

Prognostic Value of QT Interval Parameters for Mortality Risk Stratification in Chagas' Disease

Results of a Long-Term Follow-Up Study

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Background—QT interval parameters are potential prognostic markers of arrhythmogenicity risk and cardiovascular mortality and have never been evaluated in Chagas' disease.

Methods and Results—Outpatients (738) in the chronic phase of Chagas' disease were enrolled in a long-term follow-up study. Maximal heart rate–corrected QT (QTc) and T-wave peak-to-end (TpTe) intervals and QRS, QT, JT, QT_{apex}, and TpTe dispersions and variation coefficients were measured manually and calculated from 12-lead ECGs obtained on admission. Clinical, radiological, and 2-dimensional echocardiographic data were also recorded. Primary end points were all-cause, Chagas' disease–related, and sudden cardiac mortalities. During a follow-up of 58±39 months, 62 patients died, 54 of Chagas' disease–related causes and 40 suddenly. Multivariate Cox survival analysis revealed that the QT-interval dispersion (QTd) (hazard ratio, 1.45; 95% confidence interval, 1.29 to 1.63; $P<0.001$, for 10-ms increments) and left ventricular (LV) end-systolic dimension (hazard ratio, 1.36; 95% confidence interval, 1.21 to 1.53; $P<0.001$, for 5-mm increments) were the strongest independent predictors for all end points. The maximum QTc interval (QT_{cmax}) could substitute for QTd with a worse predictive performance. Other predictors were heart rate, presence of pathological Q waves, frequent premature ventricular contractions (PVCs), and isolated left anterior fascicular block (LAFB) on the ECGs. Kaplan-Meier survival curves demonstrated that a QTd ≥ 65 ms or a QT_{cmax} ≥ 465 ms^{1/2} discriminated the 2 groups with significantly different prognoses.

Conclusions—Electrocardiographic QTd and echocardiographic LV end-systolic dimension were the most important mortality predictors in patients with Chagas' disease. Heart rate, the presence on ECG of pathological Q waves, frequent PVCs, and isolated LAFB refined the mortality risk stratification. (*Circulation*. 2003;108:305-312.)

Key Words: cardiomyopathy ■ mortality ■ death, sudden ■ electrocardiography ■ echocardiography

Chagas' disease remains an important health problem in Latin American countries, where it is estimated that nearly 20 million are infected,¹ and it has also become a potential problem in Europe and the United States because of immigration.² Cardiac involvement is the most prominent manifestation, as 25% to 30% of those infected will develop congestive heart failure, ventricular arrhythmias, or thromboembolism.³ In endemic areas, it is the leading cause of cardiovascular mortality, either sudden arrhythmic or from progressive heart failure.³

Since its original description,⁴ the QT-interval dispersion (QTd), defined as the greatest interlead variability of QT intervals, is presumed to represent a measurement of ventricular repolarization heterogeneity and a potential marker of arrhythmogenicity risk and of cardiovascular morbidity and mortality. Within the last decade, various ECG repolarization parameters have been evaluated as prognostic indicators in several conditions, such as long-QT syndromes,⁵ coronary artery disease,^{6,7} heart failure of different etiologies,^{7,8} other

cardiopathies,⁹ diabetes mellitus,¹⁰ and in population-based studies,¹¹ with controversial results.¹²

Although Chagas' disease has several characteristics suggesting the importance of abnormal ventricular repolarization in its pathogenicity, such as a chronically evolving myocarditis with fibrosis, hypertrophy, and dilatation and accompanying autonomic dysfunction and a high incidence of serious ventricular arrhythmias and sudden death,¹ to date, no study has reported on the prognostic value of any repolarization parameter in chagasic patients. Thus, the aim of this long-term, follow-up study was to evaluate the prognostic importance for mortality of several ECG repolarization parameters in a cohort of patients in the chronic phase of Chagas' disease.

Methods

Subjects and Baseline Methods

The population characteristics and the baseline methods have been detailed elsewhere.¹³ In summary, we studied 814 adult patients

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attending the Chagas' disease outpatient clinic of Evandro Chagas Hospital (Oswaldo Cruz Foundation, Rio de Janeiro, Brazil), from January 1989 to December 1999. All patients were subjected to a thorough clinical examination, with special attention to signs and symptoms of cardiovascular disease. Standard/resting 12-lead ECGs (recorded at 25 mm/s paper speed and 10 mm/mV amplitude), chest x-rays, and 2-dimensional echocardiograms were obtained within 1 week of the medical visit. The same independent observers, unaware of other patient data, performed all examinations. Seventy-six patients were excluded because of ECG criteria, as previously described,¹³ leaving a total of 738 patients, who represent the study population for this report. The study complied with the Declaration of Helsinki, the local ethics committee approved its protocol, and all patients gave written, informed consent.

ECG abnormalities were classified according to the modified Minnesota code for Chagas' disease.¹⁴ Specifically, pathological Q waves (Q-wave MIs) were defined by Minnesota codes 1.1 and 1.2. For repolarization parameter measurements, ECGs were digitized, 100% amplified (corresponding to 50 mm/s paper speed), and manually measured on screen with commercial imaging software (resolution, 0.25 mm=10 ms). QRS duration, QT apex (QTa), and total QT intervals were measured in each lead, and JT and T-wave peak-to-end (TpTe) intervals were calculated. The end of the T wave was defined as the visual return to the TP baseline or as the nadir between T and U waves. Whenever possible, 3 consecutive cycles were measured, and mean values were approximated to the nearest 5 ms. The precedent RR intervals to the measured cycles were measured, and the mean RR interval used to calculate the mean heart rate-corrected QT (QTc) interval with Bazett's formula. The repolarization parameters recorded were maximal QTc (QTcmax) and TpTe (TpTemax) intervals and QRS, QT, JT, QTa, and TpTe interval dispersions (QRSd, QTd, JTd, QTad, and TpTed, respectively, defined as the difference between the maximum and minimum values obtained in any of the 12 leads) and their respective variation coefficients (defined according to the formula: $VC = [SD/mean] \times 100$). Forty-five randomly chosen ECGs were analyzed again at least 6 months after the first measurement to assess intraobserver reproducibility.

The echocardiographic measurements were performed according to the recommendations of the American Society of Echocardiography, left ventricular ejection fraction (LVEF) was calculated with the Teicholz and Kreulen method, and mass was calculated according to the formula of Devereux and Reichek. Moderate or severe LV systolic dysfunction was defined by an LVEF <45% and subjective 2-dimensional echocardiographic classification. Cardiomegaly on chest x-ray was defined as a cardio-thoracic ratio >0.5.

Follow-Up and End Points

The patients were evaluated at least 2 times a year until December 2000. Those who failed to attend the hospital were contacted annually to determine vital status. The observation period for each patient was the number of months from the date of the measured ECG to the date of death or December 31, 2000. Eighty-nine patients (12%) were lost to follow-up, and observations were considered censored at the date of their last hospital visit.

Causes of death during the follow-up period were ascertained from medical records (most of the in-hospital deaths occurred in Evandro Chagas Hospital), death certificates, and interviews with their physicians and families by using a standard questionnaire reviewed by an independent observer. Causes of death were coded according to the International Classification of Diseases (ICD, ninth revision, was used until December 1995; ICD, 10th, afterward). The primary end points were all-cause, Chagas' disease-related, and sudden cardiac deaths. Sudden death was defined as that occurring instantaneously or within 1 hour after the onset of symptoms in patients known to be previously stable.¹⁵ Chagas' disease-related mortality included deaths due to progressive heart failure, embolic cerebrovascular and pulmonary disease, and sudden death.

Statistical Analysis

All statistics were performed with the STATA statistical package. Continuous data were described as means and SDs. Intraobserver reproducibility of ECG repolarization measurements was evaluated by intraclass correlation coefficients and by the graphic method proposed by Bland and Altman.¹⁶ Survival analysis was performed by use of Kaplan-Meier estimation of survival curves (with repolarization parameters dichotomized at the upper quartile), compared by log-rank tests, as well as by univariate and multivariate proportional-hazards Cox models. Variables in univariate analysis that showed a value of $P < 0.10$ were included in the multivariate models. When 2 or more selected variables were intimately associated (correlation coefficient >0.60), the one chosen was that with the greatest Wald statistics. Different multivariate models were fitted in a backward stepwise strategy for all 3 end points by using each repolarization parameter separately. Distinct models were also fitted with all chagasic patients and excluding those with normal ECGs at baseline, because this subgroup has a generally good prognosis.³ Assumptions of the proportional-hazards models and interactions were tested,¹⁷ and no violation was observed. Results are presented as hazard ratios (HRs) with their 95% confidence intervals (95% CIs). A 2-tailed probability value <0.05 was considered statistically significant.

Results

Baseline Characteristics and Follow-Up End Points

During a mean follow-up of 58 ± 39 months (range, 1 to 144 months), there were 62 deaths, 54 from Chagas' disease-related causes (40 sudden deaths, 12 from progressive heart failure, and 2 from embolic stroke). Table 1 shows the baseline characteristics of survivors and deceased patients. Because all variation coefficients of ECG intervals were intimately associated with their respective interval dispersions, only the results of the QT interval variation coefficient (QT-VC) are presented. Nonsurvivors had significantly increased repolarization parameters and worse LV systolic function than did survivors, as well as a greater prevalence of ECG abnormalities, radiological cardiomegaly, and clinical signs and symptoms of cardiovascular disease at baseline. Patients lost to follow-up had baseline characteristics identical to those with complete data, except for being younger (43.4 ± 11.0 vs 47.1 ± 11.6 years, $P = 0.003$).

Reproducibility of Repolarization Measurements

Intraclass correlation coefficients for QTcmax and QTd were 0.96 and 0.75, respectively ($P < 0.001$ for both). In the graphic method of Bland and Altman applied to QTd, the mean intraobserver difference was 1.74 ms, with an SD of 7.39 ms and a range between -15 and +25 ms. This means that 95% of the intraobserver measurement variability lies within -14 and +16 ms ($\pm 2SD$), corresponding to a mean relative error of 11%.

Univariate Survival Analysis

Table 1 shows the results of univariate Cox analyses for Chagas' disease-related mortality. QTd, which had the greatest Wald statistics among interval dispersions and variation coefficients, as well as QTcmax, was the best univariate predictor of mortality among the ECG intervals (including maximum and mean QRS duration). Also, among the echocardiographic measurements, LV end-systolic diameter had the strongest univariate association with survival. Kaplan-Meier survival curves of QTd (dichotomized at 65 ms) and QTcmax (dichotomized at $465 \text{ ms}^{1/2}$)

TABLE 1. Baseline Characteristics of Survivors and Deceased Patients and Results of Univariate Cox Survival Analysis for Prediction of Chagas' Disease-Related Mortality

	Survivors (n=676)	Nonsurvivors (n=62)	Hazard Ratio	95% CI
Clinical variables				
Age (10 years)	45.90 (11.59)	51.03 (11.39)	1.34	1.09–1.66†
Male gender	45.7%	51.6%	1.31	0.80–2.16
Heart failure	5.9%	51.6%	12.34	7.49–20.32*
Syncope	2.2%	22.6%	8.20	4.52–14.88*
Radiological variables				
Cardiomegaly	12.9%	33.9%	11.66	6.86–19.83*
Electrocardiographic variables				
Isolated RBBB	14.6%	8.1%	0.46	0.19–1.15
Isolated LAFB	2.7%	12.9%	5.00	2.37–10.53*
RBBB+LAFB	22.2%	46.8%	2.88	1.72–4.66*
LBBB	2.4%	12.9%	5.93	2.81–12.49*
Q-wave MIs	1.8%	24.2%	12.81	7.12–23.04*
Ischemia	6.5%	21.0%	4.09	2.21–7.59*
PVCs	12.0%	41.9%	5.12	3.09–8.49*
First/second AV block	5.6%	16.1%	2.28	1.08–4.79‡
Maximum QRS duration (10 ms)	99.76 (25.86)	123.71 (28.11)	1.32	1.21–1.44*
QRSd (10 ms)	36.81 (13.37)	38.71 (14.85)	1.10	0.92–1.32
Heart rate (10 bpm)	69.03 (11.42)	71.82 (16.29)	1.24	1.01–1.52‡
Echocardiographic variables				
Diastolic LV (5 mm)	51.77 (6.14)	63.31 (10.58)	1.96	1.76–2.19*
Systolic LV (5 mm)	33.89 (7.77)	51.92 (13.48)	1.74	1.61–1.89*
Ejection fraction (5%)	63.31 (11.46)	37.16 (17.42)	0.64	0.59–0.68*
LV mass (50g)	186.33 (59.01)	261.35 (84.53)	1.67	1.50–1.88*
Mod/sev LV systolic dysfunction	9.3%	74.2%	24.20	13.65–42.93*
LV aneurysm	13.3%	33.9%	3.04	1.80–5.15*
ECG repolarization parameters				
QTcmax (50 ms ^{1/2})	437.77 (34.82)	482.65 (41.12)	4.03	2.98–5.45*
TpTmax (10 ms)	100.21 (13.85)	112.74 (21.23)	1.64	1.42–1.90*
QTd (10 ms)	49.68 (13.41)	80.00 (26.08)	1.59	1.49–1.70*
QT-VC (1%)	4.32 (1.03)	6.31 (1.71)	2.10	1.89–2.34*
JTd (10 ms)	57.29 (17.21)	82.34 (30.30)	1.43	1.33–1.53*
QTad (10 ms)	47.16 (17.42)	72.34 (30.30)	1.49	1.38–1.61*
TpTed (10 ms)	49.27 (13.52)	67.02 (19.51)	2.03	1.75–2.35*

Values are mean (SD) or frequency percentages. RBBB indicates right bundle branch block; LAFB, left anterior fascicular block; LBBB, left bundle branch block; Mod/sev, moderate or severe. Other abbreviations are as in text.

* $P < 0.001$, † $P < 0.01$, ‡ $P < 0.05$ for univariate survival analysis.

for Chagas' disease-related and sudden deaths are shown in Figure 1. Both parameters discriminated the 2 groups with significantly different prognoses. Figure 2 shows sudden death-free survival curves for patients grouped according to upper-quartile values of QTd and QTcmax and stratified according to the presence or absence of LV systolic dysfunction. It demonstrates that either QTd or QTcmax was capable of distinguishing the 2 groups with different mortalities in both subgroups.

Multivariate Survival Analysis

Results of multivariate Cox analysis for the 3 end points are shown in Table 2 with QTd as the repolarization parameter in

the model and in Table 3 with QTcmax. Both parameters were independent predictors of mortality, but the models with QTd had a better predictive performance than did the models with QTcmax, assessed by the maximum-likelihood estimate of each model. Echocardiographic LV systolic dimension was also a strong, independent predictor of mortality in any fitted Cox models. LV mass, though a univariate predictor of mortality, was not an independent one in multivariate analyses. Other frequently selected predictors were heart rate (only in models with QTd) and the ECG abnormalities of Q-wave MIs, frequent PVCs, and isolated LAFB. No QRS parameter showed additional prognostic value; in addition, exclusion

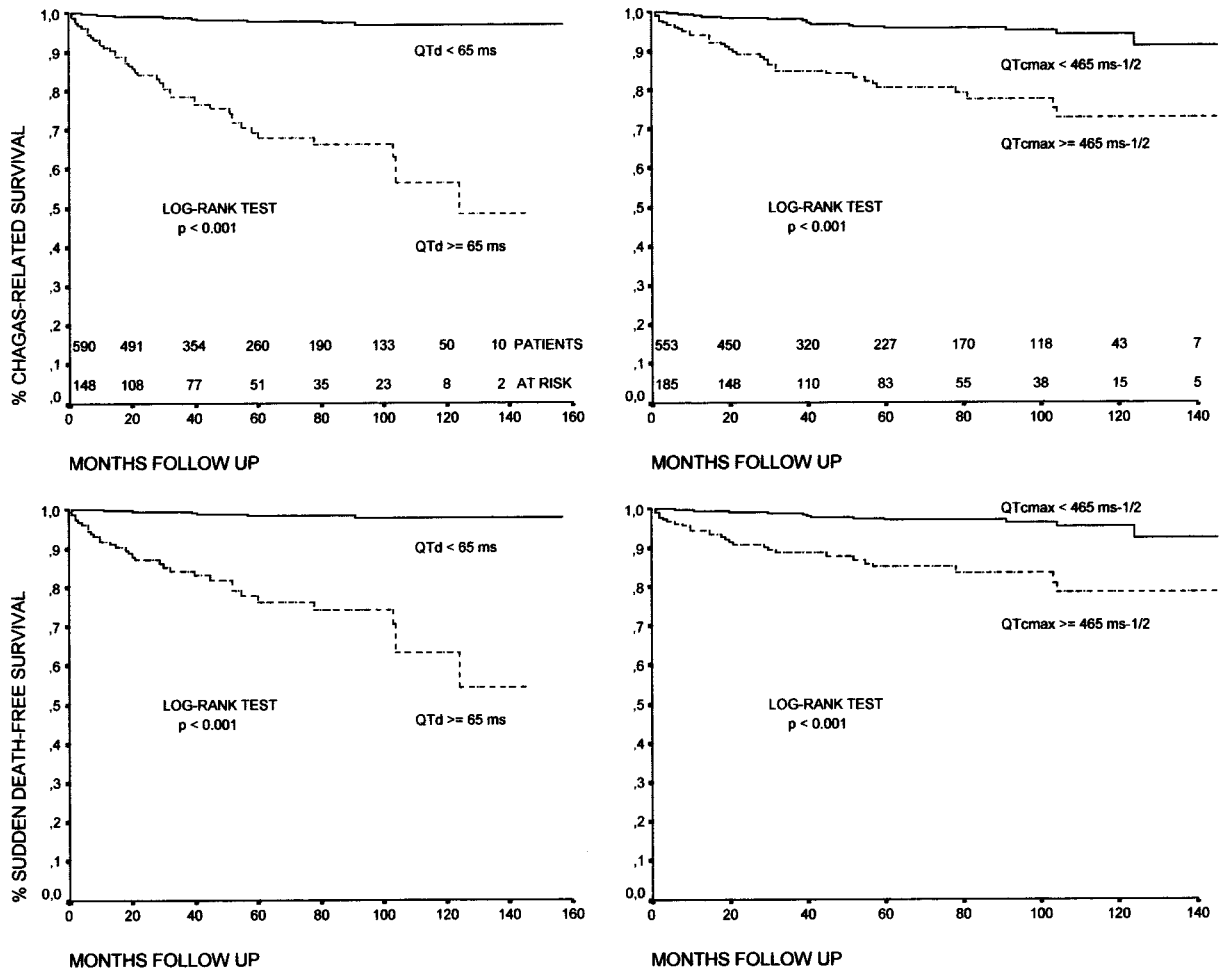


Figure 1. Kaplan-Meier estimation of cumulative Chagas’ disease–related survival (top) and sudden death–free survival (bottom) curves in patients grouped according to upper quartile of QTd (left) and QTcmax values (right).

from analyses of the 86 patients with a QRS duration >120 ms also did not change the final predictive models.

Discussion

The present study is, to the best of our knowledge, the first to investigate in a follow-up study of up to 12 years the prognostic importance for mortality of ECG parameters of ventricular depolarization-repolarization in patients with Chagas’ disease. Its major finding is that both QTcmax interval duration and QTd were independent predictors of all-cause, Chagas’ disease–related, and sudden arrhythmic deaths. Based on the results of univariate and multivariate survival analyses, it also appeared that QTd was a better mortality risk stratifier than was QTcmax interval. Echocardiographic LV systolic internal diameter was also a strong mortality predictor. Others independent predictors were heart rate and the presence of Q-wave MIs, frequent PVCs, and isolated LAFB on baseline ECGs. Not only did this study involve a large number of patients, but also a reasonable number of end points were observed. This permitted performance of a meaningful multivariate survival analysis and suggested that criteria for overfitting data were not violated.¹⁷

There are 2 recognizably relevant aspects in mortality risk stratification in Chagas’ disease. First is the presence of any ECG abnormality that characterizes Chagas’ cardiomyopathy. It has been convincingly demonstrated that Chagas’ disease patients with persistently normal ECGs have prognoses identical to the nonchagasic general population.^{3,18} Second is the presence of LV systolic dysfunction.^{19,20} Patients with overt congestive heart failure have a specially ominous prognosis, with mortality rates between 50% and 80% after 3 years.^{20,21} The present study showed that, even in the subgroup of patients with abnormal ECGs, QTcmax interval and particularly, QTd added prognostic information beyond that obtained by echocardiographically derived LV systolic function, independent of the presence of intraventricular conduction disturbances. It was also apparent that QTd and QTcmax were capable of identifying high-risk patients for sudden death among those with or without moderate or severe LV systolic dysfunction. The additional presence of specific ECG abnormalities, frequent PVCs, Q-wave MIs, and isolated LAFB refined the mortality risk stratification.

Recent studies^{22,23} have demonstrated that QTd probably does not represent true spatial dispersion of ventricular

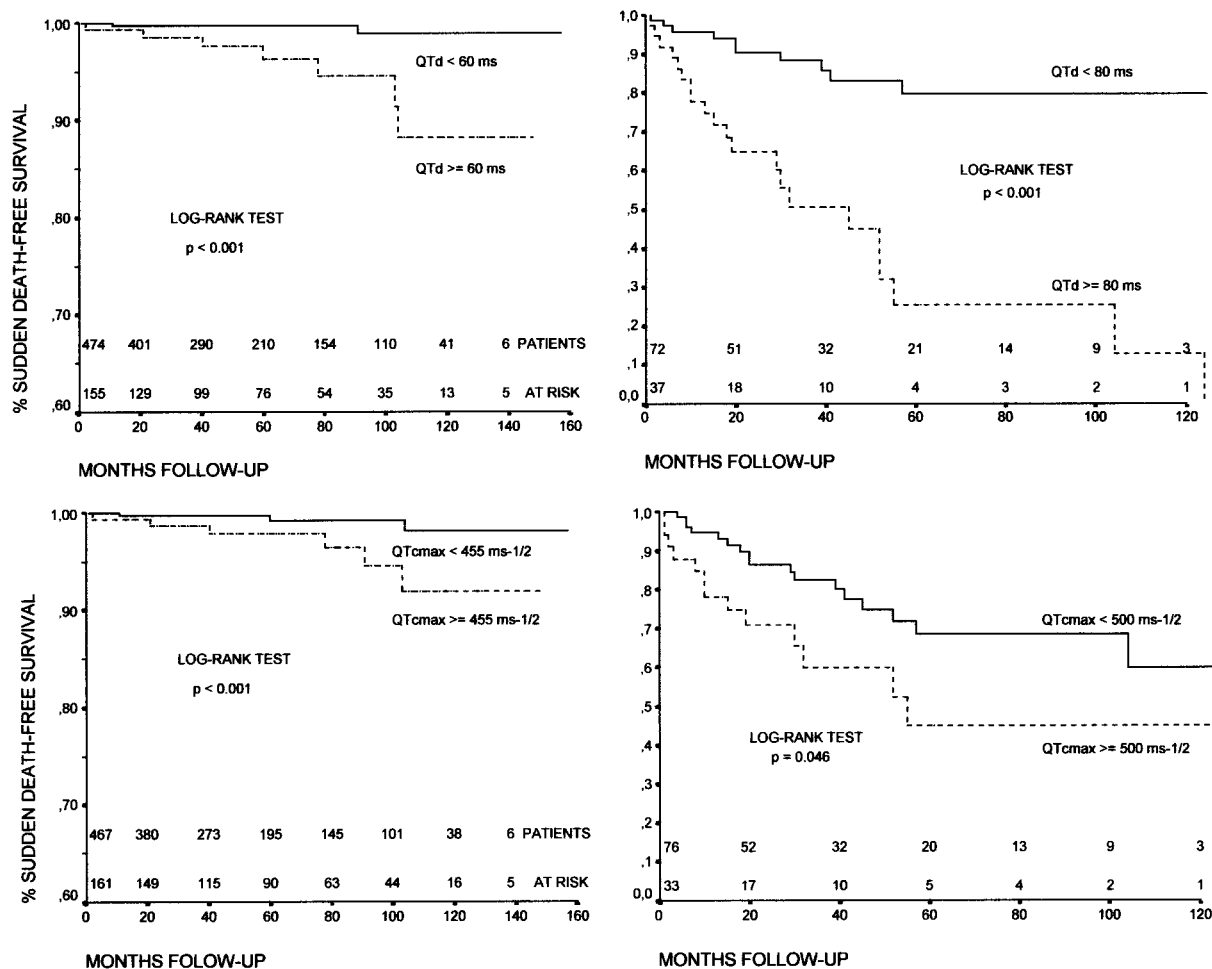


Figure 2. Kaplan-Meier estimation of sudden death-free survival curves in patients grouped according to upper quartile values of QTd (top) and QTcmax (bottom) and stratified according to the absence (left) or presence (right) of moderate or severe LV systolic dysfunction.

recovery times, a measure of regional heterogeneity of ventricular repolarization, as originally proposed.⁴ It probably constitutes a measurement of a global abnormal pattern of ventricular repolarization, reflected by an uncommon projection of a more complex vectorcardiographic T-wave loop morphology.¹² With this new perspective, we hypothesized that altered ventricular repolarization is important in the pathophysiology of Chagas' disease mortality, particularly in determining sudden death, because almost 70% of the observed deaths were classified as sudden arrhythmic. Sudden death in Chagas' disease is almost always due to ventricular fibrillation, generally preceded by sustained ventricular tachycardia.²⁴ Reentry constitutes the main electrophysiologic mechanism involved in the chain of events leading to these life-threatening ventricular tachyarrhythmias. The risk of this terminal event is conditioned by the presence of structural myocardial abnormalities and modulated by functional variations.²⁵ Abnormal ventricular repolarization, reflected by an increased QTd or a prolonged QTc interval, could be due to cardiac autonomic dysfunction, which is frequent and generally precocious in Chagas' heart disease,²⁶ or to the relentless myocarditis process itself, with its conse-

quent myocardial fibrosis and dilatation. In this respect, we have recently reported that QTd was correlated with LV systolic impairment in chagasic patients.¹³ Altered ventricular repolarization (the functional factor) could then act concomitantly with LV dysfunction and myocardial fibrotic areas (the anatomic substrates) and with myocardial electrical instability, reflected by frequent PVCs on ECG (the electrical trigger factor), to create the conditions that predispose Chagas' disease patients to serious ventricular arrhythmias and sudden death.

Although QT parameters convincingly appear to constitute risk markers for cardiovascular mortality in the general population^{11,27} and in patients with diabetes,^{10,28} their prognostic value in patients with various cardiopathies remains unsettled.^{6-9,12} Chagas' cardiomyopathy has unique pathophysiological and clinical characteristics,^{1,2} a slowly evolving chronic myocarditis due to low-grade parasitism, and autoimmune aggression, leading ultimately to extensive myocardial fibrosis, hypertrophy, and dilatation, with early cardiac autonomic denervation and a high incidence of life-threatening arrhythmias, sudden deaths, and thromboembolic complications. These aspects distinguish Chagas' heart dis-

TABLE 2. Results of Multivariate Cox Regression Analysis With QTd as the Sole Ventricular Repolarization Parameter

All Chagas' Disease Patients (n=738)			Patients With Abnormal ECGs (n=403)		
Variable	HR	95% CI	Variable	HR	95% CI
All-cause mortality					
QTd (10 ms)	1.45	1.29–1.63*	QTd (10 ms)	1.35	1.21–1.51*
Systolic LV (5 mm)	1.36	1.21–1.53*	Systolic LV (5 mm)	1.37	1.21–1.55*
Heart rate(10 bpm)	1.33	1.12–1.57*	Q-wave MIs (y/n)	2.86	1.52–5.40*
Q-wave MIs (y/n)	2.82	1.48–5.37†	Heart rate (10 bpm)	1.29	1.08–1.54†
Cardiomegaly (y/n)	2.40	1.29–4.47†	Cardiomegaly (y/n)	2.31	1.21–4.41‡
Age (10 years)	1.30	1.02–1.66‡			
Chagas' disease-related mortality					
QTd (10 ms)	1.51	1.35–1.68*	QTd (10 ms)	1.46	1.30–1.64*
Systolic LV (5 mm)	1.42	1.25–1.60*	Systolic LV (5 mm)	1.41	1.24–1.59*
Q-wave MIs (y/n)	3.35	1.71–6.54*	Q-wave MIs (y/n)	3.14	1.62–6.08*
PVCs (y/n)	2.38	1.34–4.23†	Heart rate (10 bpm)	1.28	1.07–1.53†
Heart rate (10 bpm)	1.29	1.08–1.53†	PVCs (y/n)	2.11	1.18–3.78‡
Isolated LAFB (y/n)	2.59	1.17–5.71‡	Isolated LAFB (y/n)	2.40	1.08–5.31‡
Sudden cardiac death					
QTd (10 ms)	1.52	1.35–1.72*	QTd (10 ms)	1.43	1.26–1.62*
Systolic LV (5 mm)	1.39	1.20–1.60*	Systolic LV (5 mm)	1.43	1.24–1.64*
Q-wave MIs (y/n)	2.62	1.14–6.01‡	Heart rate (10 bpm)	1.29	1.05–1.59‡
Heart rate (10 bpm)	1.26	1.03–1.55‡	Q-wave MIs (y/n)	2.31	1.02–5.32‡
PVCs (y/n)	2.16	1.09–4.25‡			
Isolated LAFB (y/n)	2.79	1.11–7.02‡			

y/n indicates present vs absent; other abbreviations are as in Table 1 and text.

* $P < 0.001$, † $P < 0.01$, ‡ $P < 0.05$.

ease from other cardiopathies and probably explain the greater importance of abnormal ventricular repolarization in determining mortality demonstrated here than that reported in other cardiac diseases.

The present report has some limitations. Some potential important prognostic variables were not explored, such as the presence of complex ventricular arrhythmias and RR variability on 24-hour Holter monitoring or inducibility of ventricular tachyarrhythmias on invasive electrophysiologic study. The presence of frequent PVCs on baseline ECGs, a prognostic predictor demonstrated here, could possibly substitute for the prognostic information given by quantification of ventricular arrhythmias on Holter monitor records. It has been shown that frequent or repetitive PVCs on standard/resting ECGs was correlated with the presence of more complex ventricular arrhythmias on 24-hour Holter monitoring in chagasic patients.²⁹ RR variability in Chagas' disease has mainly been associated with the presence of cardiac dysautonomia,³⁰ a feature probably also reflected by QT-interval prolongation or increased dispersion.³¹ Invasive electrophysiologic study is not currently a routine examination in Chagas' disease, so its prognostic value is only studied in patients with syncope or documented nonsustained ventricular tachycardia.³² Another possible drawback is the question of how far our findings could be applied to the general Chagas' disease population. Although our patients constituted

an urban cohort from a Chagas' disease reference center, their baseline characteristics were similar to those reported from rural cohorts of Chagas' endemic areas.³³ This suggests that our results possibly could be extended to the whole chagasic population; nevertheless, other follow-up studies are necessary to address this point. Finally, the well-known poor reproducibility and lack of standardization impose limitations on the general applicability of QTd data to mortality risk stratification. In this regard, our measured intraobserver reproducibility of QTd is reasonably good, suggesting that our results could not be accounted for simply on measurement errors. Obviously, the QTcmax interval duration does not have the same restriction.

Conclusions

The present study demonstrated that both ECG ventricular repolarization parameters, QTcmax interval duration and QT interval dispersion, were important mortality risk predictors in patients with Chagas' disease, together with 2-dimensional echocardiographically derived LV systolic function. Heart rate and the specific ECG abnormalities of pathological Q waves, frequent PVCs, and isolated LAFB improved mortality risk stratification in these patients. Further prospective investigations are necessary to address the predictive value of changes in QT interval duration and dispersion over time as well as intervention studies to evaluate whether these mor-

TABLE 3. Results of Multivariate Cox Regression Analysis With QTcmax as the Sole Ventricular Repolarization Parameter

All Chagas' Disease Patients (n=738)			Patients With Abnormal ECGs (n=403)		
Variable	HR	95% CI	Variable	HR	95% CI
All-cause mortality					
Systolic LV (5 mm)	1.42	1.27–1.60*	Systolic LV (5 mm)	1.43	1.28–1.61*
Q-wave MIs (y/n)	3.35	1.79–6.27*	Q-wave MIs (y/n)	3.11	1.65–5.87*
QTcmax (50 ms ^{1/2})	1.96	1.37–2.80*	Cardiomegaly (y/n)	2.57	1.38–4.78†
Cardiomegaly (y/n)	2.92	1.59–5.37*	QTcmax (50 ms ^{1/2})	1.76	1.20–2.58†
Isolated LAFB (y/n)	2.40	1.05–5.46‡	Isolated LAFB (y/n)	2.21	0.97–5.03
Chagas' disease-related mortality					
Systolic LV (5 mm)	1.45	1.29–1.64*	Systolic LV (5 mm)	1.48	1.31–1.67*
QTcmax (50 ms ^{1/2})	2.13	1.43–3.16*	Q-wave MIs (y/n)	3.55	1.86–6.76*
Q-wave MIs (y/n)	3.18	1.61–6.28*	QTcmax (50 ms ^{1/2})	1.95	1.29–2.96†
Cardiomegaly (y/n)	2.51	1.28–4.92†	Isolated LAFB (y/n)	2.97	1.27–6.94‡
Isolated LAFB (y/n)	3.11	1.31–7.37†	Cardiomegaly (y/n)	2.15	1.10–4.22‡
PVCs (y/n)	2.06	1.15–3.69‡	PVCs (y/n)	1.84	1.01–3.36‡
Syncope (y/n)	1.98	1.00–3.90‡			
Sudden cardiac death					
Systolic LV (5 mm)	1.48	1.29–1.69*	Systolic LV (5 mm)	1.47	1.29–1.69*
QTcmax (50 ms ^{1/2})	2.65	1.70–4.11*	QTcmax (50 ms ^{1/2})	2.41	1.50–3.88*
Isolated LAFB (y/n)	4.19	1.65–10.69†	Isolated LAFB (y/n)	3.86	1.48–10.04†
Q-wave MIs (y/n)	3.03	1.35–6.78†	Q-wave MIs (y/n)	2.87	1.27–6.46‡
PVCs (y/n)	2.07	1.09–3.92‡	PVCs (y/n)	1.90	0.98–3.69

Abbreviations are as in Table 1 and text.

* $P < 0.001$, † $P < 0.01$, ‡ $P < 0.05$.

tality risk markers could be modified in patients with Chagas' cardiomyopathy.

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