Relation Between QT Dispersion and Ventricular Arrhythmias In Uncomplicated Isolated Mitral Valve Prolapse

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Complications of mitral valve prolapse (MVP), among which serious ventricular arrhythmia and sudden death are of major importance, affect many individuals due to the high incidence of MVP itself in the community despite the actual low incidence of these complications. The present study investigated the incidence and distribution of ventricular arrhythmias according to their severity and relationship with the QT interval and dispersion of repolarization in uncomplicated isolated MVP (IMVP) cases. Fifty-eight uncomplicated IMVP patients, 33 patients with accompanying tricuspid valve prolapse (TVP), to compare its relationship with ventricular arrhythmia, and 60 age- and sex-matched control subjects were enrolled in the study. Individuals with accompanying cardiac or systemic disease, or who were on drug therapy that could potentially affect QT characteristics, were excluded. The incidence of ventricular arrhythmia was 48% in the IMVP group and 64% in the TVP group; the difference was statistically insignificant. In addition, the differences of the QT and Q peak T values were insignificant, whereas QT dispersion (QTd) and Q peak T dispersion (QpeakTd) values were significantly higher in the patient group (60 ± 14 , 54 ± 14 ms, respectively) compared with the control group (42 ± 10 , 38 ± 10 ms, respectively, $p < 0.001$). Complex ventricular arrhythmias (Lown Grade $\geq$ III) in the IMVP group had a significant relationship with QTd and QpeakTd ($p < 0.001$), but not with QT or QpeakT. As a result of the study, it is concluded that TVP accompanying MVP does not increase the incidence of ventricular arrhythmia, that ventricular arrhythmia is related to QT dispersion rather than QT interval in IMVP, that the QT dispersion is a fairly good marker for identifying the high-risk group for serious ventricular arrhythmia and sudden death, and that QpeakT dispersion measurement is an additional indicator that could be an alternative when QT is difficult to determine in conditions such as high heart rate or the presence of U wave. (*Jpn Circ J* 1999; 63: 929–933)

Key Words: Mitral valve prolapse; QT dispersion

Mitral valve prolapse (MVP) is the most commonly diagnosed valvular heart disease, especially in the young, and affects 5% of the community! Although it is reported that MVP has a good prognosis and a low incidence of complications,² it is obvious that even a rare complication will affect many individuals due to the high incidence of MVP in the general population.³

However, some reports point out that these complications are not as rare as was thought;^{4,5} the main entities being endocarditis, cerebrovascular accidents, sudden death, ventricular tachycardia and ventricular fibrillation. Arrhythmia and sudden death are significant complications in MVP cases; a 0.5% incidence of sudden death has been reported in different MVP studies^{3,6} and it is suggested that the underlying mechanism of the sudden death is arrhythmogenic. It was also claimed that the prolonged QT intervals in MVP cases could be related to arrhythmia and sudden death.^{7,8} Furthermore, there are studies that found that, instead of a prolonged QT interval increase, intrinsic QT dispersion can be related to arrhythmia in these cases.^{9,10}

In the present study, we aimed to determine the relationship between intrinsic QT dispersion and ventricular

arrhythmias and sudden death in young individuals suffering from uncomplicated isolated MVP (IMVP). In this respect, cases without leaflet thickening (≥ 5 mm), severe mitral regurgitation or left ventricular systolic dysfunction were included in the study. Although a few reports have concentrated on the clinical significance of MVP accompanying tricuspid valve prolapse (TVP), the clinical significance of TVP and its relation to the arrhythmias of MVP has not yet been clearly documented. Therefore, we excluded MVP cases with accompanying TVP after beginning the study. Our main aim was to investigate the incidence and distribution of ventricular arrhythmias, according to their severity and relation to the QT interval, and to the dispersion of repolarization in uncomplicated IMVP.

Methods

Study Groups

The current study was carried out in the Department of Cardiology, Faculty of Medicine, Dicle University between May 1996 and April 1998. We registered 91 individuals who underwent echocardiographic examination and were diagnosed as MVP; the group included 33 cases with accompanying TVP. Those patients who had disorders such as ischemic or rheumatic heart disease, systemic and/or pulmonary hypertension, diabetes mellitus, hyperthyroidism, stenotic valvular heart disease, congenital heart diseases, severe mitral regurgitation (> 3 cm² regurgitant jet length in color flow mapping), or severe left ventricular dysfunction

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Table 1 Lown Grading of the Study Population Distributed to its Subgroups

Lown Grade	MVP		MVP+TVP		Control	
	(n)	(%)	(n)	(%)	(n)	(%)
0	30	51.7	12	36.4	43	71.7
I	12	20.7	9	27.3	10	16.7
II	5	8.6	5	15.2	5	8.3
III	4	6.9	2	6.1	1	1.7
IVa	3	5.2	3	9.1	1	1.7
IVb	4	6.9	2	6.1	0	0.0
Complex VA	11	19.0*	7	21.2†	2	3.3
Total	28	48.3*	21	63.6†	17	28.3

Complex VPC were defined as the sum of grade III, IVa and IVb. MVP, mitral valve prolapse; TVP, tricuspid valve prolapse; complex VA, complex ventricular arrhythmias.

When compared with the control group * $p < 0.05$, † $p < 0.01$.

were excluded. Those patients whose clinical condition and findings evoked suspicion of a disease and who were taking QT prolonging drugs were excluded as well. In the cases of IMVP there was a history of palpitation in 66%, atypical chest pain in 72%, fatigue and dyspnea in 55%, presyncope in 9%, and syncope in 7%.

An age- and sex-matched healthy control group ($n=60$) was randomly formed from individuals without any cardiac disease or history of arrhythmia. Those with a QRS segment ≥ 120 ms and/or atrial fibrillation on the electrocardiogram were excluded from both groups in the study.

The patient group was divided into 2 subgroups: (i) IMVP group ($n=58$) and (ii) MVP+TVP group ($n=33$). All subjects underwent 24-h ambulatory ECG.

Echocardiographic Examination

In all subjects, transthoracic 2-dimensional and Doppler echocardiographic examinations were performed using a Vingmed CFM 800 echocardiographic system, using 2.5–3.5 MHz transducers. The measurements were carried out according to the standards of the American Society of Echocardiography,¹¹ using the parasternal long axis and apical 4-chamber windows.

MVP was defined as a systolic excursion of any leaflet that exceeded 3 mm from the mitral valve annulus proximally in the parasternal long axis and apical 4-chamber windows, and TVP was defined as a systolic excursion of any leaflet that exceeded 3 mm from the tricuspid valve annulus proximally in the same views. The echocardiographic examinations were recorded on a video recorder (Sony SVO-9500-MDP VHS) for further evaluation.

Each echocardiogram was evaluated by 2 experienced cardiologists. Echocardiograms that were difficult to evaluate due to technical defects, and the cases in which the cardiologists could not agree, were excluded from the study.

ECG Evaluation

ECG recordings of all subjects were done with a Hewlett Packard Page Writer, which records 12 derivations simultaneously at a paper speed of 50 mm/s with a calibration of 0.5 mV/cm. In each derivation the QT intervals were measured as the time from the beginning of the QRS to the end of the T wave in milliseconds. In the presence of a U wave, QT intervals were measured to the notch between the T and U waves. The distance between the beginning of the QRS complex and the highest point of the T wave was used to measure the Q peak T interval. If the T wave was biphasic,

Table 2 Mean Values of QT, QpeakT, QTc, QpeakTc and Their Dispersions in Isolated MVP and Control Groups

	MVP	Control	p value
QT (ms)	343±32	336±32	>0.05
QpeakT (ms)	266±33	253±33	>0.05
QTc (ms)	399±25	393±29	>0.05
QpeakTc (ms)	306±29	296±28	>0.05
QTd (ms)	60±14	42±10	<0.001
QpeakTd (ms)	54±14	38±10	<0.001
QTdc (ms)	71±16	49±11	<0.001
QpeakTdc (ms)	63±17	43±12	<0.001

QTc, corrected QT interval; QpeakTc, corrected QpeakT interval; MVP, mitral valve prolapse.

the second peak was used. Two QT and Q peak T interval measurements from each measurable derivation were carried out by 2 observers who were uninformed about the clinical status of the patients. Derivations with an uncertain T wave end and/or peak points, or with premature complexes, were excluded. Following the measurements, the average values were calculated. QT and Q peak T intervals were corrected (QTc) according to the Bazett formula.¹² QTc prolongation was accepted as ≥ 440 ms. The differences between maximum QT and Q peak T intervals in their own category in any of the 12 derivations were calculated as QT dispersion (QTd) and Q peak T dispersion (QpeakTd), respectively.

Ambulatory ECG Recordings The 24-h ambulatory ECG was performed by a Holter system (Del-Mar Avionics, Irvine, CA, USA) during the daily activities of all participants using CM-V₁, CM-V₅, CM-D_{II} derivations. Analysis was performed by an observer who was uninformed about the diagnosis. Premature ventricular contractions (PVC) were evaluated according to Lown and Wolf criteria (grade 0: no PVC; grade I: <30 PVC/h; grade II: >30 PVC/h; grade III: multiform PVC; grade IVa: couplets; grade IVb: ventricular tachycardia runs).¹³ PVC evaluated as Lown Grade $\geq$ III were defined as complex ventricular arrhythmia.

Statistical Analysis

The data were expressed as mean $\pm$ SD. The differences between the groups were analysed by Student's t-test, or chi-squared test. The correlation between the variances was investigated, and $p < 0.05$ was assessed as significant.

Results

Ninety-one MVP patients and 60 control subjects were enrolled. Of 58 IMVP patients, 38 (66%) were female and 20 (34%) were male with an average age of 27 ± 7 years; of the 33 patients suffering from both MVP and TVP, 22 (66%) were female and 11 (34%) were male with an average of 28 ± 7 years. The control group comprised asymptomatic healthy volunteers, in whom neither clinical evaluation nor echocardiographic examination could detect any kind of valvular prolapse; there were 39 females (65%) and 21 (35%) males with an average age of 28 ± 7 years. From the view-point of age and sex, statistically there was no significant difference between the patient and control groups. All of the subjects were in sinus rhythm on their resting ECG.

Table 3 QT Measurements Related to Ventricular Arrhythmia According to Lown Grade of Arrhythmia in Isolated MVP Cases

Lown Grade	QT	QpeakT	QTc	QpeakTc	QTd	QpeakTd	QTdc	QpeakTdc
0	331±34	255±32	386±22	297±25	53±9*	48±10**	62±11*	57±13**
I	350±23	265±32	401±22	304±29	60±8*	48±10**	69±9*	57±13**
II	363±23	270±37	419±29	334±38	58±10*	53±7**	76±5*	65±12**
III	355±12	256±18	422±17	306±25	80±14	75±7	95±14	82±15
IVa	360±27	293±40	414±16	334±23	83±13	78±8	96±14	89±10
IVb	363±39	279±40	415±10	319±28	83±5	74±6	95±13	85±9

QTc, corrected QT; QTd, QT dispersion; QpeakTc, corrected QpeakT; QpeakTd, QpeakT dispersion; QTdc, corrected QT dispersion; QpeakTdc, corrected QpeakT dispersion.

*QTd, QTdc, Lown Grade 0, I, II vs III, IVa, IVb $p<0.001$, $p<0.001$.

*QpeakTd, QpeakTdc, Lown Grade 0, I, II vs III, IVa, IVb $p<0.001$, $p<0.001$.

Echocardiographic Results

In the patient group, 58 (64%) had IMVP and 33 (36%) had MVP+TVP. The prolapse was observed in the anterior leaflet only in 29 (50%), in the posterior leaflet only in 9 (15.5%), and in both leaflets in 20 (34.5%) of the IMVP patients.

Ambulatory Results

Mean heart rates were 78 ± 16 and 70 ± 12 beats/min in the patient and control groups, respectively ($p<0.01$). Premature ventricular contractions were seen in 28 of the 58 IMVP cases (48%) and 21 of the 33 MVP+TVP cases (64%). When compared with the control group, the frequency of VPC was significantly higher in both of these subgroups ($p<0.05$, $p<0.01$, respectively). Complex ventricular arrhythmia (Lown Grade $\geq$ III) was detected in 11 cases of IMVP (19%), in 7 cases of MVP+TVP (21%) and in only 2 control subjects (3.3%). These results were significant ($p<0.05$, $p<0.01$, respectively). Ventricular premature complexes were seen less frequently in the IMVP (48%) group than in the MVP+TVP (64%) group, but it was not significant ($p<0.05$) (Table 1).

QT Dispersion Results

QT, QpeakT, QTd, and QpeakTd values were calculated in both the IMVP ($n=58$) and control groups ($n=60$). In each group, the minimum and mean numbers of measured derivations were 9 and 11.5, respectively. The mean $\pm$ SD difference between the QTd measurements of the 2 independent observers (interobserver variability) was 2.74 ± 9.35 ($n=58$), and the correlation coefficient was $r=0.83$ ($p<0.001$). The values of QT, QpeakT, QTc, and QpeakT in the IMVP and control groups are presented in Table 2. Mean values were higher in the IMVP group, but it was not significant ($p>0.05$).

In the patient group, the QTc value of 3 of 5 subjects who were defined as having at least one presyncopal attack exceeded 440 ms. Two of them had Grade II and the third had Grade III PVC. Three of 4 patients who were defined as having syncope had a QTc >440 ms, and VPC were classified as Lown Grade II in 2 and Grade IVa in the third. Ventricular arrhythmia of Grade I and II, respectively, occurred in 2 patients with prolonged QT intervals. Dispersions of QT, QpeakT, QTc, QpeakTc were calculated and the results are shown in Table 2. In IMVP cases, QTd and QpeakTd values were higher than those of the control group, which was statistically significant ($p<0.001$). In IMVP cases, there was no significant relationship between the grade of VPC and the QT, QpeakT, QTc or QpeakTc values. However, that kind of relation was established with QTd and QpeakTd ($p<0.001$) (Table 3).

Discussion

The incidence of PVC in MVP has been reported between 49 and 89% and it varies according to the patient study group and the MVP diagnostic criteria.¹⁴⁻¹⁷ The incidence is reported to increase in complicated cases such as those with an increased anterior and/or posterior leaflet thickness (≥ 5 mm), and those with severe mitral regurgitation or severe left ventricular systolic dysfunction; moreover, these patients are accepted as having high risk.^{18,19} In the current study, we found the incidence to be 48% in uncomplicated cases of MVP and 64% if MVP was accompanied by TVP ($p>0.05$), a lower incidence for MVP than has been reported earlier. This might reflect our relatively uncomplicated IMVP cases; in fact, there were no patients with severe mitral regurgitation and/or severe left ventricular systolic dysfunction secondary to mitral regurgitation in our study group. The presence of MVP accompanied by TVP increased the incidence; however, the difference was not significant. Previous reports have noted a 43–56% incidence of serious ventricular arrhythmia, but a lower incidence (2–17%) has been found in uncomplicated MVP.^{5,20} We established an incidence of 19% for complex ventricular arrhythmia Lown Grade $\geq$ III in IMVP cases and of 21% in MVP+TVP cases. Although the mechanism of arrhythmia has not been clarified yet, different mechanisms, such as diastolic depolarization of the muscle fibers of the anterior mitral leaflet in response to stretch, initiation of ventricular ectopia and arrhythmia as a result of extreme tension on the papillary muscles, mechanical stimulation due to thickened chordae, endocardial plaque-friction lesions, increased excitability consequent to adrenergic system activation and others, can be speculated.

It is suggested that QT prolongation is related to arrhythmic sequelae in MVP cases,^{3,7,21,22} but controversies still exist.²¹ Different studies present the incidence of QTc prolongation between 8 and 75% in MVP,^{7,21} whereas the Framingham Study reported no relation between these entities.¹⁷ Our results suggest that QTc prolongation is not a common finding. In fact, we determined neither a significant difference between the patient and control groups from the view-point of QT interval prolongation incidence nor a significant correlation between QTc and ventricular arrhythmia in MVP, which is consistent with previous studies.^{9,10} In spite of the contradictory information on the relation between QT prolongation and MVP, it is focused on the link between nonspecific repolarization changes and potentially malign arrhythmia.²² The inter-lead variability of the QT interval measured in the 12-lead ECG is defined as QTd. Mirvis²³ and others²⁴ showed variability in QTd and established the QTd²⁵ A close relation between disper-

sions of QT and QTc, which are noninvasive measurements of regional variability of ventricular recovery time and serious ventricular arrhythmia, has been put forward in various reports²⁶⁻²⁸. This kind of relation has been shown particularly in congenital long QT syndromes^{25,29} in drug intoxication, in hypertrophic cardiomyopathy³⁰ and following acute myocardial infarction. In fact, through experimental studies, it has been concluded that the heterogeneous repolarization could contribute to ventricular arrhythmia^{26,31,32}. Therefore, increased dispersion of refractoriness may be the arrhythmic mechanism underlying MVP. Tieleman et al⁹ and Kulan et al¹⁰ determined that dispersions of QT and QTc were higher than in controls. Kulan et al reported that MVP patients who had a higher incidence of complex ventricular arrhythmias (Lown $\geq$ III) had higher QTd and QTc compared with the those with a lower Lown grade of arrhythmia. However, Tieleman et al did not determine such a relation; moreover, it is not clear in these studies whether they excluded other triggering factors of arrhythmia, such as severe mitral regurgitation, severe left ventricular systolic dysfunction and dilatation, and thickening of the mitral leaflets. As well, in some reports, TVP is probably present in cases of ventricular fibrillation and sudden cardiac death³³. We excluded the cases of MVP accompanied by TVP after the beginning of the study, and the cases of thickened fibrotic or calcified mitral leaflets, severe mitral regurgitation, severe left ventricular systolic dysfunction and/or dilated heart chambers. We determined that the QTd and QTcd values were higher in uncomplicated IMVP than in the controls ($p < 0.001$), and higher in patients having complex ventricular arrhythmias compared to those having Lown grade I–II arrhythmia ($p < 0.001$).

Recently, it has been highlighted that, especially when difficulties are encountered in measuring the QT interval, such as in cases of a high heart rate with united T and P waves, the presence of U waves or an indefinite end of the T wave, measurement of QpeakT might be of great benefit³⁴⁻³⁷. We measured QpeakT and QpeakTd values in the MVP cases. Mean values of QpeakT and QpeakTc were not significantly different between the patient and control groups. However, the dispersion values of QpeakT and corrected QpeakT were significantly higher in the patient group and in those having complex ventricular arrhythmias in the subgroup analysis compared with those having simple PVC ($p < 0.001$, $p < 0.001$, respectively). Our results comparing QTd values to the severity of the arrhythmia are similar to those of Kulan et al. However, our study group comprised uncomplicated and IMVP cases, which we did to try and exclude other factors thought to be responsible for the pathogenesis of the arrhythmia in MVP. Nevertheless, it is not clear enough whether increased dispersion of the refractoriness is the underlying reason of the arrhythmia in MVP or not. Therefore, further studies of IMVP consisting of cases having serious ventricular arrhythmia are needed.

Previous studies have pointed out that increased QT variability reflects regional shortening as well as regional prolongation of repolarization intervals. This regional variability of the action potential interval may occur secondary to adrenergic stimulation, locally increased wall stress or ischemia. Various authors have reported high levels of and increased sensitivity to catecholamines along with their abnormal regulation in MVP patients in addition to abnormal baroreceptor modulation. An experimental animal

model showed an increased dispersion of refractoriness via both prolonged and shortened regional ventricular refractoriness by the activation of the sympathetic nervous system³⁸. Another reason for an increased dispersion of refractoriness may be the regional differences in wall stresses. Increased stress on chordae due to the increased valvular surface area in MVP may create differences in wall dynamics. In this respect, a shorter action potential related to increased wall stretch was measured in an experimental model³⁹.

It is concluded that, first, the frequency of serious ventricular arrhythmia and changes in repolarization were found to be increased and a significant relationship was observed between these 2 parameters in IMVP. Second, both QpeakTd, especially if the end of the T wave was not evident, and QT were found to be favorable parameters, in addition to other risk factors, in identifying high-risk patients such as those likely to experience serious arrhythmia or sudden death. Third, cases with MVP and associated TVP have an insignificant increase in ventricular arrhythmia over the IMVP cases.

References

1. Savage DD, Garrison RJ, Devereux RB, Castelli WP, Anderson SJ, Levy D, et al: Mitral valve prolapse in general population. I. Epidemiologic features: The Framingham Study. *Am Heart J* 1983; **106**: 571–576
2. Devereux RB, Perloff JK, Reichek N, Josephson ME: Mitral valve prolapse. *Circulation* 1976; **53**: 749–751
3. Kligfield P, Levy D, Devereux RB, Savage DD: Arrhythmias and sudden death in mitral valve prolapse. *Am Heart J* 1987; **113**: 1298–1307
4. Dören DR, Becker AE, Dunning AS: Long term follow-up of idiopathic mitral valve prolapse in 300 patients: a prospective study. *J Am Coll Cardiol* 1988; **11**: 42–47
5. Farb A, Tang AL, Atkinson JB, McCarthy WF, Virmani R: Comparison of cardiac findings in patients with mitral valve prolapse who die suddenly to those who have congestive heart failure from mitral regurgitation and to those with fatal non-cardiac conditions. *Am J Cardiol* 1992; **70**: 234–29
6. Nishimura RA, McGoon MD, Shub C, Miller FA Jr, Ilstrup DM, Tajik AJ: Echocardiographically documented mitral valve prolapse. *N Engl J Med* 1985; **313**: 1305–1309
7. Bekheit SG, Ali AA, Deglin SM, Jain AC: Analysis of QT interval in patients with idiopathic mitral valve prolapse. *Chest* 1982; **81**: 620–625
8. Puddu PE, Pasternac A, Tubau JF, Krol R, Farley L, de Champlain J: QT interval prolongation and increased plasma catecholamine levels in patients with mitral valve prolapse. *Am Heart J* 1983; **105**: 422–428
9. Tieleman RG, Crijns HJ, Wiersfeld AC, Posma J, Hamer HP, Lie KI: Increased dispersion refractoriness in the absence of QT prolongation in patients with mitral valve prolapse and ventricular arrhythmias. *Br Heart J* 1995; **73**: 37–40
10. Kulan K, Komsuoglu B, Tuncer C, Kulan C: Significance of QT dispersion on ventricular arrhythmias in mitral valve prolapse. *Int J Cardiol* 1996; **54**: 251–257
11. Henry WL, DeMaria A, Gramiak R, King DL, Kisslo JA, Popp RL, et al: Report of the American Society of Echocardiography Committee on Nomenclature and Standards in two dimensional imaging. *Circulation* 1980; **62**: 212–217
12. Bazett HC: An analysis of time relations of electrocardiograms. *Heart* 1920; **7**: 353–370
13. Lown B, Wolf M: Approaches to sudden death from coronary heart disease. *Circulation* 1971; **44**: 130–142
14. Kligfield P, Devereux RB: Arrhythmias in mitral valve prolapse. *Clin Prog Electrophysiol Pacing* 1985; **3**: 403–418
15. Winkle RA, Lopes MG, Fitzgerald JW, Goodman DJ, Schroeder JS, Harrison DC: Arrhythmias in patients with mitral valve prolapse. *Circulation* 1975; **52**: 73–81
16. DeMaria AN, Amsterdam EA, Vismara LA, Neumann A, Mason DT: Arrhythmias in the mitral valve prolapse syndrome: Prevalence, nature and frequency. *Ann Intern Med* 1976; **84**: 656–660
17. Savage DD, Levy D, Garrison RJ, Castelli WP, Kligfield P,

- Devereux RB, et al: Mitral valve prolapse in general population. III. Dysrhythmias: The Framingham Study. *Am Heart J* 1983; **106**: 582–586
18. Sanfilippo AJ, Abdollah H, Burggraf GW: Quantification and significance of systolic mitral leaflet displacement in mitral valve prolapse. *Am J Cardiol* 1989; **64**: 1349–1355
  19. Babuty D, Cosnay P, Breuillac JC, Charniot JC, Delhomme C, Fauchier L, et al: Ventricular arrhythmia factors in mitral valve prolapse. *PACE* 1994; **17**: 1090–1099
  20. Devereux RB, Kramer-Fox R, Kligfield P: valve prolapse: causes, clinical manifestations and management. *Ann Intern Med* 1989; **111**: 305–317
  21. Levy D, Savage D: Prevalence and clinical features of mitral valve prolapse. *Am Heart J* 1987; **113**: 1281–1290
  22. Jeresaty RM: Sudden death in the mitral valve prolapse click syndrome. *Am J Cardiol* 1976; **37**: 317–318
  23. Mirvis DM: Spatial variation of QT intervals in normal persons and patients with acute myocardial infarction. *J Am Coll Cardiol* 1985; **5**: 625–631
  24. Sylven JC, Horacek BM, Spencer LA: QT interval variability on the body surface. *J Electrocardiol* 1984; **17**: 179–188
  25. 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
  26. Kuo CS, Munakata K, Reddy CP, Surawicz B: Characteristics and possible mechanisms of ventricular arrhythmia dependent on the dispersion of action potential duration. *Circulation* 1983; **67**: 1356–1367
  27. Merx W, Yoon MS, Han J: The role of local disparity in conduction and recovery time on ventricular vulnerability to fibrillation. *Am Heart J* 1977; **94**: 603–610
  28. Cowan CJ, Yussuf CK, Moore M, et al: Importance of lead selection in QT interval measurement. *Am Heart J* 1988; **61**: 83–87
  29. Priori SG, Napolitano C, Diehl L, Schwartz PJ: Dispersion of the QT interval: A marker of therapeutic efficacy in the idiopathic long QT syndrome. *Circulation* 1994; **89**: 1681–1689
  30. Dristas A, Sbarouni E, Gilligan D, Nihoyannopoulos P, Oakley CM: QT interval abnormalities in hypertrophic cardiomyopathy. *Clin Cardiol* 1992; **15**: 739–742
  31. Surawicz B: Electrophysiologic substrate of torsades de pointes: Dispersion of repolarization or early after repolarization. *J Am Coll Cardiol* 1985; **14**: 172–184
  32. Surawicz B, Kuo CS, Varro A: Dispersion of refractoriness in experimental and clinical arrhythmias. In: Fisch C, Surawicz B, editors. *Cardiac electrophysiology and arrhythmias*. New York: Elsevier Science Publishing, 1991: 108–120
  33. Martini B, Nava A, Thiene G, Buja GF, Canciani B, Scognamiglio R, et al: Ventricular fibrillation without apparent heart disease: Description of six cases. *Am Heart J* 1989; **118**: 1203–1209
  34. Lax KG, Okin PM, Kligfield P: Electrocardiographic repolarization measurements at rest and during exercise in normal subjects and in patients with coronary artery disease. *Am Heart J* 1994; **128**: 271–280
  35. Stoletniy LN, Pai RG: Usefulness of QTc dispersion in interpreting exercise electrocardiograms. *Am Heart J* 1995; **130**: 918–921
  36. Dibs SR, Childs DB, Tenaglia AN: QT peak dispersion: a potential adjunct in non-invasive diagnosis of coronary artery disease (abstract). *Circulation* 1995; **92**(Suppl I): I-540
  37. Stoletniy LN, Pai RG: Value of QT dispersion in the interpretation of exercise stress test in women. *Circulation* 1997; **96**: 904–910
  38. Opthof T, Misier AR, Coronel R, Vermeulen JT, Verberne HJ, Frank RG, et al: Dispersion of refractoriness in canine ventricular myocardium: Effects of sympathetic stimulation. *Circ Res* 1991; **68**: 1204–1215
  39. Lab MJ: Contraction and excitation feedback in myocardium physiological basis and clinical relevance. *Circ Res* 1982; **50**: 757–766