ventricular arrhythmias. Br Heart J. 1995; 73: 37-40.

[19] Spargias KS, Lindsay SJ, Kawar GI, et al. QT dispersion as a predictor of long term mortality in patients with acute myocardial infarction and clinical evidence of heart failure. Eur. Heart J. 1999; 20: 1158-1165.

[20] Darbar D, Luck J, Davidson N, et al. Sensitivity and specificity of QTc dispersion for identification of risk of cardiac death in patients with peripheral vascular disease. BMJ. 1996; 312: 874-879.

[21] Antzelevitch C, Shimizu W, Yan GX, et al. Cellular basis for QT dispersion. J Electrocardiol. 1998; 30 Suppl: 168-175.

[22] Kautzner J, Gang Y, Camm AJ. Short- and long-term reproducibility of QT, QTc and QT dispersion measurement in healthy subjects. PACE. 1994; 17: 928-937.

[23] Glancy JM, Weston PJ, Bhullar HK, et al. Reproducibility and automatic measurement of QT dispersion. Eur Heart J. 1996; 17: 1035-1039.

[24] Elming H, Jun l, Kober L, et al. Measurement of QT interval dispersion. Card Electrophysiol Rev. 1997; 3: 372-376.

[25] Malik M, Camm AJ. Correct the QT interval correctly: Should QTc be expressed in the same unit as the QT interval? PACE. 1996; 19: 1531-1534.

[26] Malik M, Camm AJ. Mystery of QTc interval dispersion. Am J Cardiol. 1997; 79: 785-787.

[27] Gang Y, Guo X-h, Crook R, et al. Computerized measurements of QT dispersion in healthy subjects Heart. 1998; 80: 459-466.

[28] Savelieva I, Yi G, Guo X, et al. Agreement and reproducibility of automatic versus manual measurement of QT interval and QT dispersion. Am J Cardiol. 1998; 81: 471-477.

[29] Kors JA, van-Herpen G. Measurement error as a source of QT dispersion: a computerised analysis Heart. 1998; 80: 453-458.

[30] Molnar J, Rosenthal JE, Weiss JS, et al. QT interval dispersion in healthy subjects and survivors of SCD: circadian variation in a twenty-four-hour assessment. Am J Cardiol. 1997; 79: 1190-1193.

[31] Priori SG, Napolitano C, Diehl L, et al. Dispersion of the QT interval. A marker of therapeutic efficacy in the idiopathic long QT syndrome. Circulation. 1994; 89: 1681-1689.

[32] Perkiomaki JS, Koistinen MJ, Yli Mayry S, et al. Dispersion of QT interval in patients with and without susceptibility to ventricular tachyarrhythmias after previous myocardial infarction. J Am Coll Cardiol. 1995; 26: 174-179.

[33] Karagounis LA, Anderson JL, Moreno FL, et al. Multivariate associates of QT dispersion in patients with acute myocardial infarction: primacy of patency status of the infarct-related artery. TEAM-3 Investigators. Am Heart J. 1998; 135: 1027-1035.

[34] Kelly RF, Parillo JE, Hollenberg SM. Effect of coronary angioplasty on QT dispersion. Am Heart J. 1997; 134: 399-340.

[35] Endoh Y, Kasanuki H, Ohnishi S, et al. Influence of early coronary reperfusion on QT interval dispersion after acute myocardial infarction. PACE. 1997; 20: 1646-1653.

[36] Yunus A, Gillis AM, Traboulsi M, et al. Effect of coronary angioplasty on precordial QT dispersion. Am J Cardiol. 1997; 79: 1339-1342.

[37] Suzuki M, Nishizaki M, Arita M, et al. Increased QT dispersion in patients with vasospastic angina. Circulation. 1998; 98: 435-440.

[38] Tamura A, Nagase K, Mikuriya Y, et al. Relation of QT dispersion to infarct size and left ventricular wall motion in anterior wall acute myocardial infarction. Am J Cardiol. 1999; 83: 1423-1426.

[39] Sporton SC, Taggart P, Sutton PM, et al. Acute ischaemia: a dynamic influence on QT dispersion Lancet 1997; 349: 306-309.

[40] Barr CS, Naas AA, Fenwick M, et al. Enalapril reduces QTc dispersion in mild congestive heart failure secondary to coronary artery disease. Am J Cardiol. 1997; 79: 328-333.

[41] Bogun F, Chan KK, Harvey M, et al. QT dispersion in nonsustained ventricular tachycardia and coronary artery disease. Am J Cardiol. 1996; 77: 256-259.

[42] Macfarlane PW, McLaughlin SC, Rodger JC. Influence of lead selection and population on automated measurement of QT dispersion. Circulation. 1998; 98: 2160-2167.

[43] De Bruyne MC, Hoes AW, Kors JA, et al. QTc dispersion predicts cardiac mortality in the elderly: the Rotterdam study. Circulation. 1998; 97: 467-472.

[44] Grimm W, Steder U, Menz V, et al. QT dispersion and arrhythmic events in idiopathic dilated cardiomyopathy. Am J Cardiol. 1996; 78: 458-461.

[45] Fei L, Goldman JH, Prasad K, et al. QT dispersion and RR variation on 12-lead ECGs in patients with congestive heart failure secondary to idiopathic dilated cardiomyopathy. Eur Heart J. 1996; 17: 258-263.

[46] Fu GS, Meissner A, Simon R. Repolarization dispersion and SCD in patients with impaired left ventricular function. Eur Heart J. 1997; 18: 281-289.

[47] Galinier M, Vialette JC, Fourcade J, et al. QT interval dispersion as a predictor of arrhythmic events in congestive heart failure. Importance of etiology. Eur Heart J. 1998; 19: 1054-1062.

[48] Kulan K, Komsuoglu B, Tuncer C, et al. Significance of QT dispersion on ventricular arrhythmias in mitral valve prolapse. Int J Cardiol. 1996; 54: 251-257.

[49] Conti JB, Mills RM Jr, Woodard DA, et al. QT dispersion is a marker for life-threatening ventricular arrhythmias after atrioventricular nodal ablation using radiofrequency energy. Am J Cardiol. 1997; 79: 1412-1414.

[50] Mayet J, Shahi M, Senior R, et al. QT dispersion in athletic left ventricular hypertrophy. AM Heart J. 1999; 137: 678-681.

[51] González-Juanatey JR, Garcia-Acuna JM, Pose A, Varela A, et al. Reduction of QT and QTc dispersion during long-term treatment of systemic hypertension with enalapril. Am J Cardiol. 1998; 81: 170-174.

[52] Bonnar CE, Davie AP, Caruana L, et al. QT dispersion in patients with chronic heart failure: beta blockers are associated with a reduction in QT dispersion. Heart. 1999; 81: 297-302.

[53] Leonardo F, Fragasso G, Rosano GMC, et al. Effect of atenolol on QT interval and dispersion patients with syndrome X. Am J Cardiol. 1997; 80: 789-790.

[54] Fesmire S I, Marcoux LG, Lyyski DS, et al. Effect of selective versus nonselective beta blockade on QT dispersion in patients with nonischemic dilated cardiomyopathy. Am J Cardiol. 1999; 84: 350-354.

[55] Singh BN. Amiodarone and homogeneity of ventricular repolarization and refractoriness. J Cardiovasc Pharmacol Ther. 1996; 1: 265-270.

[56] Mattioni TA, Zheutin TA, Sarmiento JJ, et al. Amiodarone in patients with previous drug-mediated torsade pointes. Ann Intern Med. 1989; 111: 5745-5780.

[57] Papp JGy, Németh M, Krassói I, et al. Differential electrophysiologic effects of chronically administered amiodarone on canine Purkinje fibers versus ventricular muscle. J Cardiovasc Pharmacol Therapeut 1996; 1: 287-296.

[58] Siccouri S, Moro S, Litowsky S, et al. Chronic amiodarone reduces transmural dispersion of repolarization in canine heart. J Cardiovasc Electrophysiol 1997; 8: 1269-1279.

[59] Drouin E, Lande G, Cherpentier F. Amiodarone reduces transmural heterogeneity of repolarization in the human heart. J Am Coll Cardiol. 1998; 32: 1063-1067.

[60] Sarubbi B, Ducceshi V, Briglia N, Mayer MS, Santangelo L, Iacono A. Compared effects of sotalol, flecainide and propafenone on ventricular repolarization in patients free of underlying structural heart disease. Int. J. Cardiol. 1998; 66: 157-164.