QT Interval Dispersion Analysis in Patients Undergoing Left Partial Ventriculectomy (Batista Operation)

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Background: QT interval dispersion (QTd) has been valued as a marker of increased vulnerability for cardiac arrhythmias. QTd was analyzed in patients undergoing the left partial ventriculectomy (LPV) or Batista operation, a palliative surgery for patients in the line for heart transplantation, which is associated with complex arrhythmia and death from sustained ventricular tachyarrhythmia (SVT).

Methods: Pre- and postoperative R-R, QT, QTc, JT (QT – QRS), and aT (apex to end of T wave) intervals were obtained by 87-lead body surface mapping from 24 patients (18 male), mean age 46.4 ± 9.15 years. Dispersions of QT, QTc, JT, and aT intervals were calculated, and the total number of arrhythmic events were assessed, aiming to verify a possible risk predictor for the occurrence of SVTs. Subgroups of patients who survived and who died after LPV were also compared, aiming to obtain a QTd cutoff value that could be used prognostically.

Results: No difference between pre- and postoperative mean values were found, but a very significant difference was seen when comparing QTd and QTcD values for surviving and dead patients: QTd, cutoff value was 95 ms, while QTcD value was 114 ms.

Conclusion: There were no significant differences between pre- and postoperative variables or the number of arrhythmic events, but there were significant differences between both pre- and postoperative QTd and QTcD data from surviving and dead patients; this enabled the determination of cutoff values that we believe may be useful for the prognosis of the LPV outcome.

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The left partial ventriculectomy (LPV) or Batista operation, reported by Dr. Randas Batista¹ in 1996, is a palliative surgery for patients suffering from end-stage chronic congestive heart failure (CHF), who remain in NYHA Function Classes III and IV after all kinds of clinical management have been tried, and are therefore in the line for heart transplantation. The operation consists of the resection of a large wedge of muscle from the left ventricle lateral wall, beginning at the apex, extending between the papillary muscles, and ending proximal to the mitral annulus (Fig. 1). This can reverse some aspects of the cardiac remodeling, such as hypertrophy, dilation, change in left ventricular

shape, and augmented wall stress (law of Laplace). Reduced left ventricular diameters, along with increased wall thickness-to-chamber radius ratio, can result in decrease in wall stress valve regurgitation, fiber slippage, and myocardial oxygen demand, with consequent enhancement of ventricular performance.

The resection of part of the cardiac muscle can result in myocardial infarction and is a substrate for ventricular tachycardia. Patients undergoing LPV frequently present with sustained ventricular tachyarrhythmias (SVT) that are the cause for 30% mortality from sudden death in this group.²

Figure 1. Schematic representation of the heart in the Batista operation.

In the last 30 years, many investigators have associated ventricular extra-systoles that cause complex arrhythmias, with increased risk of sudden death.^{3,4} Disturbances of impulse formation and conduction can also originate SVTs. Many studies have associated the inhomogeneous refractoriness of myocardial tissue with increased vulnerability to SVTs.⁵⁻¹² Wilson¹⁴ had already reported in the 1930s that ventricular repolarization could vary throughout the different ECG leads. Han and Moe¹⁵ have demonstrated an association between increase in the dispersion of ventricular repolarization and reduction in the threshold for ventricular fibrillation, concluding that inhomogeneity of the myocardium recovery of excitability contributed to increased vulnerability to ventricular fibrillation.

An increased QT interval dispersion (QTd) observed in the electrocardiogram reflects the asynchronous myocardium refractoriness, which results from regional differences in ventricular recovery times, and is an indicator of electrical instability.¹⁶ Studies investigating the long-QT syndrome,^{5,6,17,18} drug-induced torsades des pointes,⁷ unexpected sudden death in congestive heart failure,^{8,9} ischemic coronary heart disease,¹⁰⁻¹² and

metabolic disorders^{19,20} have all associated QT interval dispersion with the occurrence of ventricular arrhythmias.

Analysis of QT interval dispersion consists in observing the difference between maximum and minimum QT intervals in any two of the 12 ECG leads.¹³ The objectives of the present study were to investigate, in a homogeneous cohort of patients undergoing LPV, (1) possible differences between pre- and postoperative measurements of variables involved in the dispersion of myocardium refractoriness (R-R, QT, QTd, QTc, QTcD, JT, and aTd); (2) to compare the number of arrhythmic events in the pre- and postoperative periods of LPV; (3) to compare data from patients who survived with values from patients who died during the follow-up period; and (4) to determine cut-off values to stratify patients at risk of death in the postoperative period of LPV.

MATERIALS AND METHODS

Study Population

From January 1995 to June 2001, 43 consecutive patients of the outpatient chronic heart failure

service were selected to undergo the left partial ventriculectomy. All the patients had history of cardiogenic shock and were in NYHA classes III and IV, with persistent functional impairment, although they had undergone target drug therapy, and had at least one hospitalization for heart failure treatment during the previous 6 months. Left ventricular ejection fraction in the group was equal to or below 25%, as determined by technetium radioisotopic angiography, and they all presented with pulmonary hypertension. Etiology of heart failure was idiopathic dilated cardiomyopathy. The final study group consisted of 24 patients, 18 (75%) male, mean age 46.4 (range 32–68, SD 9.15) years, who could have a body surface potential mapping (BSPM) examination performed in both the pre- and postoperative periods.

The 19 patients excluded could not have a BSPM performed postoperatively either due to death in the immediate postoperative period, or because the aggravation of their condition hindered them from undergoing the second examination. Preliminary analysis of only preoperative values of these latter patients did not substantially alter the results; therefore, it was decided not to include them in that study.

Follow-up of patients was discontinued after November 15, 2001. All the patients signed a special informed consent form according to our Ethical and Scientific Review Board.

METHODS

All the patients underwent Technetium 99m radioisotopic angiography, obtained with a Siemens model LEM camera (Siemens Corp., USA) and analyzed in a model 3300 Microvac computer (Siemens Corp), to register left ventricle ejection fraction (LVEF). Left ventricle diastolic diameter (LVDD) was determined by echocardiography.

Patients were monitored by 24-hour Holter electrocardiography pre- and postoperatively, by a Marquette MARS 8000 equipment (Marquette Co., Milwaukee, WI), using a 4.0 software. Complex SVT arrhythmic events were defined as all the recordings of three or more ventricular beats per minute.

Body surface potential mapping was performed with a Fukuda Denshi model 7100 equipment (Fukuda Denshi Co., Inc., Tokyo, Japan) in a mean interval of 45.35 (range 4–205) days before, and mean 16.77 (range 6–65) days after LPV. Signals were acquired by 87 leads placed 59 on the anterior

chest and 28 on the back, as displayed in Figure 2. Maps were constructed from the 87 simultaneous recordings acquired in the frontal, horizontal, and sagittal planes, visualized on a color screen where each lead can have the beginning and end of the PQRS complex precisely identified and manipulated by the observer through two cursors on the screen. The observer is thus able to automatically obtain measurements of QT, JT, and aT intervals. Pre- and post-extra-systole beats are not considered by the BSPM equipment, which also obtains instant heart rate (HR) measurements. Recordings are magnified with double voltage keeping constant velocity for easier visualization of the precise beginning of QRS and end of T wave recordings. By placing one cursor at the beginning of the QRS complex, the observer can manipulate the second cursor to intersect the end of the T wave with the baseline, in order to measure QT intervals, following the Van de Loo criteria.²¹ The same criteria were used to determine JT intervals, where J was defined as the area where the QRS complex ends and the ST segment begins. The aT interval was measured from the apex of the T wave to its end. QT intervals were corrected by the HR, according to the formula of Bazett: $QT_c = QT / \sqrt{RR}$.²² QT dispersion was determined for each of the QT values found, Bazett-corrected before calculation of differences in all BSPM examinations. From all these measurements, maximum and minimum interval values were calculated, and their dispersion was defined as the difference between maximum and minimum QT, JT, aT, and QTc values, respectively, in milliseconds.

Statistical Analysis

Data are expressed as mean $\pm$ SD, unless otherwise specified. Data comparisons were performed by Student's *t*-test, and Wilcoxon's method was used to compare nonparametric variables. Pearson's method assessed the correlations between LVDD and HR with R-R, QTd, QTcD, JTd, and aTd data. McNemar's test was used to evaluate pre- and postoperative occurrence of SVT episodes. Logistic regression was used to obtain cutoff values for QTd and QTcD associated with mortality. A significance level of $P < 0.05$ was used.

RESULTS

Pre- and postoperative data from patients showed no statistically significant difference when comparing preoperative with postoperative data,

BSPM: (Fukuda Denshi, model 7100)

Figure 2. Body surface potential mapping—sites for lead placement.

with the exception of the minimum JT interval mean value, with $P = 0.0150$, which is significantly increased postoperatively (Table 1). No other data showed any statistically significant difference.

The difference in the number of arrhythmic events did not show statistical significance either, when pre- and postoperative periods are compared ($P = 0.2207$), but SVT events were found in 36% of patients (5 patients in 14) who already presented with SVT before the surgery, whereas only 10% (1 patient in 10) who did not have arrhythmic events

before the surgery, presented with them postoperatively.

Pearson's method did not provide evidence of any significant correlation among LVDD, LVEF, QTd, QTcD, JTd, and aTd mean values. Left ventricle diastolic diameter and ejection fraction did not correlate with any of the other variables ($r = 0.11369$ and $P = 0.6144$).

Comparison between groups of patients who survived and who died during the postoperative follow-up period did not provide evidence of significant differences between the two groups in pre- and postoperative mean R-R, QT, QTc, JTd, and aTd values. However, QTd and QTcD showed significant differences between mean values for the two groups, both pre- and postoperatively.

The association between QTd and QTcD was evaluated by logistic regression. Cutoff values were calculated for QTd and QTcD associated with the event death, with QTd = 95 ($P = 0.0305$) and QTcD = 114 ($P = 0.0207$).

Eight patients died in the postoperative follow-up period. Table 2 displays mean data for subgroups of patients who survived, in comparison with those who died during the follow-up period. JT and aT

Figure 3. QTd and QTcD: subgroups surviving versus dead patients.

Table 1. Comparison of Preoperative and Postoperative Data

	Pre-op		Post-op		P
	μ	σ	μ	σ	
HR	97.17	22.75	87.46	14.01	0.0918
R-R	644.25	125.26	704.63	123.75	0.1049
QTd	91.63	18.25	96.50	26.49	0.1302
QTcD	115.96	26.56	115.17	28.81	0.8467
JTd	78.46	26.49	75.25	25.40	0.5918
aTd	47.13	14.53	47.17	28.86	0.1370
QT max	420.00	40.24	434.63	55.38	0.1700
QT min	328.38	27.17	338.13	42.16	0.2590
QTc max	528.83	56.10	520.75	61.03	0.6593
QTc min	412.86	45.30	405.54	50.82	0.6240
JT max	273.83	40.13	285.21	28.62	0.1480
JT min	195.38	32.26	209.96	26.30	0.0150*

μ = mean; σ = standard deviation; HR = heart rate; R-R = R-R interval; QTd = QT interval dispersion; QTcD = dispersion of QT intervals corrected by the heart rate; JTd = JT interval dispersion; aTd = dispersion of the interval from apex to end of the T wave; QT min = minimum QT interval; QT max = maximum QT interval; QTc min = minimum corrected QT interval; QTc max = maximum corrected QT interval; JT max = maximum JT interval; JT min = minimum JT interval; * = statistically significant.

dispersions did not show statistically significant difference, but it was possible to note a trend toward higher mean values in the subgroup of dead patients, and toward decreased mean values in the surviving subgroup, respectively, for these variables.

Figure 3 compares QTd and QTcD data; in both the pre- and postoperative periods, these variables were characteristically shorter for the subgroup of surviving patients, when compared with the subgroup of dead subjects. QTd for surviving patients was 85.94 ms pre- and 87.81 postoperatively, and the values from patients who died were 105.43 ms pre- and 117.86 ms postoperatively ($P = 0.0067$). QTcD mean values were 106 ms pre- and 105 ms postoperatively for surviving patients, and 138 ms

in both the pre- and postoperative periods ($P = 0.0037$) for the patients who died.

DISCUSSION

In congestive heart failure, 35% to 59% of patients have sudden cardiac death without prior signs of their clinical or hemodynamic condition worsening,²³ and one of the possible explanations for the high mortality rate could be that the main cause was alteration of the ventricular repolarization. Many mechanisms can contribute to such abnormalities of repolarization:

- Malignant remodeling to compensate for maintaining cardiac output and blood flow, with

Table 2. Comparison of Subgroups of Patients Who Survived Versus Those Who Died Following Batista Operation

	QTd		QTcD		JTd		aTd	
	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op
Dead patients	105.43	117.86	138.00	138.12	78.14	92.43	46.71	57.86
Surviving patients	85.94	87.71	106.88	105.71	78.59	68.18	47.29	42.76
<i>p</i>	0.0067		0.0037		0.2265		0.3477	
P	Subgroup Dead >> Surviving (both pre- & post-op)				Subgroup Dead :Trend ↑ vs. Surviving: Trend ↓ (from pre- to post-op)			

QTd = QT interval dispersion; QTcD = dispersion of corrected QT interval; JTd = JT interval dispersion; aTd = dispersion of interval apex to end of the T wave; pre-op = preoperative; post-op = postoperative; p = probability; >> = higher; ↑ = increase; ↓ = decrease.

consequent dilatation of ventricular chambers and augmented wall stress during diastoles, leading to increased dispersion in myocardium refractoriness.²⁴

- Frank-Starling mechanism
- Adrenergic autonomic release, with consequent chronotropic action.
- Myocardium hypertrophy
- Alterations of the inotropic mechanism in calcium-dependent channels, modifying the plateau phase of the action potential²⁵

All these mechanisms lead to reduction of the action potential rest phase in transmembranes, and to a shortening of the action potential duration at the ischemic site, with consequential shortening of the QT interval. However, the time for repolarization is prolonged in this same hypoperfused area, and this leads to increased QT interval dispersion.

QT dispersion is reported as ranging from 30 to 60 ms in most studies,^{26–29} and from 30 to 70 ms in some others.^{30,31} However, Malik considered that only values QTd $\geq$ 100 ms should be taken safely as substantial proof of disturbances in the repolarization process.³² In our group of patients, QT dispersion mean value was 91.63 ± 18.25 ms, which is significantly increased in comparison with values reported as normal, although not as high as the 100 ms recommended by Malik.

The comparison between preoperative and postoperative QTd, QTcD, JTd, and aTd data did not show statistically significant difference in any of these variables. The number of arrhythmic events did not show significant difference from the pre- to the postoperative moment either. It is only worth mentioning that the occurrence of arrhythmic events was more prevalent among patients who already presented with SVT before surgery, than among those who did not. Alterations of myocardium refractoriness and of electrical impulse conduction are under the influence of the autonomous nervous system (ANS). Some investigators^{33,34} reported that catecholamines inhomogeneously reduce the threshold for ventricular fibrillation in ischemia due to the nonuniform distribution of beta-receptors in the myocardium. From the above, we hypothesize that the autonomic retrocession of alterations that might have occurred before surgery were not strong enough to modify the arrhythmic process. Myocardial fibers are greatly damaged in CHF, similar to the necrosis seen in infarcted myocardial tissue; the increased

QT dispersion, reflecting the block in impulse conduction, would lead us to expect the occurrence of arrhythmia caused by reentry mechanisms. However, the damaged heart fibers and the consequent autonomic and physiological sequels, which impair both cell dynamics and the balance between rest and action potentials, along with the duration of myocardium refractoriness, were already present before the surgery, because of CHF. This might be an explanation for the fact that no significant differences could be found between pre- and postoperative values of the variables we analyzed.

The comparison between subgroups of patients who survived and patients who died in the follow-up period evidenced higher QTd and QTcD mean values for the group of dead patients, and also a trend toward higher JTd and aTd values in the same group. This contradicts data reported by Brendorp et al. (2001),³⁵ in a substudy of the DIAMOND-CHF trial with 1518 patients with severe CHF and significant left ventricular dysfunction. The QTd and QTcD mean values of their study subjects, as assessed by 12-lead ECG, did not disclose any difference between surviving and dead patients. Also, the QTd mean value of their population was 70 ms, and no prognostic QTd information could be extracted from any of the mortality causes (CHF or arrhythmia). The other two studies, one with postinfarction CHF patients³⁶ and the other with dilated cardiomyopathy patients,³⁷ also found similar results, thus concluding that QTd could not be considered a good prognostic marker.

On the other hand, consistent with our results, Barr et al. (1994),⁹ found increased QTd values in patients with ischemic cardiomyopathy and sudden death, thereby inaugurating the analysis of QTd as a prognostic marker for CHF patients. Additionally, Anastasiou-Nana et al. (1999)³⁸ found significantly increased QTd values in CHF patients who died in the 19.6-month follow-up term of their study (QTd of 95 vs 54, $P < 0.03$). Death among patients with QTd > 90 ms were 2.8 times as high as among those with QTd < 90 ms. Also, Fu et al. (1997)³⁹ followed 163 patients with LVEF $< 40\%$, 126 with ischemic disease, and 37 with dilated cardiomyopathy, for 26 ± 15 months, finding significantly different QTd and JTd values for CHF patients who suffered sudden cardiac death or a higher number of cardiac events than among those who survived (QTd 95 ± 19 ms vs 54 ± 9 ms, $P < 0.001$).

Galinier et al. (1998)⁴⁰ concluded that QTd > 80 ms has a prognostic value for prediction of

sudden cardiac death and death from arrhythmia in patients with dilated cardiomyopathy, although he could not find a prognostic QTd value for patients with CHF due to ischemic disease. Pinsky et al. (1997)⁴¹ agreed with that result and found QTd higher than 140 ms in all patients who died before they could have a heart transplantation performed. Grimm et al. (1996)²⁹ compared 107 patients with dilated cardiomyopathy, of whom 12 presented with complex arrhythmic events (sudden death, SVTs, or demanded implantation of pacemaker). QTd was found to be higher in those patients, in comparison with those who did not have progression to complex arrhythmic events (76 ± 17 ms vs 60 ± 26 ms, $P = 0.03$).

The studies mentioned above are consistent with our findings, and support our evidence that QTd and QTcD are substantial prognostic markers for patients undergoing LPV, with cutoff mean QTd value of 95 ms and mean QTcD value of 114 ms.

Limitations

The number of patients had to be reduced to 24, since the other 19 patients could not have a body surface potential mapping performed postoperatively, either due to immediate death or aggravation of their clinical condition precluding its performance. Preliminary analysis of preoperative variables of these patients did not significantly alter the overall mean value; therefore, we decided not to include an additional preoperative analysis of the total ventriculectomy patients.

We attempted to overcome the difficulties in measuring the QT interval dispersion (determination of the end of the T wave, small number of ECG leads, intra- and inter-observer data reproducibility, etc.) reported in several studies,^{21,42–46} by using the 87-lead BSPM computerized analysis of ECG data, which, apart from enabling better determination and visualization of the end of the T wave, and of the U wave when it is present, also comprises a larger number of leads—87—to minimize the chance of error, and allows for better visualization of the QRSTU complex, with magnification of the complex on the screen and automatic measurement of the intervals. Automatic BSPM measurement has been used since the last decade for a more practical investigation of coronary artery disease, to determine the infarction site and size,⁴⁷ and also to localize abnormal conduction pathways

in the Wolff-Parkinson-White syndrome, as well as in studies of the arrhythmic process.⁴⁸

CONCLUSIONS

In our QT dispersion analysis of CHF patients undergoing LPV, we concluded that no statistical difference was found in R-R, QT, QTd, QTcD, JT, JTd, and aTd measurements from the pre- to the postoperative BSPM examinations; no difference in the number of arrhythmic events could be seen by comparing data collected before and after surgery; a significant difference in QTd and QTcD mean values was found in the comparison of subgroups of patients who survived and who died in the follow-up period; and cutoff values for QTd and QTcD (95 ms and 114 ms, respectively) were established, which we think may be of value as predictors of worse outcome for patients undergoing LPV.

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REFERENCES

1. Batista RV. Partial ventriculectomy: A new concept in surgical treatment of end-stage cardiomyopathies. *Rev Bras Circ Cardiovascular* 1996;II:1–6.
2. Moreira LFP, Stolf NAG, Higuchi ML, et al. Current perspectives of partial left ventriculectomy in the treatment of dilated cardiomyopathy. *Eur J Cardiothorac Surg* 2001;19(1):54–60.
3. Moss AJ, Camilla J, Mietlowski W, et al. Prognostic grading and significance of ventricular premature beats and mortality after myocardial infarction. *Circulation* 1975;51(suppl. III):204–209.
4. Chiang B, Perlman L, Ostrander L, et al. Relationship of premature systoles to coronary heart disease and sudden cardiac death in the Tecumseh epidemiologic study. *Ann Intern Med* 1969;79:1159–1165.
5. Moss AJ. Long QT syndrome. In Podrid P, Kowey P (eds.), *Textbook of Cardiac Arrhythmia, Mechanisms, Diagnosis and Management*. Baltimore, Williams & Wilkins, 1995:1110–1120.
6. Priori SG, Napolitano C, Diehl L, et al. Dispersion of the QT interval. A marker of therapeutic efficacy in idiopathic long QT interval. *Circulation* 1994;89:1681–1689.
7. Cui G, Sem L, Sager P, et al. Effects of amiodarone, sotalol and sotalol on QT dispersion. *Am J Cardiol* 1994;74:896–890.
8. Zardi M. Dispersion of ventricular repolarization in dilated cardiomyopathy. *Eur Heart J* 1997;18:1129–1134.
9. Barr CS, Naas A, Freeman M, et al. QT dispersion and sudden unexpected death in chronic heart failure. *Lancet* 1994;343:327–329.
10. Zareba W. Dispersion of ventricular repolarization and arrhythmic cardiac death in coronary artery disease. *Am J Cardiol* 1994;74:550–553.
11. Higham PD, Campbell RWF, Furniss S. QT dispersion and components of the QT interval in ischaemia and infarction. *Br Heart J* 1995;73:32–36.

12. Tomassoni G, Pisano LM, Gardner KMW, et al. QT prolongation and dispersion in myocardial ischemia and infarction. *J Electrocardiol* 1995;30:187-190.
13. Campbell RWF, Gardiner P, Amos P. Measurement of the QT interval. *Eur Heart J* 1985;6:81-83.
14. Wilson FN, Macleod AD, Barker PS, et al. The determination of the significance of the areas of the ventricular deflections of the electrocardiogram. *Am Heart J* 1934;10:46-61.
15. Han J, Moe GK. Nonuniform recovery of excitability in ventricular muscle. *Circ Res* 1964;14:44-60.
16. Zareba W, Moss AJ, Badilini F. Noninvasive electrocardiology. Clinical aspects of Holter monitoring. In Moss AJ, Stern S (eds.), *Dispersion of Repolarization: Noninvasive Marker of Nonuniform Recovery of Ventricular Excitability*. London, Saunders, 1996:405-418.
17. Schwartz PJ, Periti M, Malliani A. The long Q-T syndrome. *Am Heart J* 1975;89:378-390.
18. Schwartz PJ, Wolf S. QT interval prolongation as predictor of sudden death in patients with myocardial infarction. *Circulation* 1978;57:1074-1077.
19. Burgess CD, Siebers RW, Purdie GL, et al. The relationship between the QT interval and plasma amiodarone concentration in patients on long-term therapy. *Eur J Clin Pharmacol* 1987;33:115-118.
20. Schouten EG, Dekker MP, Kok FJ, et al. QT interval prolongation predicts cardiovascular mortality in an apparently healthy population. *Circulation* 1991;84:1516-1523.
21. Van de Loo A, Arendts W, Hohnloser SH. Variability of QT dispersion measurements in the surface electrocardiogram in patients with acute myocardial infarction and in normal subjects. *Am J Cardiol* 1994;74:1113-1118.
22. Bazett HC. An analysis of the time-relations of electrocardiograms. *Heart* 1920;7:353-70.
23. Gradman A, Deedwania P, Cody R, et al. For the Captopril-Digoxin study group. Predictions of total mortality and sudden death in mild to moderate heart failure. *J Am Coll Cardiol* 1989;14:564-570.
24. Cohn JN. Structural basis for heart failure: Ventricular remodeling and its pharmacological inhibition. *Circulation* 1995;91:2504-2507.
25. Braunwald E. Mechanisms of cardiac contraction and relaxation; pathophysiology of heart failure. In *Heart Disease. A Textbook of Cardiovascular Medicine*. New York, Saunders, Chapters 13, 14, 1995:351-418.
26. Kautzner J, Malik M. QT dispersion and its clinical utility. *PACE* 1997;20:2625-2640.
27. Murray A, MacLaughlin NB, Campbell RWF. Measuring QT dispersion: Man versus machine. *Heart* 1997;77:539-542.
28. Vloka ME, Babaa A, Ehlert FA, et al. Poor correlation of automated and manual QT dispersion measurements in patients and normal subjects. (abstract) *J Am Coll Cardiol* 1999;33(Suppl. A):350A.
29. Grimm W, Steder U, Menz V, et al. Clinical significance of increased QT dispersion in the 12-lead standard ECG for arrhythmia risk prediction in dilated cardiomyopathy. *PACE* 1996;19:1886-1889.
30. Berul CI, Sweeten TL, Hill SL, et al. Provocative testing in children with suspect congenital long QT syndrome. *ANE* 1998;3:3-11.
31. Zaidi M, Robert A, Fesler R, et al. Dispersion of ventricular repolarisation: A marker of ventricular arrhythmias in patients with previous myocardial infarction. *Heart* 1997;78:371-375.
32. Malik M, Satcharov V. In: Camm JA, Ed. *QT Dispersion. Clinical Approaches to Tachyarrhythmias*. v. 12. New York: Futura, 2000.
33. Calkins H, Allman K, Bolling S, et al. Correlation between scintigraphic evidence of regional sympathetic neuronal dysfunction and ventricular refractoriness in the human heart. *Circulation* 1993;88:172-179.
34. Stanton MS, Tuli MM, Radtke NL. Regional sympathetic denervation after myocardial infarction in humans detected non-invasively using I-123-metaiodobenzylguanidine. *J Am Coll Cardiol* 1998;14:1519-1526.
35. Brendorp B, Elming H, Kober L, et al. QT dispersion has no prognostic information for patients with advanced congestive heart failure and reduced left ventricular systolic function. *Circulation* 2001;103:831-838.
36. Spargias KS, Lindsay SJ, Kawar GL, 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.
37. Fei L, Goldman JH, Prasad K, et al. QT dispersion and RR variations on 12-lead ECGs in patients with congestive heart failure secondary to idiopathic dilated cardiomyopathy. *Eur Heart J* 1996;17:258-263.
38. Anastasiou-Nana MI, Nanas JN, Karagounis LA, et al. Dispersion of QTS and QT in patients with advanced congestive heart failure: Relation to cardiac and sudden cardiac death mortality (Abstract). *Eur Heart J* 1999;20:117.
39. Fu G-S, Meissner A, Simon R. Repolarization dispersion and sudden cardiac death in patients with impaired left ventricular function. *Eur Heart J* 1997;18:281-289.
40. Galinier M, Vialette JC, Fourcade J, et al. QT dispersion as a predictor of arrhythmic events in congestive heart failure. Importance of aetiology. *Eur Heart J* 1998;19:1054-1062.
41. Pinsky DJ, Sciacca RR, Steinberg JS. QT dispersion as a marker of risk in patients awaiting heart transplantation. *J Am Coll Cardiol* 1997;27:1576-1584.
42. Yi G. Computerized measurements of QT dispersion in healthy subjects. *Heart* 1998;80:459-466.
43. Kors JA. Measurement error as a source of QT dispersion: A computerized analysis. *Heart* 1998;80:453-458.
44. Lepeschkin E, Surawicz B. The measurement of the QT interval of electrocardiogram. *Circulation* 1952;6:378-388.
45. Malik M, Camm AJ. Mystery of QTc interval dispersion. *Am J Cardiol* 1997;79:785-787.
46. Glancy JM, Weston PJ, Bhullar HK, et al. Reproducibility and automatic measurement of QT dispersion. *Eur Heart J* 1996;17:928-937.
47. SippensGroenewegen A, Spekhorst H, van Hemel NM, et al. Value of body surface mapping in localizing the site of origin of ventricular tachycardia in patients with previous myocardial infarction. *J Am Coll Cardiol* 1994;24(7):1708-1724.
48. Pastore CA. Mapeamento eletrocardiográfico de superfície na localização de vias acessórias na síndrome de Wolff-Parkinson-White (Body Surface Potential Mapping for identification of accessory pathways in the Wolff-Parkinson-White syndrome). Doctoral dissertation presented to the University of São Paulo Medical School. São Paulo, 1992:69.