The Relation of QT Dispersion and Localized QT Difference to Coronary Pathology in a Population with Unstable Coronary Artery Disease

Milos Kesek, M.D.,* Anders Englund, M.D. Ph.D.,† Tomas Jernberg, M.D. Ph.D.,‡ Bo Lagerqvist, M.D. Ph.D.,‡ and Bertil Lindahl, M.D. Ph.D.‡

From the *Department of Cardiology, Norrland University Hospital, 901 85 Umea, Sweden;

†Department of Cardiology, University Hospital, 701 85 Örebro, Sweden; ‡Department of Cardiology,

Akademiska Hospital, 751 85 Uppsala, Sweden

Background: QT dispersion (QTd) contains prognostic information in several patient groups. The variable increases in several conditions with ischemia. Originally, it was thought to reflect the local repolarization inhomogeneity. Even though this explanation has been questioned lately, it continues to be put forward. In order to elucidate a possible local mechanism, we investigated the relation between QT dispersion, an ECG parameter reflecting the local dispersion, and angiographical measures in a population with unstable coronary artery disease.

Methods: The 276 patients were recruited from the FRISC II trial. As the QTd parameter we used the mean value of automatically measured QTd during 27 hours after admission (QTdMean). As a local repolarization measure we used the maximal difference in QT between two adjacent ECG leads (QTdiffMean). The computations were performed on all available ECG leads and on a restricted set without the V₁-V₂ combination. Previously published angiographic scoring tools were adapted for rating and localizing the coronary pathology by two approaches and applied on 174 patients undergoing angiography.

Results: QTdMean was significantly higher than that reported in previous material with unselected chest pain patients (55 vs 40 ms). QTdiffMean correlated strongly with QTdMean. No differences in QTdMean were detected between patients with different angiographical scores. No relation could be shown between the region with dominating coronary pathology as expressed by the scoring tools and the localization of QTdiffMean.

Conclusions: QTd in ischemia seems to be increased by a mechanism unrelated to localization and severity of coronary disease.

A.N.E. 2003;8(1):22-29

QT dispersion; repolarization; coronary artery disease; coronary angiography

QT dispersion (QTd) is an easily accessible parameter obtained from surface ECG that contains prognostic information in several patient groups. QTd is known to increase in several conditions with ischemia, such as during spontaneous episodes of angina,¹ during and immediately after inflation of a PTCA-balloon,² and after incremental atrial pacing in patients with coronary triple-vessel disease.³ QTd is decreased by PTCA⁴ and increased by restenosis.⁵ QTd increases during the initial course of acute myocardial infarction^{6,7} whereas successful thrombolysis decreases QTd.⁸ The variable has been thought to reflect the local repo-

larization inhomogeneity,⁹⁻¹² and ischemia is one possible cause of the inhomogeneity. The repolarization inhomogeneity will result in a difference in the QT duration between adjacent areas of the myocardium if QTd is caused by local factors. Lately, the local explanation of QTd has been questioned.¹³⁻¹⁵ Projections of the t-wave vector onto the scalar ECG leads result in varying QT durations and can thus generate QTd.¹⁶⁻²¹ This hypothesis has not, however, still been generally accepted and the local explanation continues to be put forward.^{7,22,23} The main objective of the present study was to relate QT dispersion to

the extent and localization of coronary pathology in a population of ischemic patients. We investigated the relation of automatically measured QTd to a derived localized ECG parameter that reflects the dispersion and to angiographical measures of coronary artery disease in a population with unstable coronary artery disease. Previously published angiographic scoring tools were adapted for rating and localization of coronary pathology.

METHODS

Patients

The present study was carried out as a substudy of the Fragmin and Fast Revascularization during InStability in Coronary artery disease (FRISC II) trial, a prospective randomized trial involving 58 Scandinavian centers that has been reported in detail elsewhere.^{24,25} Patients were included if they had symptoms suggestive of an acute coronary syndrome and signs of ischemia (ST-segment depression or t-wave inversion) on the ECG or positive biochemical markers for myocardial damage. The main trial had a factorial design with parallel groups. Patients were allocated to one of four treatment groups: Invasive strategy + 3 months subcutaneous dalteparin, invasive strategy + 3 months placebo, noninvasive strategy + 3 months subcutaneous dalteparin, noninvasive strategy + 3 months placebo. In the invasive strategy the aim was to perform coronary angiography, and revascularization within 7 days from admission if appropriate. Patients following the noninvasive strategy underwent coronary angiography only if refractory or recurrent symptoms occurred or if they showed signs of severe ischemia at a predischARGE exercise test. The 276 patients, object to current analysis, were recruited into the FRISC II trial at the seven trial centers equipped for continuous recording of 12-lead ECG. They were in sinus rhythm and exhibited no conduction disturbance. A total of 174 patients underwent coronary angiography, either as a part of the invasive strategy or due to a clinical indication in the noninvasive group. See Figure 1 for the details of the current study profile. Based on our findings, we also analyzed subgroups selected for disease mainly confined to one region and clinically more aggressive coronary artery disease. Written consent was obtained from all patients

and the protocol was approved by all local ethics committees.

ECG Recordings

Sampling of the ECG signal started at the coronary care unit immediately on admission. Each minute, a signal from the 12 conventional scalar ECG leads was collected for 10 seconds at 240 samples per second by a commercial system (TRAM 200SL patient monitors connected to ST-Guard system, GE Medical Systems, Information Technologies, Milwaukee, WI, USA). The signal was digitized by a 16-bit A/D converter and a median ECG complex was computed.

The method only used the ECG complexes with dominating morphology within the 10-second window, thus excluding complexes with grossly aberrant morphology. The QT was computed by a commercial algorithm²⁶ (QT-Guard, GE Medical Systems) that has previously been evaluated.^{27,28} The program defined a simultaneous Q-onset for all leads and a T-end for each lead as the intercept of the baseline and a straight line computed by a least-squares fitting through seven points around the maximum slope of the T wave after a final T-peak. QT in each lead was computed by the commercial program as T-end-Q-onset and QTd as $QT_{max} - QT_{min}$ across all available ECG leads. The program also registered the number of leads excluded due to noisy signal, extremely low t-wave amplitude or undetermined t-wave shape. The parameters from all recordings in each patient were exported to a custom software package.

QTd Measurements

The ECG recordings with valid registrations from at least 10 leads were considered satisfactory and used for subsequent processing. The custom software computed the mean QTd during the registration time (QTdMean). Local differences in QT between adjacent ECG leads were quantified by an approach similar to the one used by Benn et al.²⁹: For each satisfactory ECG recording, the variable QTdiff was computed as the maximal difference in QT between two adjacent ECG leads (precordials and extremity leads ordered in Cabrera sequence). The software then computed QTdiffMean as the mean value of QTdiff for all satisfactory

Figure 1. Study profile.

recordings during the observation time. QT_{diff} in each recording was localized to one of three electrocardiographic regions: anterior when the maximal difference was found in V_1-V_2 , V_2-V_3 , V_3-V_4 , or I-aVR; lateral (V_4-V_5 , V_5-V_6 or aVL-I), and inferior (aVR-II, II-aVF, or aVF-III) (see Figs. 2 and 3). In each patient, the most common localization of QT_{diff} was taken as the localization of $QT_{diffMean}$. The computations were repeated after exclusion of the lead V_1 and the V_1-V_2 lead combination (for justification of this approach see discussion).

Coronary Angiograms

The angiogram was prospectively analyzed by the operator for stenoses. A predefined classification scheme based on a subdivision of the coronary artery tree into fifteen segments³⁰ was used. The operator's analysis was used for computing the de-

gree of stenotic changes in the coronary artery tree and localizing the pathology to one of three angiographical regions (Fig. 1). Two different strategies were used in parallel.

Figure 2. Computation of QT_d and QT_{diff} from an ECG recording.

Figure 3. Division of the coronary tree into three angiographical regions and classification of the ECG leads into three electrocardiographic regions.

1. A simple CASS score³¹ was computed by evaluating LAD (3 segments), LCX including the sulcus branch (2 segments), and RCA (three segments). We assigned a regional CASS score of 1 to an artery with at least one stenosis of >70% whereas an artery with no stenoses or stenoses ≤70% received a regional CASS score of 0. Left main coronary artery stenosis >70% was treated as a combination of LAD and LCX stenoses. By adding the regional scores, the CASS score with a possible range of 0–3 was obtained. This approach did not take into account the stenoses in the seven segments covering the peripheral vessels.
2. A hemodynamically weighted stenosis score (HW score) was computed by the following procedure: Each of the 15 segments was assigned an anatomical coefficient 0.5–5 after Gensini³² (Table 1) and a stenosis coefficient 0–4 (slightly modified after previously published scoring designs:^{30,33} 0 for normal vessel, 1 for <50% stenosis, 2 for 50–70% stenosis, 3 for >70%–<100% stenosis, and 4 for occlusion). For each arterial segment the anatomical coefficient was multiplied by the stenosis coefficient for a segmental product. By adding the segmental products separately for each region, a regional HW score was computed. The three regional scores were added together for a global HW score with a theoretical maximal value of 82.

Table 1. Anatomical Coefficients Modified After Gensini³² and the 15 Coronary Artery Segments After Austen et al.,³⁰ Subdivided into Regions

Coefficient	Anterior Region	Lateral Region	Inferior Region
5	LM (2.5)	LM (2.5)	
2.5	LADprox	LCXprox	
1.5	LADmid		
1	LADdist, D1	LCXdist, OM1	RCA (3 segments), PDA
0.5	D2	OM2	

The left main coronary artery (LM) is assigned a coefficient of 5 that is divided between the anterior and lateral regions.

For both strategies the region with the highest regional score was considered as the region of dominating coronary pathology.

Statistical Analysis

The data were analyzed in SPSS, release 9 (SPSS Inc., Chicago, IL). Values are given as median (interquartile range) unless stated otherwise. Two-tailed Mann-Whitney test was used for testing of differences in continuous variables between two groups; for more than two groups the Kruskal-Wallis test was used. Kappa statistics was used for estimating agreement between categories. Kappa expresses the agreement with values ranging from +1 (perfect agreement) via 0 (no agreement above that expected by chance) to –1 (complete disagreement). Spearman's rho was used for evaluating correlation between variables. A P-level of <0.05 was considered as significant.

RESULTS

General Findings

The baseline characteristics and outcome for the patients included in the present material were similar to those in the main FRISC II study population^{24,25} (Table 2). In the entire studied population of 276 patients, the median number of ECG recordings per patient was 1514 (1294–1980), recorded during a median time of 27 hours (23–36). In median, 824 (213–1344) ECG recordings/patient were satisfactory. For the 174 patients who underwent angiography, the median number of ECG recordings per patient was 1512 (1293–2038), recorded during a median time of 27 hours (23–37). In

Table 2. Basal Characteristics and Outcome for the Investigated Patients

	Patients with QTd-Data	Patients with QTd-Data and Coronary Angiogram
N	276	174
Age	66 (59–73)	64 (58–71)
Men	199 (72%)	122 (70%)
Previous AMI	72 (26%)	41 (24%)
Diabetes mellitus	39 (14%)	26 (15%)
Hypertension	87 (32%)	62 (36%)
Hyperlipidemia	40 (14%)	27 (16%)
Ejection fraction < 45% (by echo)	37 (13%)	18 (10%)
Death during follow-up	8 (3%)	4 (2%)
Death or AMI follow-up	33 (12%)	29 (17%)

median, 810 (212–1295) ECG recordings/patient were satisfactory.

QTd Measurements

The median QTdMean for the 276 patients was 56 ms (40–70 ms). When the V₁ lead was excluded, the resulting restricted median QTdMean was 49 ms (33–66 ms). After dichotomizing the population with respect to known risk factors, no significant difference in QTdMean was found between the groups (Table 3).

The median value of each patient's mean QT_{min} was 370 ms (352–392); the corresponding median of mean QT_{max} was 426 ms (404–450). QTdMean exhibited a significant correlation with mean QT_{max} (Spearman's $\rho = 0.50$, $P < 0.001$) but not with mean QT_{min} ($\rho = -0.08$, $P = 0.16$).

The QTdiffMean was in median 42 ms (27–58). It correlated strongly with QTdMean (Spearman's

$\rho = 0.93$, $P < 0.001$). The restricted QTdiffMean after exclusion of the V₁–V₂ lead combination was in median 33 ms (19–48 ms). It correlated with the restricted QTdMean with $\rho = 0.91$ ($P < 0.001$). According to the criteria above, the QTdiffMean was localized anteriorly in 181 cases, laterally in 61, and inferiorly in 34 cases. The most common localization of QTdiffMean was V₁–V₂, being responsible for the maximal local difference of QT in 95 cases. The restricted QTdiffMean was localized anteriorly in 92, laterally in 88, and inferiorly in 96 cases.

Angiography

Angiography in the 174 patients was performed in median 5 days (3–8) after the inclusion and recording of the ECG. The CASS score was 0 in 26 patients (14.9%), 1 in 84 patients (48.3%), 2 in 42 patients (24.1%), and 3 in 22 patients (12.6%). The HW score was in median 14.5 (6.5–25.5). The CASS score and HW score were significantly higher in groups with previous acute myocardial infarction, ejection fraction <45%, and troponin-T values ≥ 0.1 ug/L (Table 4).

No significant differences in QTdMean were detected between the patients grouped according to their CASS score ($P = 0.34$, Kruskal-Wallis test). QTdMean showed no correlation with the HW-score (Spearman's $\rho = -0.08$, $P = 0.29$). No significant difference in the CASS score or the HW score was seen between two groups dichotomized at QTdMean 40 ms (the median value in a material with unselected chest pain³⁴).

By the angiographic scoring outlined above, the HW score located the region of dominating coronary pathology anteriorly in 110 cases, laterally in 35 cases, and inferiorly in 29 cases. No significant relation could be shown between the region with dominating coronary pathology and the localization

Table 3. QTd in 276 Patients Dichotomized with Respect to Risk Factors

	No		Yes		P (Mann-Whitney)
	n	Median QTdMean	n	Median QTdMean	
Previous AMI	204	56.2	72	51.4	0.32
Diabetes mellitus	237	54.2	39	56.2	0.35
Hypertension	189	54.9	87	54.9	>0.5
Hyperlipidemia	236	55.2	40	49.9	0.11
Ejection fraction < 45% ^a	226	56.1	37	56.2	>0.5
Troponin-T ≥ 0.1 ug/L ^b	119	50.8	152	56.8	0.09

^a Not available in 13 cases. ^b Not available in five cases.

Table 4. Coronary Stenosis Scores in Groups Dichotomized with Respect to Risk Factors

	CASS score (proportion of patients with score < 2)			HW-score (median)		
	No	Yes	P (Mann-Whitney)	No	Yes	P (Mann-Whitney)
Previous AMI	71%	37%	<0.001	12	25	<0.001
EF < 45%	66%	33%	0.01	14	22.75	0.02
Troponin-T $\geq$ 0.1 ug/L	66%	60%	0.03	16	12.5	0.03
Hyperlipidemia	66%	48%	0.27	14	16.5	>0.5
Diabetes mellitus	64%	58%	0.46	14.5	14.5	>0.5
Hypertension	67%	56%	0.38	14	15.25	0.39
Male sex	60%	65%	>0.5	14.25	15.5	>0.5
QTdmean $\geq$ 40 ms	63%	63%	>0.5	15.5	13.5	>0.5

of QTdiffMean, computed either with or without the V₁-V₂ lead combination ($\kappa = -0.018$, $P > 0.5$ and $\kappa = -0.067$, $P = 0.24$, respectively) (see Table 5). Similar results were obtained for the comparison of localization of QTdiffMean with localization of the coronary pathology by the CASS score ($\kappa = -0.057$, $P = 0.27$ and $\kappa = 0.08$, $P > 0.5$ for QTdiffMean computed with and without V₁-V₂, respectively).

Subgroup Analysis

A subpopulation with the coronary pathology mainly confined to one region was selected by examining the patients with CASS score of 1 (84 patients). No significant relation could be shown between the region with dominating coronary pathology and the localization of QTdiffMean in this group. A subpopulation with a clinically more aggressive coronary artery disease was selected by focusing on the 68 patients initially randomized to the noninvasive strategy but undergoing coronary angiography due to clinical indication. No significant relation could be shown between the region with dominating coronary pathology and

the localization of QTdiffMean in this group. After dichotomization with respect to the risk factors (from Table 3), the median QTdMean was significantly greater for the 32 patients with troponin-T $\geq$ 0.1 ug/L when compared to the 34 patients with troponin-T < 0.1 ug/L (64 vs 48 ms and 59 vs 39 ms, $P = 0.011$ and $P = 0.018$, Mann-Whitney, for calculations with and without V₁-V₂, respectively; two patients missing).

DISCUSSION

We have shown that the differences in QT underlying the QT dispersion for a given patient are not equally distributed across the measured leads. Instead, a localized difference in QT between adjacent leads stands for about three fourths of the QT dispersion. This would in itself be consistent with local factors causing QTd. Our attempt to connect the localized electrocardiographical measure to the angiographical localization was, however, unsuccessful. This is in line with the unsuccessful attempt of Shimizu et al. to relate QT dispersion to scintigraphically quantified regional cardiac sympathetic nerve activity.²³ The

Table 5. Localization of QTdiffMean Versus Region of Dominating Coronary Pathology

		Localization of QTdiffMean ^a				Localization of QTdiffMean (V ₁ -V ₂ excluded) ^b			
		Anterior	Lateral	Inferior	Total	Anterior	Lateral	Inferior	Total
Region of dominating coronary pathology by HW score	Anterior	66	26	18	110	32	35	43	110
	Lateral	27	6	2	35	12	13	10	35
	Inferior	16	10	3	29	10	10	9	29
	Total	109	42	23	174	54	58	62	174

^a $\kappa = -0.067$, $P = 0.24$. ^b $\kappa = -0.018$, $P > 0.5$.

findings make a local mechanism less probable as an explanation for QTd. The distribution of the QT durations over the ECG leads is known to be asymmetrical with V₁ diverging from the others. It exhibits most frequently the shortest QT interval and smallest t-wave amplitude, making it more liable to measurement error.^{20,35} We therefore performed the computations on all available ECG leads in each satisfactory recording, as well as on a restricted set where the V₁-lead and the V₁-V₂ combination were excluded. Our observation that the QT dispersion relates moderately to the longest but not to the shortest QT in an individual patient is in accordance with previously published data.^{7,36} The automatically measured QTdMean has in a previous study by our group been related to the outcome in patients with unselected chest pain.³⁴ In comparison, the current material exhibited a significantly higher QTdMean (median 55 vs 40 ms, $P < 0.001$). It was comparable to the mentioned material with unselected chest pain in median age (66 vs 67 years), prevalence of diabetes (14% vs 16%), hypertension (32% vs 37%), and previous myocardial infarctions (26% vs 28%) whereas the mortality in the current material was somewhat lower (3% vs 4%). The large difference in QTdMean does not thus seem to relate to the current patients being generally sicker. However, the present study included only patients with ischemic heart disease, with a great majority exhibiting ST depression on admission, whereas about half of the patients in the previous study did not have acute ischemic heart disease. Furthermore, the dichotomized QTdMean lost its prognostic power when it was adjusted for ST-T changes on admission ECG.

LIMITATIONS

It is exceedingly difficult to construct a scoring scheme that adequately quantifies the severity and anatomical localization of coronary pathology. Two different algorithms were, therefore, used. Our approach will still be crude and for an individual patient error-prone due to the large normal anatomical variability. The relation between a repolarization abnormality of the myocardium and stenotic changes or measures of flow in the supplying coronary arteries is complex. The ischemic area is not always identical with an anatomical extrapolation from the angiogram. The definition of the regions based on the schematic coronary angiogram may significantly differ from the definition of the re-

gions as seen from the ECG. Thus, a local mechanism may still be active although it may not directly correspond to the coronary pathology as we quantify it. Averaging a large number of automatically analyzed ECG recordings is a powerful approach but it also means that any possible time-related information will remain uncovered. We have previously addressed this issue.³⁴ The current analysis was performed in a retrospective manner, although the data collection was done prospectively in a large study and consecutive eligible patients were analyzed.

In conclusion, it seems that QT dispersion in ischemia is increased by a mechanism unrelated to localization and severity of coronary disease as reflected in risk factors (Table 3) and viewed by angiography (Table 5). From our, and others' work it seems that the measure is an indicator of future risk. The clinical value of the measure for stratification of broad populations will, however, remain restricted. The limitations are inherent in its properties and will probably not be removed by the development of better measurement methods.

REFERENCES

1. Dilaveris P, Andrikopoulos G, Metaxas G, et al. Effects of ischemia on QT dispersion during spontaneous anginal episodes. *J Electrocardiol* 1999;32:199-206.
2. Michelucci A, Padeletti L, Frati M, et al. Effects of ischemia and reperfusion on QT dispersion during coronary angioplasty. *Pacing Clin Electrophysiol* 1996;19:1905-1908.
3. Stierle U, Giannitsis E, Sheikhzadeh A, et al. Relation between QT dispersion and the extent of myocardial ischemia in patients with three-vessel coronary artery disease. *Am J Cardiol* 1998;81:564-568.
4. Yunus A, Gillis AM, Traboulsi M, et al. Effect of coronary angioplasty on precordial QT dispersion. *Am J Cardiol* 1997;79:1339-1342.
5. Koide Y, Yotsukura M, Tajino K, et al. Use of QT dispersion measured on treadmill exercise electrocardiograms for detecting restenosis after percutaneous transluminal coronary angioplasty. *Clin Cardiol* 1999;22:639-648.
6. Glancy JM, Garratt CJ, de Bono DP. Dynamics of QT dispersion during myocardial infarction and ischaemia. *Int J Cardiol* 1996;57:55-60.
7. Chauhan VS, Tang AS. Dynamic changes of QT interval and QT dispersion in non-Q-wave and Q-wave myocardial infarction. *J Electrocardiol* 2001;34:109-117.
8. 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.
9. Mirvis DM. Spatial variation of QT intervals in normal persons and patients with acute myocardial infarction. *J Am Coll Cardiol* 1985;5:625-631.
10. Franz MR, Zabel M. Electrophysiological basis of QT dispersion measurements. *Prog Cardiovasc Dis* 2000;42:311-324.
11. Zabel M, Portnoy S, Franz MR. Electrocardiographic indexes of dispersion of ventricular repolarization: An isolated heart validation study. *J Am Coll Cardiol* 1995;25:746-752.

12. Zabel M, Lichtlen PR, Haverich A, et al. Comparison of ECG variables of dispersion of ventricular repolarization with direct myocardial repolarization measurements in the human heart. *J Cardiovasc Electrophysiol* 1998;9:1279-1284.
13. Punske BB, Lux RL, MacLeod RS, et al. Mechanisms of the spatial distribution of QT intervals on the epicardial and body surfaces. *J Cardiovasc Electrophysiol* 1999;10:1605-1618.
14. Lux RL, Fuller MS, MacLeod RS, et al. QT interval dispersion: Dispersion of ventricular repolarization or dispersion of QT interval? *J Electrocardiol* 1998;30(Suppl.):176-180.
15. Malik M, Acar B, Gang Y, et al. QT dispersion does not represent electrocardiographic interlead heterogeneity of ventricular repolarization. *J Cardiovasc Electrophysiol* 2000;11:835-843.
16. Kors JA, van Herpen G, van Bommel JH. QT dispersion as an attribute of T-loop morphology. *Circulation* 1999;99:1458-1463.
17. Rautaharju PM. QT and dispersion of ventricular repolarization: The greatest fallacy in electrocardiography in the 1990s. *Circulation* 1999;99:2477-2478.
18. Coumel P, Maison-Blanche P, Badilini F. Dispersion of ventricular repolarization: Reality? Illusion? Significance? *Circulation* 1998;97:2491-2493.
19. Macfarlane PW, McLaughlin SC, Rodger JC. Influence of lead selection and population on automated measurement of QT dispersion. *Circulation* 1998;98:2160-2167.
20. Lee KW, Kligfield P, Okin PM, et al. Determinants of precordial QT dispersion in normal subjects. *J Electrocardiol* 1998;31(Suppl.):128-133.
21. Lee KW, Kligfield P, Dower GE, et al. QT dispersion, T-wave projection, and heterogeneity of repolarization in patients with coronary artery disease. *Am J Cardiol* 2001;87:148-151.
22. Zabel M, Franz MR. The electrophysiological basis of QT dispersion: Global or local repolarization? *Circulation* 2000;101:E235-E236.
23. Shimizu M, Ino H, Okeie K, et al. Increased QT dispersion does not reflect the increased regional variation of cardiac sympathetic nervous activity in hypertrophic cardiomyopathy. *Am Heart J* 2001;142:358-362.
24. FRISC II Investigators. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. *Lancet* 1999;354:708-715.
25. FRISC II Investigators. Long-term low-molecular-mass heparin in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. FRagmin and Fast Revascularisation during InStability in Coronary artery disease. *Lancet* 1999;354:701-707.
26. Xue Q, Reddy S. Algorithms for computerized QT analysis. *J Electrocardiol* 1998;30(Suppl.):181-186.
27. 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.
28. Gang Y, Guo XH, Crook R, et al. Computerised measurements of QT dispersion in healthy subjects. *Heart* 1998;80:459-466.
29. Benn M, Hansen PS, Pedersen AK. QT dispersion in patients with arrhythmogenic right ventricular dysplasia. *Eur Heart J* 1999;20:764-770.
30. Austen WG, Edwards JE, Frye RL, et al. A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease, Council on Cardiovascular Surgery, American Heart Association. *Circulation* 1975;51:5-40.
31. Principal Investigators of CASS. The National Heart, Lung, and Blood Institute Coronary Artery Surgery Study (CASS). *Circulation* 1981;63:1-39.
32. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. *Am J Cardiol* 1983;51:606.
33. Sullivan DR, Marwick TH, Freedman SB. A new method of scoring coronary angiograms to reflect extent of coronary atherosclerosis and improve correlation with major risk factors. *Am Heart J* 1990;119:1262-1267.
34. Kesek M, Jernberg T, Lindahl B, et al. QT dispersion measured by an automatic continuous method early in patients admitted for chest pain. *Int J Cardiol* 2002; In press.
35. Glancy JM, Garratt CJ, Woods KL, et al. Use of lead adjustment formulas for QT dispersion after myocardial infarction. *Br Heart J* 1995;74:676-679.
36. Krahn AD, Nguyen-Ho P, Klein GJ, et al. QT dispersion: An electrocardiographic derivative of QT prolongation. *Am Heart J* 2001;141:111-116.