The Prognostic Accuracy of Different QT Interval Measures

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Background: The QT intervals accuracy for predicting arrhythmic death varies between studies, possibly due to differences in the selection of the lead used for measurement of the QT interval. The purpose of this study was to analyze the prognostic accuracy of all known ways to select the lead.

Methods and Results: Three institutions that used different methods for measuring QT intervals provided their QT databases. They included more than 3500 twelve-lead surface ECGs. The data represented low- and high-risk patients of the normal population (survivors vs dead from cardiovascular causes), acute myocardial infarction (survivors versus death from all causes) and remote myocardial infarction (with vs without a history of ventricular arrhythmia). The prognostic accuracy was defined as the area under the Receiver Operator Curve (ROC-area). The most accurate standard leads were I and aVL and the least accurate was AVR. The most accurate precordial lead was V₄. The prognostic accuracy of the longest QT interval was higher than for any standard lead. The prognostic accuracy of the mean of the three longest QT intervals was equal to or slightly lower than for the longest QT interval.

Conclusions: The highest prognostic accuracy is obtained with the longest QT interval. The accuracies of the lead selection methods are so different that it can explain a substantial part of the differences between otherwise similar studies in the literature. We recommend the use of the mean value of the three longest QT intervals.

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A prolonged QT interval is associated with an increased risk of death. It has been observed in individuals with a variety of heart diseases including the long QT syndrome,¹⁻³ post myocardial infarction patients,^{4,5} in the general population,^{6,7} and in the newborn.⁸ Prolonged QT intervals can also be caused by drugs or electrolyte disturbances.⁹⁻¹² The intraobserver reproducibility mea-

sured as the standard deviation (SD) of the measurement errors in a single lead is about 10-15 ms.¹³⁻¹⁸ The interobserver bias is about 10 ms^{19,20} for the longest QT interval. The intraobserver reproducibility can be improved by averaging the QT interval over all leads. However troublesome, the size of these errors is small compared to the inter-lead variability as revealed by the QT dispersion.^{6,21-23}

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Campbell et al.²⁴ noticed in 1988 that different studies used different criteria for selecting the QT interval: such as lead II,^{8,25} modified lead V₅,²⁶ the lead with the tallest T wave,²⁷ the longest QT interval in any limb lead,²⁸ the longest QT in any lead of the 12-lead electrocardiogram,^{4,29} or the mean QT interval.^{6,12} In some studies no criteria are defined.^{5,10,30} Campbell et al.²⁴ showed that lead V₂ and V₃ approximated the longest QT interval best, but concluded that the QT interval should be measured in all leads in order to locate the longest QT interval. There is still not a standard for the selection of the QT interval, but the longest is probably the most used definition in research projects. The longest QT interval might have the highest predictive accuracy, but it has the lowest reproducibility of all the QT intervals.^{13,31}

The literature on the QT interval is extensive and a study of QT interval changes has become a standard requirement during evaluation of new drugs. It is, therefore, surprising that there does not exist any standard for the measurement of the QT intervals nor in which lead it should be measured.³²

The purpose of this study is to analyze all known methods for selecting the lead(s) in which the QT interval should be measured. The study was designed to have a high external validity by (1) including a wide range of patients from the normal population, patients with remote myocardial infarction, and patients with acute myocardial infarction, and (2) including populations where the QT interval was measured by different methods.

METHOD

Study Population

Subjects with less than three QT intervals in the precordial or the frontal leads were excluded. Framingham's correction for heart rate has been found to be superior to Bazett's formula and was consequently used in the entire study.³³ See also the Discussion.

The EpiSet database consisted of a random sample of 3781 individuals from a general Danish population recruited in 1982 to 1984 and followed for 11 years by the Copenhagen County Centre for Preventive Medicine.⁶ The medical history was obtained by interview. The medical staff performed a physical examination and an ECG12 was recorded at 25 mm/s at a gain of 10 millimeters per millivolt and a paper format of 3*4 leads. The QT interval

was measured in one beat using a digitizer tablet. The endpoint of the T wave was defined as the point of return to the isoelectric line. In the presence of a U wave, the end of the T wave was defined as the nadir between the two waves. Leads were rejected if the T wave was too flat or in case of a TU-merger without nadir. Subjects with bundle branch block (N = 28), atrial fibrillation (N = 10), death from noncardiovascular causes (N = 167), missing or too low quality ECG12s (N = 78), or too few QT intervals (N = 4) were excluded. The 3248 subjects accepted for this study consisted of two groups. The high-risk group (N = 92) with subjects that died from cardiovascular causes during follow-up, and the low risk group (N = 3156) with subjects who were alive at the end of the follow-up. The age was 44 ± 10 years. Notice that the majority of the subjects died from noncardiovascular causes (N = 167 vs N = 92 who died from cardiac causes). The prevailing hypothesis is that they cannot be identified using the QT interval. They were excluded in order to improve the contrast between high- and low-risk subjects. Reproducibility was analyzed for 122 subjects for whom two repeated measurements were available.

The arrhythmia database (ArrSet)³⁴ included 110 subjects with a remote myocardial infarction in a case-control design with matching for age and sex. The leads were recorded at a paper-speed of 50 mm/sec at a gain of 10 millimeters per millivolt and a paper format of 2*6 leads. The QT interval was measured in two successive beats as the intersection between the tangent of the terminal part of the T wave and the baseline. Leads were rejected if the amplitude of the T wave was considered too low, if the baseline was considered too unstable, or if the start of QRS was ill defined. The QT interval was averaged over the two successive beats after rejection of subjects (N = 15) where the number of QT intervals was too small due to one or two missing beats (N = 21 beats). The 95 subjects accepted for this study came from a low-risk group (N = 47) and a high-risk group including (N = 48) who had a recent history of ventricular tachycardia or ventricular fibrillation or had been resuscitated from cardiac arrest. The age was mean $\pm$ SD = 54 ± 9 years. The reproducibility was analyzed by considering the measurement of QT in two successive beats as two repeated measurements.

The Acute Myocardial Infarction database (AmiSet)³⁵ included 247 subjects who were hospitalized for acute myocardial infarction and fol-

lowed for 14 ± 6 months. Two hundred one subjects had an ECG12 taken early after hospitalization. Twenty-three subjects died from all causes of death in this period. Eighty-eight survived and the status was unknown for 90 subjects. We classified the 90 patients with unknown status as survivors, because 9.3% (23 dead of the 247 included subjects) is the expected mortality of an unselected population of acute myocardial infarction patients.³⁶ The QT interval was measured using a semiautomatic method applied to the averaged QRS-T complex of 10 seconds of ECG12 plus Frank's orthogonal XYZ leads. A startpoint for QRS and an endpoint for the T wave were determined from Frank's orthogonal leads and displayed on a computer screen as common start- and endpoints for the QT interval in all leads. The operator then adjusted the endpoints when necessary. ECG12s with too few QT intervals ($N = 1$) were excluded. Of the 201 ECGs one was lost. The 200 subjects accepted for this study came from a low-risk group with ($N = 178$) patients that survived and a high-risk group ($N = 22$) who died. The age was 64 ± 12 years.

Reorganization of the QT Intervals

Organizing the QT intervals according to the anatomical position of the leads has previously revealed a trend in the duration of the QT intervals.³⁷ It might, therefore, reveal a trend in the prognostic value of the QT intervals too. The QT intervals are organized as follows: I, aVR, II, aVF, III, aVL, I, aVR, II, aVF, III, and aVL for the frontal leads and V_1 , V_2 , V_3 , V_4 , V_5 , V_6 , V_1 , V_2 , V_3 , V_4 , V_5 , and V_6 for the precordial leads. The sign of the leads was omitted since it does not influence QT.

Rejection of QT Outliers and Estimation of Missing QT Intervals

We have extensively studied the rejection of erroneous QT intervals before the calculation of the QT dispersion.³⁷ We, therefore, analyzed how these methods influence the prognostic accuracy of the QT interval. In short, erroneous QT intervals were detected and rejected by measuring whether the difference between the shortest and second shortest or the longest and the second longest QT intervals exceed the threshold in equation 1.³⁷

Equation 1: Calculation of the threshold for QT-outliers. The multiplier 5 and the offset 60 ms were identified previously.³⁷

$$th = 5 * \alpha + 60$$

Symbols: th is the calculated threshold ; α : is the slope was estimated as the difference between the second longest and the second shortest QT intervals divided by $N-3$ where N is the number of measured QT intervals.

The analysis of trends in the prognostic accuracy is much easier if all patients are represented by 12 QT intervals. We therefore estimated the missing QT intervals by linear interpolation of the QT intervals organized as shown above.³⁷ This reorganization revealed a trend in the QT intervals³¹ and is the reason why linear interpolation is presumably better than substitution by the mean of the measured values.

Selection of the QT Interval

The known methods of selecting the QT interval consist of, the mean QT interval,^{6,12} lead II,^{8,25} modified lead V_5 ,²⁶ the lead with the tallest T wave,²⁷ the maximum QT in any limb lead,²⁸ the maximum QT in any lead,^{4,29} and lead V_2 and V_3 .²⁴

All these methods can be analyzed by calculating the prognostic accuracy of: the QT interval for each standard lead, the mean QT interval, and the QT intervals sorted according to size from the shortest to the longest QT interval. We also analyzed the mean of the following QT intervals; the two shortest, the two longest, the three shortest, and the three longest. These methods are meant as more reproducible replacements for the shortest and longest QT intervals. All methods were analyzed after rejection of erroneous QT measurements. The best methods were also analyzed without rejection of erroneous QT measurements and without interpolation of missing QT intervals.

Prognostic Accuracy

The prognostic accuracy is the ability of the method to classify patients correctly into the high- and low risk groups described in the section "Study Population." The prognostic accuracy is frequently reported as the sensitivity and the specificity at a given threshold for the QT interval. This makes it impossible to compare the prognostic accuracy of the QT interval in different studies. The Receiver Operator Curve (ROC) shows the sensitivity and the specificity of the test at all thresholds for the QT interval. The area under the ROC summarizes the test's overall accuracy and is in fact propor-

Figure 1. The variation of the accuracy of the QT interval with the orientation of the lead. Figures A and B show the accuracy of the limb- and the precordial- leads over 360°. Erroneous QT intervals were rejected and missing QT intervals interpolated.

tional to the standardized normal deviate of Mann-Whitney for a given number of patients.³⁸ The larger the ROC area, the higher the sensitivity and the specificity will be for most, but not necessarily for all thresholds. The ROC area is independent of the prevalence of the disease and avoids the issue of selecting specific thresholds for the classification of patients.³⁹ The ROC area varies between 50 and 100 corresponding to no and perfect discriminative power, respectively.

We did not calculate confidence intervals or P values to state whether the ROC-areas were significantly different. The results show that a satisfactory calculation of the P value should be based on a statistical model that takes into account the trend in the ROC area from the shortest to the longest QT interval. The development of such a statistical model is beyond the scope of this study. Furthermore, we believe that the only rational choice is to select the QT interval with the highest ROC area,

eventually with some concern for the reproducibility.

RESULTS

One or two erroneous QT intervals were rejected from N = 0, N = 1, and N = 48 subjects for the ArrSet, AmiSet, and the EpiSet, respectively.

Figure 1 shows the prognostic accuracy of the standard leads organized according to the anatomical orientation of the standard leads. The accuracy follows approximately the same highly organized pattern for all databases. This is in particular true for the EpiSet and the ArrSet, whereas the pattern in the AmiSet is slightly displaced and not as systematic. The best accuracy for the limb leads was found in the interval from lead III—aVL—I and for the precordial leads in the interval from V₃ to V₄. The highest accuracy was located in different leads and was never located in the precordial leads: 67 (II,III), 78 (aVL), and 66 (I) for AmiSet, ArrSet, and EpiSet, respectively.

Figure 2 shows that the prognostic accuracy increased quasi systematically from the shortest to the longest QT interval. The accuracy increased from about 56 to 68 for the AmiSet and the EpiSet, and from 65 to 79 for the ArrSet. The AmiSet seems at first sight to deviate from this pattern by forming a plateau from QT-7 to QT-12. This is, however, a consequence of the measurement method. In fact, each patient in the AmiSet had five identical longest QT intervals, whereas there was only one longest QT interval in the ArrSet and the EpiSet per patient.

Figure 2. Variation of the prognostic accuracy of QT intervals with the rank of the sorted QT intervals. QT-1 is the shortest interval and QT-12 is the longest interval. Erroneous QT intervals were rejected and missing QT intervals interpolated.

Table 1. Prognostic Accuracy According to the Length of the QT Interval with and without Rejection of Erroneous Measurements and Interpolation of Missing QT Intervals

	AmiSet (L, H = 178, 22)		ArrSet (L, H = 47, 48)		EpiSet (L, H = 3156, 92)	
	Y	N	Y	N	Y	N
Shortest QT	57	57	65	65	56	57
Mean of two shortest QT	58	58	66	66	59	59
Mean of three shortest QT	57	57	66	66	60	60
Mean QT	66	65	75	75	65	65
Mean of three longest QT	68	68	78	78	67	67
Mean of two longest QT	68	68	78	78	67	68
Longest QT	68	68	79	79	68	68

L = number of low risk patients; H = number of high risk patients; "Y" = rejection of erroneous QT intervals and interpolation of missing QT intervals; "N" = no rejection of erroneous QT intervals and no interpolation of missing QT intervals.

Table 1 shows that the rejection of erroneous QT intervals and the interpolation of missing QT intervals in column "Y" did not improve the prognostic accuracy compared to no rejection of erroneous QT intervals and no interpolation of missing QT intervals in column "N". The longest QT interval is the most accurate, but the accuracy of the mean of the two or three longest QT intervals is almost as good: AmiSet 68 versus 68, ArrSet 79 versus 78, and EpiSet 68 versus 67.

We have previously shown that the QT interval measured in the lead with the tallest T wave correspond to the median QT interval.³¹ Its accuracy corresponds to the accuracy of QT-6 and QT-7 in Figure 2 and is consequently lower than the accuracy of the longest QT interval.

The highest prognostic accuracy in any standard lead is lower than for the longest QT interval in all databases: 67 (II,III) versus 68 (longest QT), 78 (aVL) versus 79 (longest QT), and 66 (I) versus 68 (longest QT) for AmiSet, ArrSet, and EpiSet, respectively.

The reproducibility of the mean QT interval is about 50% better than for the shortest and longest QT intervals in the ArrSet (4 vs 7 and 10 ms, $P < 0.001$) and the EpiSet (10 vs 18 and 23 ms, $P < 0.001$). The reproducibility of the mean of the three shortest and the mean of the three longest QT intervals was about 38% better than for the shortest and the longest QT interval respectively in both datasets ($P < 0.001$).

DISCUSSION AND CONCLUSION

This study shows that the longest QT interval consistently has the highest prognostic accuracy of

all known methods of selecting the QT interval including the mean QT interval, the QT interval of the tallest T wave, and the QT intervals of any standard lead. The rejection of erroneous QT intervals and the interpolation of missing QT intervals did not improve the prognostic accuracy of any of the QT interval measures, which is contrary to the improvement we found previously for the QT dispersion.³⁷ The longest QT interval has the highest prognostic accuracy irrespective of the method used to measure the QT interval. This circumstance increases the external validity of the study.

We report the absolute prognostic accuracy. However, do notice that the only information required to draw the conclusion in this study is the change in prognostic accuracy due to the selection. Whether that change takes place from an ROC area of 51% to 55% or from 75% to 78% does not matter. This implies that the conclusion does not depend on the heart-rate correction formula. It also implies that the conclusion would have been the same, had we included other clinical data in a multivariate analysis.

The advantage of using the longest QT interval as prognostic parameter is that it is always available. The disadvantage is that all leads must be measured and that the longest QT interval has the lowest reproducibility.¹³ The advantage of measuring the QT interval in a fixed standard lead is that the definition is simple and avoids bias due to operator preferences. Campbell et al.²⁴ suggested measuring the QT interval in V_2 and V_3 for patients with acute myocardial infarction, because V_2 and V_3 approximate the longest QT interval best. This is interesting because the most accurate precordial

leads were in fact V_2 and V_3 for the AmiSet, which consisted of acute myocardial infarction patients. The disadvantage of measuring the QT interval in a fixed standard lead is that there will always be patients where the QT interval cannot be measured in that lead. Furthermore the study showed that the optimal lead was not the same for different databases, probably due to differences in populations and measurement methods. For example, the precordial leads V_2 and V_3 were the most accurate for the AmiSet (patients with acute myocardial infarction), whereas V_4 , V_5 and V_6 were the most accurate for the ArrSet (remote myocardial infarction) and the EpiSet (cardiac death in the general population). That no single standard lead is best for all types of patients, is also supported by the circumstance that the orientation of the T wave's vector-loop changes according to the heart disease⁴⁰ and that this rotation will change the lead in which the longest QT interval is located.³¹

The reproducibility of the mean of the three longest QT intervals is better than for the longest QT interval, but despite this advantage the single longest QT interval has the same or a slightly better accuracy. However, reproducibility is important to the acceptance of a method, so we recommend the use of the mean of the three longest QT intervals without rejection of erroneous QT intervals and without interpolation of the missing QT intervals.

Measuring all the QT intervals in the standard leads will probably be considered impractical for clinical use until ECG analysis is computerized. Standardizing on measuring the QT interval in a single standard lead should be avoided for the following reasons. The shortest and the longest QT intervals are located in neighboring leads.³¹ It explains why the accuracy is almost the lowest in the lead before or after the most accurate standard lead. The consequence is that for the patients where the standard lead is not optimal, it has a 50% risk of being the least accurate (shortest QT interval). That is, the prognostic method does not degenerate gracefully, as it should, in situations where it fails to be optimal. An acceptable compromise could possibly be to select the longest QT interval of I and aVL or the longest QT interval of V_3 and V_4 .

Clinical trials can have an important impact on best clinical practice, and the cost of measuring ECG parameters is probably small in most clinical trials compared to the total cost. It would therefore be logical to use the method with the best compro-

mise between accuracy and reproducibility for clinical trials, namely the mean of the three longest QT intervals.

It should finally be mentioned that the differences in prognostic accuracy between lead selection methods were so large that they can explain a substantial part of the differences between otherwise similar studies in the literature.

REFERENCES

1. Schwartz PJ, Moss AJ, Vincent GM, et al. Diagnostic criteria for the long QT syndrome. An update. *Circulation* 1993;88:782-784.
2. Swan H, Saarinen K, Kontula K, et al. Evaluation of QT interval duration and dispersion and proposed clinical criteria in diagnosis of long QT syndrome in patients with a genetically uniform type of LQT1. *J Am Coll Cardiol* 1998;32:486-491.
3. Moss AJ, Schwartz PJ, Crampton RS, et al. The long QT syndrome. Prospective longitudinal study of 328 families. *Circulation* 1991;84:1136-1144.
4. Ahnve S. QT interval prolongation in acute myocardial infarction. *Eur Heart J* 1985;6:85-95.
5. Schwartz PJ, Wolf S. QT interval prolongation as predictor of sudden death in patients with myocardial infarction. *Circulation* 1978;57:1074-1077.
6. Elming H, Holm E, Jun L, et al. The prognostic value of the QT interval and QT interval dispersion in all-cause and cardiac mortality and morbidity in a population of Danish citizens. *Eur Heart J* 1998;19:1391-1400.
7. de Bruyne MC, Hoes AW, Kors JA, et al. Prolonged QT interval predicts cardiac and all-cause mortality in the elderly. The Rotterdam Study. *Eur Heart J* 1999;20:278-284.
8. Schwartz PJ, Stramba-Badiale M, Segantini A, et al. Prolongation of the QT interval and the sudden infant death syndrome. *N Engl J Med* 1998;338:1709-1714.
9. Hohnloser SH. Proarrhythmia with class III antiarrhythmic drugs: Types, risks, and management. *Am J Cardiol* 1997;80:82G-89G.
10. Kurita T, Ohe T, Shimizu W, et al. Early afterdepolarizationlike activity in patients with class IA induced long QT syndrome and torsades de pointes. *Pacing Clin Electrophysiol* 1997;20:695-705.
11. McKibbin JK, Pocock WA, Barlow JB, et al. Sotalol, hypokalaemia, syncope, and torsade de pointes. *B Heart J* 1984; 51:157-162.
12. Reilly JG, Ayis SA, Ferrier IN, et al. QTc-interval abnormalities and psychotropic drug therapy in psychiatric patients. *Lancet* 2000;355:1048-1052.
13. Lund K, Arildsen H, Perkiömäki JS, et al. Reproducibility of minimum, maximum and median QT intervals in the 12-lead resting ECG. *Ann of Noninvasive Electrocardiol* 2000;5:354-357.
14. Tran HT, Fan C, Tu QW, et al. QT Measurement: A comparison of three simple methods. *Ann Noninvasive Electrocardiol* 1998;3:228-231.
15. Glancy JM, Weston PJ, Bhullar HK, et al. Reproducibility and automatic measurement of QT dispersion. *Eur Heart J* 1996;17:1035-1039.
16. Fei L, Statters DJ, Camm AJ. QT interval dispersion on 12-lead electrocardiogram in normal subjects: Its reproducibility and relation to the T wave. *Am Heart J* 1994; 127:1654-1655.
17. Zabel M, Klingenhöben T, Franz MR, et al. Assessment of QT dispersion for prediction of mortality or arrhythmic

- events after myocardial infarction: Results of a prospective, long-term follow-up study [see comments]. *Circulation* 1998; 97:2543-2550.
18. Coumel P, Maison-Blanche P, Badilini F. Dispersion of ventricular repolarization: Reality? Illusion? Significance? *Circulation* 1998;97:2491-2493.
19. Ahnve S. Errors in the visual determination of corrected QT (QTc) interval during acute myocardial infarction. *J Am Coll Cardiol* 1985;5:699-702.
20. Murray A, McLaughlin NB, Bourke JP, et al. Errors in manual measurement of QT intervals. *Br Heart J* 1994;71:386-390.
21. 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.
22. Macfarlane PW, McLaughlin SC, Rodger JC. Influence of lead selection and population on automated measurement of QT dispersion. *Circulation* 1998;98:2160-2167.
23. Zaidi M, Robert AR, Fesler R, et al. Computer-assisted study of ECG indices of the dispersion of ventricular repolarization. *J Electrocardiol* 1996;29:199-211.
24. Cowan JC, Yusoff K, Moore M, et al. Importance of lead selection in QT interval measurement. *Am J Cardiol* 1988; 61:83-87.
25. Moller M. QT interval in relation to ventricular arrhythmias and sudden cardiac death in postmyocardial infarction patients. *Acta Med Scand* 1981;210:73-77.
26. Molnar J, Zhang F, Weiss J, et al. Diurnal pattern of QTc interval: How long is prolonged? Possible relation to circadian triggers of cardiovascular events. *J Am Coll Cardiol* 1996;27:76-83.
27. Wheelan K, Mukharji J, Rude RE, et al. Sudden death and its relation to QT interval prolongation after acute myocardial infarction: Two-year follow-up. *Am J Cardiol* 1986; 57:745-750.
28. Ahnve S, Gilpin E, Madsen EB, et al. Prognostic importance of QTc interval at discharge after acute myocardial infarction: A multicenter study of 865 patients. *Am Heart J* 1984; 108:395-400.
29. Juul-Moller S. Corrected QT interval during one year follow-up after an acute myocardial infarction. *Eur Heart J* 1986;7:299-304.
30. Veglio M, Maule S, Matteoda C, et al. Use of corrected QT interval in autonomic function testing: Assessment of reproducibility. *Clin Auton Res* 1996;6:309-312.
31. Lund K, Lund B, Arildsen H, et al. Spatial Properties of QT and the T-wave morphology. *Ann Noninvasive Electrocardiol* 2000;5:214-221.
32. Moss AJ. Drugs that prolong the QT interval: Regulatory and QT measurement issues from the United States and the European perspectives. *Annals of Noninvasive Electrocardiology* 1999;4:255-256.
33. Sagie A, Larson MG, Goldberg RJ, et al. An improved method for adjusting the QT interval for heart rate (the Framingham Heart Study). *Am J Cardiol* 1992;70:797-801.
34. Perkiömäki JS, Huikuri HV, Koistinen JM, et al. Heart rate variability and dispersion of QT interval in patients with vulnerability to ventricular tachycardia and ventricular fibrillation after previous myocardial infarction. *J Am Coll Cardiol* 1997;30:1331-1338.
35. Brohet C., Zaidi M, Robert A, et al. Risk stratification after myocardial infarction: Pre-eminence of the QT Dispersion. 1998. XIII World Congress of Cardiology - Rio de Janeiro, Brazil, Monduzzi Editore - Italy.
36. Hohnloser SH, Klingenhöben T, Zabel M. Identification of patients after myocardial infarction at risk of life-threatening arrhythmias. *Eur Heart J* 1999;20:11-20.
37. Lund K, Perkiömäki JS, Brohet C, et al. Improving the reproducibility of QT-dispersion measures. *Ann Noninvasive Electrocardiol* 2001;6:143-152.
38. Henderson AR. Assessing test accuracy and its clinical consequences: A primer for receiver operating characteristic curve analysis. *Ann Clin Biochem* 1993;30:521-539.
39. Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: A fundamental evaluation tool in clinical medicine. *Clin Chem* 1993;39:561-577.
40. Kors JA, de Bruyne MC, Hoes AW, et al. T axis as an indicator of risk of cardiac events in elderly people. *Lancet* 1998;352:601-605.