SUPPLEMENTARY DATA

Supplementary methods

Clinical setting and patient management

The Clementino Fraga Filho University Hospital (*Hospital Universitário Clementino Fraga Filho [HUCFF]*) at the Federal University of Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil, is a reference center for the treatment and research of infectious and tropical diseases covered by the Brazilian Public Health Care System (*Sistema Único de Saúde [SUS]*). It offers comprehensive and multidisciplinary care to patients with Chagas disease (ChHD). All individuals referred from the primary health care centers need to have their Chagas cardiomyopathy (CC) confirmed based on validated diagnostic criteria[1] to be followed up in the *HUCFF-CC*. Here, experienced cardiologists reviewed 12-lead electrocardiograms (ECGs). ECGs were classified using the Minnesota Code criteria, modified for ChHD.[2] In brief, the diagnosis of CC is established based on the presence of at least 2 distinct positive serologic tests for antibodies to *Trypanosoma cruzi* (indirect hemagglutination, indirect immunofluorescence, or enzyme-linked immunosorbent assay), together with the characteristic 12-lead ECG changes. After establishing a diagnosis of ChHD, patients are systematically evaluated and monitored according to the cardiac form of the disease. All patients received individualized care, invasive therapies and pharmacological treatment for ChHD according to the guidelines in effect when the study was conducted. The drugs used were part of the SUS.

In the case of patients who did not return to hospital for medical appointments, vital status (deceased or alive) was obtained from the Mortality Information System (SIM) of the Department of Informatics of the Unified Health System (DATASUS)[3] in Brazil. Upon verifying vital status, sudden cardiac arrest (SCA) and causes other than SCA were obtained from the death records of the mobile emergency care service, where on-scene care for individuals, is registered. Living relatives were also contacted to obtain copies of death certificates in cases when the patient did not die during admission in the HUCFF-UFRJ.

With respect to the medications used during the study period: *a)* Patients were monitored at a referral center where all medications and interventions, both invasive and noninvasive, were administered according to established guidelines in effect during the study period, as ensured by the Brazilian Unified Health System (SUS). *b)* Use of amiodarone treatment was guided primarily by the clinical manifestations and the severity of ventricular dysfunction

rather than solely by the presence of potentially life-threatening ventricular arrhythmias. This management approach reflects the clinical strategy commonly applied in Chagas cardiomyopathy, in which ventricular arrhythmias are frequently considered a consequence of the underlying structural myocardial disease. Therefore, treatment is often directed toward controlling ventricular dysfunction and disease progression in addition to arrhythmia suppression, aiming to improve overall prognosis rather than only modifying the mode of death.[1] *c)* Specifically, amiodarone intake was indicated only in patients with nonsustained monomorphic ventricular tachycardia asymptomatic or symptomatic and left ventricular dysfunction < 45%; sustained monomorphic ventricular tachycardia hemodynamically stable patients with an ejection fraction (EF) > 40%, patients with syncope and EF > 40%; syncope, sustained monomorphic ventricular tachycardia induced by electrophysiological study and EF > 40%; patients with a strong recommendation for implantable cardioverter-defibrillator (ICD), but with limited life expectancy or no access to the device.[1]

ECG pre-processing

We first interpolated the ECG signals at a sampling frequency of 1000 Hz to obtgain higher resolution in ECG wave delineation. Next, baseline wander was canceled using a zero-phase butterworth high-pass filter at 0.5 Hz. Electric and muscle noise were removed using a zero-phase butterworth low-pass filter at 40 Hz, and ectopic beats were detected[2] and not considered in the analysis. A fully automated delineation system[3] followed by a visual inspection to remove possible outlier errors was used to annotate QRS complex (QRS) onset and T-wave peak and end occurrences. After delineation, each T-wave was further low-pass filtered at 20 Hz [4].

Proportional hazards assumption assessment

Proportional-hazards assumptions were evaluated using the statistical test from the scaled Schoenfeld residuals in R (cox.zph() function from the “survival” package, https://github.com/therneau/survival). In our data, assumptions were supported by a nonsignificant relationship between residuals and time. The table below shows the remaining variables in the multivariate Cox model from Table 2, where ρ is the correlation coefficient between the transformed survival time and the scaled Schoenfeld residuals.

	ρ	*P*
$\Delta\alpha^{Tpe}$ [per unit increment]	0.074	.64
Hypertension (yes)	0.051	.78
Rassi Score [per unit increment]	0.187	.19

For all covariates in the multivariate Cox model, the test indicated no significant correlations between residuals and time (all *P*-values > 0.05), supporting the proportional hazards assumption.

Construction of the combined risk model

The SCA prediction model was defined according to the following equation[5,6]:

$$CRM = \sum_{i=1}^{I} \beta_i x_i$$

where combined risk model (CRM) denotes the score; I is the number of variables retained in the multivariable model; β_i is the coefficient of the i-th variable; and x_i is the i-th variable (ie, when a categorical variable, x_i takes the value 0 when the variable is below the defined cutoff point and 1 when it is above).

Final combined risk model

The SCA prediction model was calculated as follows:

$$CRM = 1.032 * x_{Hypertension} + 0.382 * x_{Rassi\ score}[per\ unit\ increment] + 2.612 * x_{\Delta\alpha^{Tpe}}[per\ unit\ increment]$$

Sex-specific analyses

Patient characteristics stratified by sex are shown in Supplementary Table 4. Male patients in the primary endpoint group, compared with patients in the control group, showed higher values of Rassi score and thyroid-stimulating hormone (TSH) levels (*P* < .001 and *P* = .023, respectively), and a higher proportion of amiodarone intake (*P* = .019), while age, BMI, type 2 diabetes mellitus (DM2), hypertension, dyslipidemia and coronary artery disease (CAD) showed no significant variations. Upon comparison of ECG variables between primary endpoint and control groups in males, significant differences were found for $\Delta\alpha^{QT}$ (*P* = .009) and $\Delta\alpha^{Tpe}$ (*P* =.013), both temporal ECG indices of ventricular restitution. Each of them was significantly higher in the primary endpoint group than in the rest of the patients.

In males, the area under the receiver operating characteristic curve (AUC) for Rassi Score, $\Delta\alpha^{QT}$ and $\Delta\alpha^{Tpe}$ was 0.835 (95%CI: 0.728-0.943), 0.711 (0.561–0.861) and 0.702 (0.550–0.854), respectively. Patients were dichotomized following the optimal thresholds

for primary endpoint risk stratification of 0.150 for $\Delta\alpha^{QT}$ and 0.036 for $\Delta\alpha^{Tpe}$. Of the 53 male patients, 39 (73.6%) were included in the Rassi Score(L) group and 14 (26.4%) in the Rassi Score(I) group, 30 (56.60%) were included in the $\Delta\alpha^{QT}$(L) group and 23 (43.4%) in the $\Delta\alpha^{QT}$(H) group, and 33 (62.3%) were included in the $\Delta\alpha^{Tpe}$(L) group and 20 (37.7%) in the $\Delta\alpha^{Tpe}$(H) group.

Multivariate Cox analysis in males showed that only Rassi score remained significantly associated with the primary endpoint, with a hazard ratio (HR) of 1.56 (*P* < .0001) (Supplementary Table 5). Consequently, a male-specific combined risk model incorporating ECG variables could not be evaluated.

In contrast, female patients in the primary endpoint group, as compared with the control group, showed significantly higher values of Rassi score (*P* <.0001) and were more likely to be hypertensive (*P* = .001) and use amiodarone (*P* < .0001). Among the ECG variables, only $\Delta\alpha^{Tpe}$ and T-peak-to-end morphology restitution (TpeMR) were significantly higher in female patients meeting the primary endpoint (*P* = .003 and .024, respectively). The AUC for Rassi Score, $\Delta\alpha^{Tpe}$ and TpeMR was 0.951 (95% confidence interval [CI]: 0.915–0.992), 0.668 (0.567–0.808) and 0.644 (95% CI: 0.516–0771), respectively. Patients were dichotomized following the optimal thresholds for primary endpoint risk stratification of 0.043 for $\Delta\alpha^{Tpe}$ and 0.021 for TpeMR. Of the 91 female patients, 56 (61.5%) were included in the Rassi Score(L) group and 35 (38.5%) in the Rassi Score(I) group, 59 (64.8%) were included in the $\Delta\alpha^{Tpe}$(L) group, and 32 (35.2%) in the $\Delta\alpha^{Tpe}$(H) group.

Multivariate Cox analysis in females showed that only Rassi score and hypertension remained significantly associated with the primary endpoint, with an HR of 1.70 (*P* <.0001) and 3.60 (P = 0.036), respectively (Supplementary Table 6). Consequently, a female-specific combined risk model incorporating ECG variables could not be evaluated.

In conclusion, our sex-stratified analyses allowed us to investigate the possible contribution to SCA-related primary endpoint risk prediction of ECG-derived repolarization indices in each sex separately. We were able to observe that $\Delta\alpha^{Tpe}$ was associated with an SCA-related event in both groups, whereas $\Delta\alpha^{QT}$ was only associated in males and TpeMR only in females. However, these associations did not remain significant after multivariable adjustment, indicating that ECG-derived ventricular restitution markers did not provide independent prognostic value beyond established clinical predictors in sex-specific models.

Sensitivity analysis excluding patients in amiodarone treatment

The characteristics of patients excluding those under amiodarone treatment are shown in Supplementary Table 7. Patients in the primary endpoint group, as compared with

those in the control group, showed lower values of BMI (*P* = .041) and higher values of Rassi score (*P* < .0001), while age, DM2, hypertension, dyslipidemia, CAD, and TSH showed no significant variations. Upon comparison of ECG variables between the primary endpoint and control groups, significant differences were found for $\Delta\alpha^{QT}$ (P = 0.038), $\Delta\alpha^{Tpe}$ (*P* =.005) and TpeMR (*P* = .005). All of them were significantly higher in the primary endpoint group than in the rest of the patients.

The AUC for the clinical variables body mass index (BMI) and Rassi Score was 0.663 (0.528–0.799) and 0.816 (0.697–0.936), respectively. The AUC for the ECG variables $\Delta\alpha^{QT}$, $\Delta\alpha^{Tpe}$ and TpeMR was 0.668 (95% CI: 0.488–0.848), 0.727 (0.581–0.874) and 0.726 (0.562–0.890), respectively. Patients were dichotomized following the optimal thresholds for primary endpoint risk stratification of 28 for BMI, 0.270 for $\Delta\alpha^{QT}$, 0.020 for $\Delta\alpha^{Tpe}$ and 0.021 for TpeMR. Of the 100 patients who did not take amiodarone, 31 (31%) were included in the BMI(L) group and 69 (69%) in the BMI(+) group, 92 (92%) were included in the Rassi Score(L) group and 8 (8%) in the Rassi Score(I) group, 87 (87%) were included in the $\Delta\alpha^{QT}$(L) group and 13 (13%) in the $\Delta\alpha^{QT}$(H) group, 46 (46%) were included in the $\Delta\alpha^{Tpe}$(L) group and 54 (54%) in the $\Delta\alpha^{Tpe}$(H) group and 67 (67%) were included in the TpeMR(L) group and 33 (33%) in the TpeMR(H) group.

Multivariate Cox analyses showed that only the Rassi score remained significantly associated with the primary endpoint (HR, 1.60, *P* < .0001; Supplementary Table 8). Consequently, in this subgroup of patients not receiving amiodarone, ECG-derived variables did not retain statistical significance after multivariable adjustment, whereas the Rassi score remained as the only independent predictor. This may reflect a reduced statistical power (only 15 patients met the primary endpoint) and also a shift in risk profile, suggesting that the contribution of $\Delta\alpha^{Tpe}$ to SCA risk stratification is stronger in individuals with intermediate Rassi scores, who are also more likely to receive amiodarone.

Electrophysiological hypothesis behind ECG-derived makers of ventricular repolarization restitution

The pathogenesis of SCA is not yet fully understood, and further research is needed to clarify its mechanisms. The Tpe interval has recently emerged as a significant indicator for predicting the risk of arrhythmias and cardiovascular death.[7,8] In 1998,[9] it was proposed that the later phase of ventricular repolarization could be used to assess arrhythmic risk, based on in vivo models in which epicardial action potential duration (APD) (the shortest APD) coincides with the peak of the T-wave, while the repolarization of the M cells (longest APD) coincides with the end of the T-wave. Consequently, the Tpe interval potentially reflects the difference in repolarization times across the heart wall, known as transmural

dispersion of repolarization (TDR), creating a vulnerable period across the ventricular wall. [10]

The action potential represents the electrical activity of individual cardiomyocytes, and spatial dispersion of APD among cells constitutes a measure of repolarization heterogeneity.[11] If this dispersion of ventricular repolarization is abnormal, it indicates an increased dispersion of APD across the ventricles.[12] This effect is not only seen at rest: the change in heart rate further emphasizes these differences, a process known as ventricular restitution, which describes how the electrical recovery of the heart adapts to varying rhythms. An abnormally slow action potential duration restitution (APDR) in the left ventricle has been shown to be one of the electrophysiological causes of SCA [13]. However, APDR assessment is invasive and costly, motivating the development and use of noninvasive techniques.

In our research, we have demonstrated that $\Delta\alpha^{Tpe}$, based on the changes with heart rate of the later phase of ventricular repolarization, showed higher values in the SCA group within a subset of patients with ChHD, suggesting that ChHD may increase TDR. A recent study has also shown that ChHD often leads to localized injuries in the endocardium [14], and therefore this damage could further contribute to an increase in TDR.

Evaluation of ECG-based indices across fixed follow-up periods

To investigate the stability of the predictive value of the ECG indices across different follow-up times, we computed the area under the receiver operating characteristic (AUC) curve and its CI for each of the 4 indices at 1 to 10 years after the Holter acquisition. Patients who died from causes other than the primary endpoint within this selected optimal period were excluded from the analysis.

Supplementary Figure 2 reveals differences in classification performance over time. $\Delta\alpha^{Tpe}$ reached peak AUCs at 2 and 3 years (≈0.75), but the CI was narrower at 3 years, indicating a more stable performance. TpeMR also peaked at 3 years (≈0.67). $\Delta\alpha^{QT}$ and T-wave morphology restitution (TMR) showed lower, relatively stable AUCs across the follow-up periods.

Based on these results, the 3-year follow-up period reached the highest discriminatory performance.

Table S1. Distribution of Rassi score and combined risk model categories according to the primary endpoint

	All	Primary endpoint group	Control group
Overall population	144 (100)	53 (36.8)	91 (63.2)
Rassi score			
Rassi score(L)	95 (66)	11 (11.6)	84 (88.4)
Rassi score(I)	49 (34)	42 (85.7)	7 (14.3)
Combined risk model			
CRM(L)	81 (56.2)	5 (6.2)	76 (93.8)
CRM(H)	63 (43.8)	48 (76.2)	15 (23.8)

CRM, combined risk model; H, high risk; I, intermediate risk; L, low risk.

The data are expressed as No. (%).

Table S2. Net reclassification index for Rassi score vs the combined risk model for primary endpoint risk prediction

Outcome: absent

		Combined risk model			
		[0, 0.3)	[0.3, 0.6)	[0.6, 1)	% reclassified
Rassi	[0, 0.3)	76	2	0	3
score	[0.3, 0.6)	1	5	0	17
	[0.6, 1]	0	1	6	14

Outcome : present

		Combined risk model			
		[0, 0.3)	[0.3, 0.6)	[0.6, 1)	% reclassified
Rassi	[0, 0.3)	7	2	0	22
score	[0.3, 0.6)	0	2	0	0
	[0.6, 1]	0	1	41	2

Combined data

		Combined risk model			
		[0, 0.3)	[0.3, 0.6)	[0.6, 1)	% reclassified
Rassi	[0, 0.3)	83	4	0	5
score	[0.3, 0.6)	1	7	0	12
	[0.6, 1]	0	2	47	4

Table S3. Characteristics of male and female patients

	Overall population (N_M = 53) (N_F = 91)	Primary endpoint (N_M = 21) (N_F = 32)	Control (N_M = 32) (N_F = 59)	*P*
Clinical variables				
Age–M, y	43.7 [13.2]	46.2 [9.8]	43.4 [13.5]	.752
Age–F, y	44.0 [13.0]	41.4 [10.4]	44.6 [14.0]	.828
BMI–M, kg/m²	28 [3]	28 [2]	29 [4]	.056
BMI–F, kg/m²	28 [2]	28 [3]	28 [2.5]	.389
Rassi score–M, points	5 [6]	8 [3]	2 [3]	**<.001**
Rassi score–F, points	3 [8]	11 [0]	3 [3]	**<.0001**
LVEF–M, %*	61 [19]	46 [14]	65.5 [10.5]	<.0001
LVEF–F, %*	55 [27]	41 [5.25]	67 [14]	<.0001
DM2–M, yes	11 (20.7)	6 (28.6)	5 (15.6)	.310
DM2–F, yes	9 (9.9)	4 (12.5)	5 (8.5)	.714
Hypertension–M, yes	40 (75.5)	17 (80.9)	23 (71.8)	.670
Hypertension–F, yes	62 (68.1)	29 (90.6)	33 (55.9)	**.001**
Amiodarone–M, yes	11 (20.7)	11 (52.4)	0 (0.0)	**<.0001**
Amiodarone–F, yes	33 (36.3)	27 (84.4)	6 (10.1)	**<.0001**
Dyslipidemia–M, yes	22 (52.8)	13 (61.9)	15 (46.8)	.429
Dyslipidemia–F, yes	35 (38.5)	16 (50)	19 (32.2)	.149
CAD–M, yes	4 (7.54)	2 (9.5)	2 (6.25)	.999
CAD–F, yes	1 (1.1)	0 (0.0)	1 (1.7)	.999
TSH–M, mUI/L	2.1 [0.7]	2 [0.5]	2.25 [0.75]	**.023**
TSH–F, mUI/L	2.3 [1]	2.35 [1.05]	2.3 [0.9]	.732
ECG variables				
$\Delta\alpha^{QT,}$ –M [a.u.]	0.141 [0.106]	0.181 [0.170]	0.124 [0.074]	**.009**
$\Delta\alpha^{QT}$–F [a.u.]	0.158 [0.107]	0.146 [0.177]	0.159 [0.100]	.910
$\Delta\alpha^{Tpe}$–M [a.u.]	0.021 [0.039]	0.038 [0.099]	0.017 [0.020]	**.013**
$\Delta\alpha^{Tpe}$–F [a.u.]	0.027 [0.049]	0.050 [0.081]	0.022 [0.025]	**.003**
TMR–M [a.u.]	0.022 [0.022]	0.031 [0.035]	0.021 [0.018]	.214

TMR–F [a.u.]	0.037 [0.026]	0.038 [0.035]	0.037 [0.024]	.907
TpeMR–M [a.u.]	0.011 [0.027]	0.015 [0.051]	0.008 [0.014]	.071
TpeMR–F [a.u.]	0.015 [0.025]	0.027 [0.037]	0.014 [0.016]	**.024**

BMI, body mass index; CAD, coronary artery disease; DM2, diabetes mellitus type 2; ECG, electrocardiogram; F, female; LVEF, left ventricle ejection fraction; M, male; TMR, T-wave morphology restitution; TpeMR, T-peak-to-end morphology restitution; TSH, thyroid-stimulating hormone. Statistical significant differences are indicated in bold.

The data are presented as median [interquartile range] for continuous variables, and as absolute number and percentages for categorical variables.

*LVEF is included in the Rassi score.

Table S4. Univariate and multivariate Cox analysis in males

	Univariate		Multivariate*	
	HR (95%CI)	*P*	HR (95%CI)	*P*
ECG variables				
$\Delta\alpha^{QT}$(per unit increment)	29.8 (1.65-536.7)	**.021**	NS	NS
$\Delta\alpha^{Tpe}$ (per unit increment)	56.8 (2.80-1159.5)	**.001**	NS	NS
Clinical variables				
Amiodarone intake (yes)	12.8 (4.71-34.8)	**<.0001**	NA	NA
TSH (per mUI/L increment)	0.29 (0.12-0.67)	**.004**	NS	NS
Rassi Score (per unit increment)	1.56 (1.60-1.88)	**<.0001**	1.56 (1.30-1.88)	**<.0001**

CI, confidence interval; ECG, electrocardiogram; HR, hazard ratio; NA, not applicable; NS, not significant; TSH, thyroid-stimulating hormone.

Significant differences are indicated in bold.

*Multivariate analysis included only the most significant ECG variable in the univariate analysis and excluded amiodarone intake to avoid multicollinearity.

Table S5. Univariate and multivariate Cox analysis in females

	Univariate		Multivariate*	
	HR (95%CI)	*P*	HR (95%CI)	*P*
ECG variables				
$\Delta\alpha^{Tpe}$ [per unit increment]	48.1 (2.45-968.3)	**.010**	NS	NS
TpeMR [per unit increment]	1.88e7 (694.4-5e11)	**.001**	NS	NS
Clinical variables				
Hypertension (yes)	5.88 (1.79-19.3)	**.003**	3.59 (1.37-2.11)	**.036**
Amiodarone intake (yes)	19.0 (7.24-50.3)	**<.0001**	NA	NA
Rassi Score [per unit increment]	1.71 (1.38-2.13)	**<.0001**	1.70 (1.37-2.11)	**<.0001**

CI, confidence interval; ECG, electrocardiogram; HR, hazard ratio; NA, not applicable; NS, not significant.

Only covariates specified in this table were included in the analyses. Significant differences are indicated in bold.

*Multivariate analysis included only the most significant ECG variable in univariate analysis and excluded amiodarone intake to avoid multicollinearity.

Table S6. Characteristics of patients after exclusion of Chagas disease patients under amiodarone treatment

	Overall population (N = 100)	Primary endpoint group (N = 15)	Control group (N = 85)	*P*
Clinical variables				
Age, y	45.1 [13.7]	48 [6.2]	44.0 [14.1]	.349
Sex, male*	42 (42)	10 (66.6)	32 (37.6)	.069
BMI, kg/m^2	28 [3]	28 [2]	29 [3]	**.041**
Rassi score, points	3 [3]	5 [5]	3 [1]	**<.0001**
LVEF, %*	66.5 [14]	53 [16]	67 [9]	.001
DM2, yes	12 (12)	2 (13.3)	10 (11.7)	1
Hypertension, yes	62 (62)	9 (60)	53 (62.3)	1
Amiodarone intake, yes	0 (0.0)	0 (0.0)	0 (0.0)	**-**
Dyslipidemia, yes	40 (40)	7 (46.6)	33 (38.8)	.775
CAD, yes	4 (4)	1 (6.6)	3 (3.5)	.483
TSH, mUI/L	2.3 [0.82]	2.1 [0.4]	2.3 [0.9]	.085
ECG variables				
$\Delta\alpha^{QT}$ [a.u.]	0.146 [0.101]	0.191 [0.205]	0.141 [0.090]	**.038**
$\Delta\alpha^{Tpe}$ [a.u.]	0.022 [0.033]	0.044 [0.100]	0.019 [0.026]	**.005**
TMR [a.u.]	0.036 [0.026]	0.047 [0.038]	0.033 [0.023]	.058
TpeMR [a.u.]	0.013 [0.022]	0.031 [0.060]	0.012 [0.016]	**.005**

BMI, body mass index; LVEF, left ventricle ejection fraction. DM2, diabetes mellitus type 2; CAD, coronary artery disease; TSH, thyroid-stimulating hormone. ECG, electrocardiogram. TMR, T-wave morphology restitution; TpeMR, T-peak-to-end morphology restitution.

The data are presented as No. (%) or median [interquartile range].

Statistical significant differences are indicated in bold.

*Sex and LVEF are included in the Rassi score.

Table S7. Univariate and multivariate Cox analysis after excluding Chagas disease patients receiving amiodarone treatment

	Univariate		Multivariate*	
	HR (95%CI]	*P*	HR (95%CI]	*P*
ECG variables				
$\Delta\alpha^{QT}$ (per unit increment)	320.2 (13.56-7560.2]	**<.01**	NA	N.A.
$\Delta\alpha^{Tpe}$ (per unit increment)	1,227.3 (30.2-4.9e4]	**<.001**	NS	N.S.
TpeMR (per unit increment)	1.48e5 (23.26-9.5e8]	**.007**	NA	N.A.
Clinical variables				
Body mass index (per kg/m^2 increment)	0.86 (0.73-1.00]	.063	-	-
Rassi Score (per unit increment)	1.60 (1.33-1.93]	**<.0001**	1.60 (1.33-1.93]	**<.0001**

CI, confidence interval; ECG, electrocardiogram; HR, hazard ratio; NA, not applicable; NS, not significant.

Only covariates specified in this table were included in the analyses. The population consisted of 100 participants, of whom 15 (15%] met the primary endpoint within the follow-up period and the remaining were controls. Significant differences are indicated in bold.

*Multivariate analysis included only the most significant ECG variable in univariate analysis.

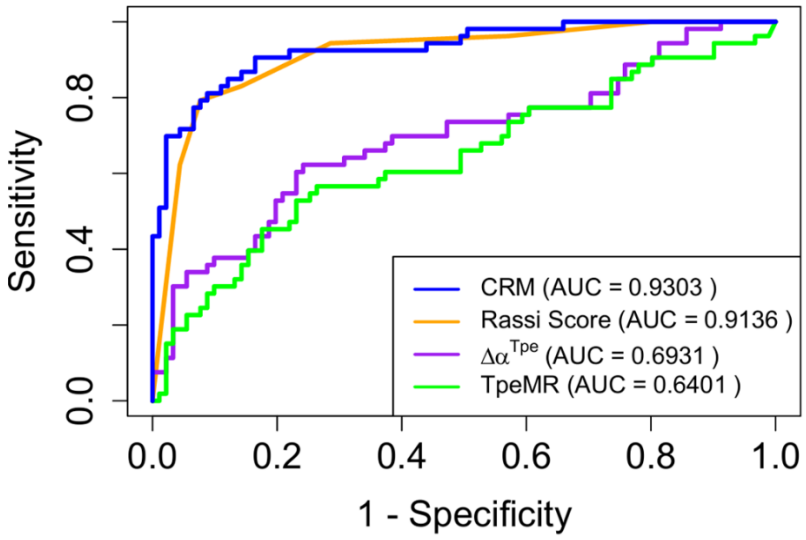
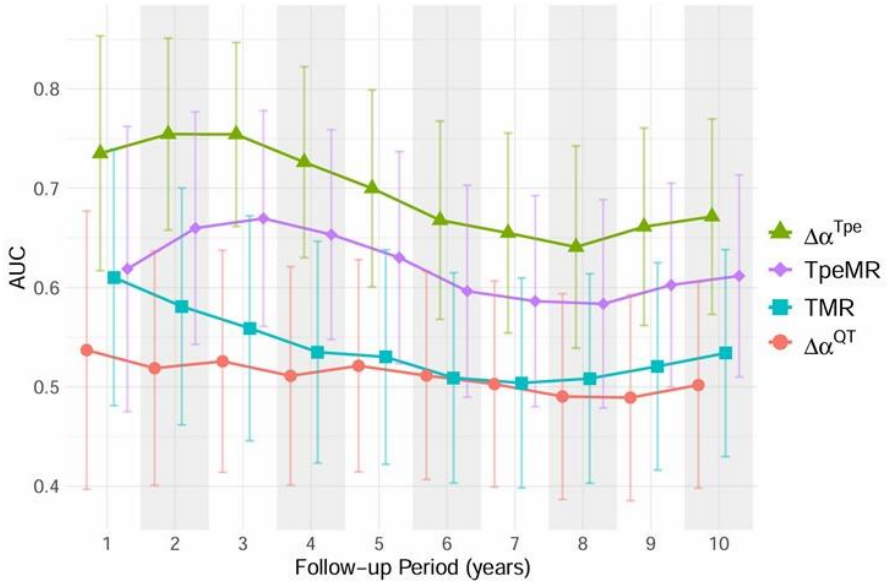


Figure S1. Area under the receiver operating characteristics (ROC) curves for the combined risk model (CRM], Rassi score, $\Delta\alpha^{Tpe}$, and TpeMRc.



Samples sizes at each follow-up period

142	142	142	141	141	141	141	141	139	139	*Overall population after exclusion criteria*
19	30	36	39	42	45	46	47	49	50	*Primary endpoint*
123	112	106	102	99	96	95	94	90	89	*Control*

Figure S2. Area under the curve (AUC] for $\Delta\alpha^{QT}$ (red circles], $\Delta\alpha^{Tpe}$ (green triangles], TMR (blue squares] and TpeMR (purple diamonds] and sample sizes over the 10-year follow-up period.

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