Doença de Chagas

&

Morte súbita

Rogério Braga Andalaft

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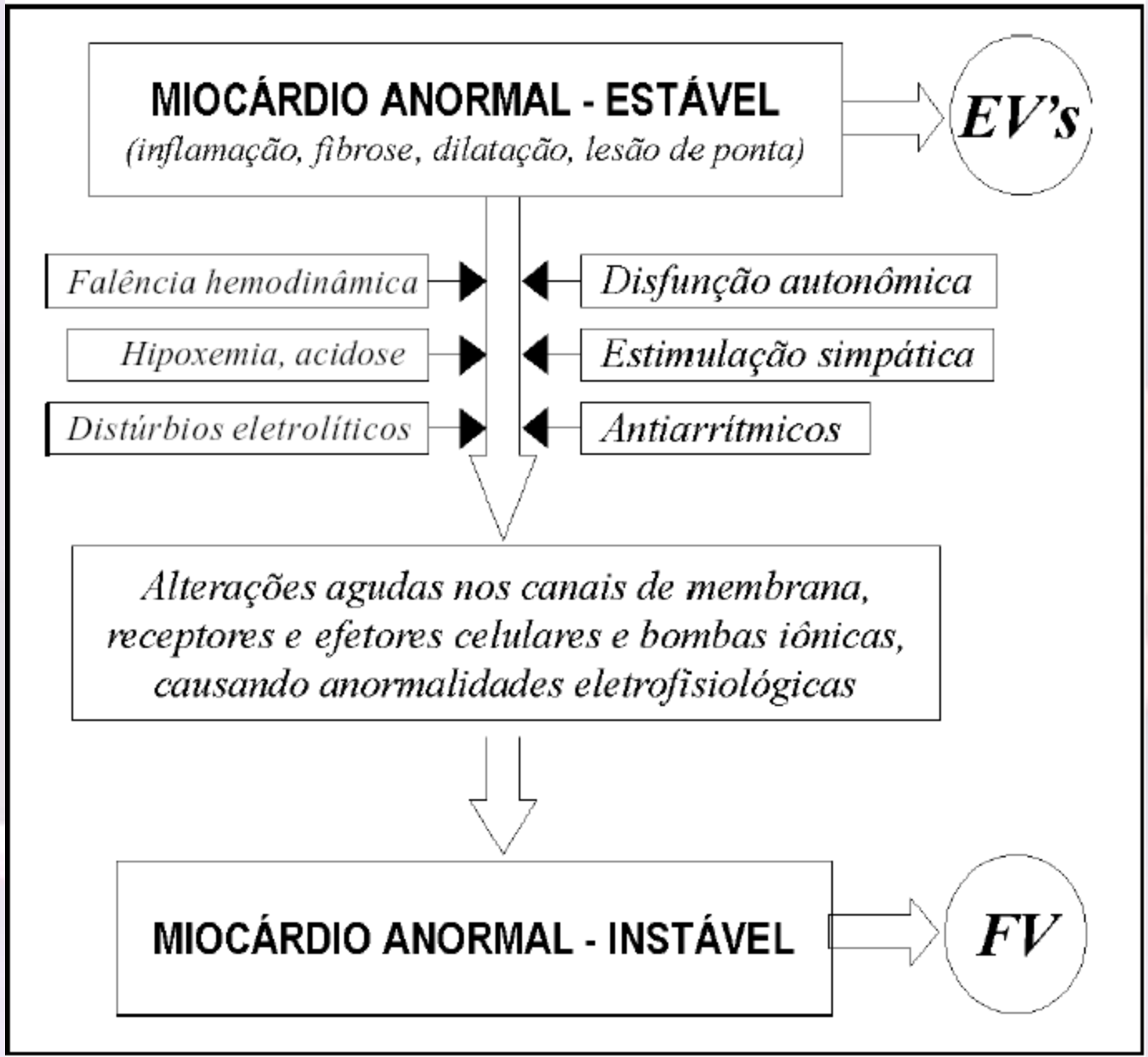
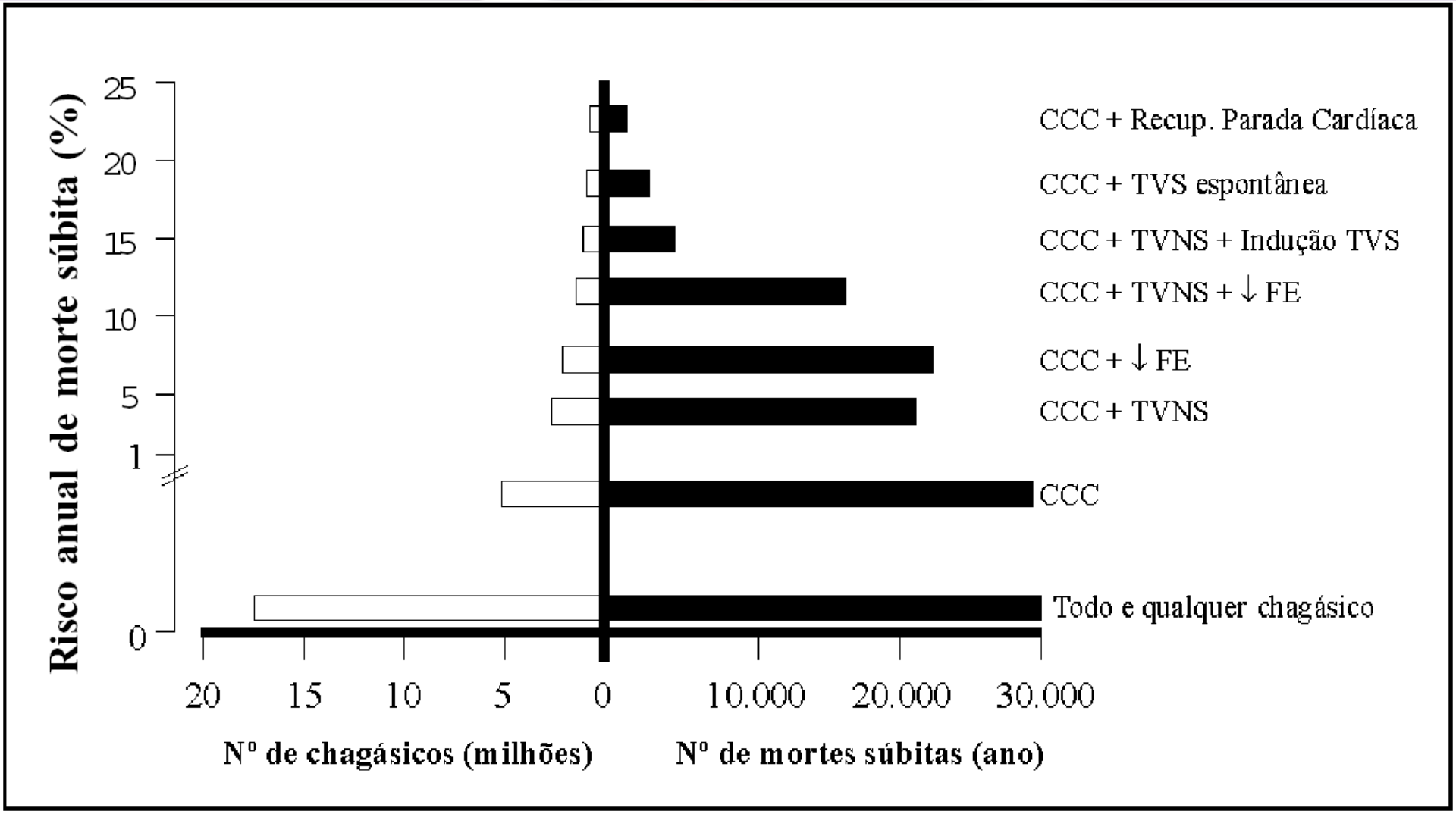
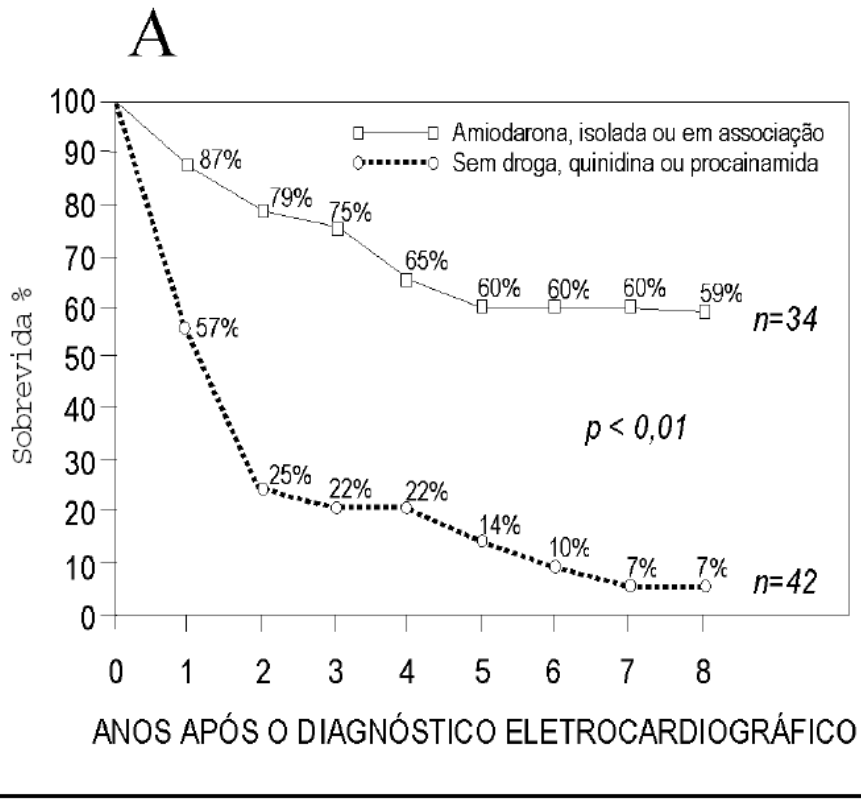
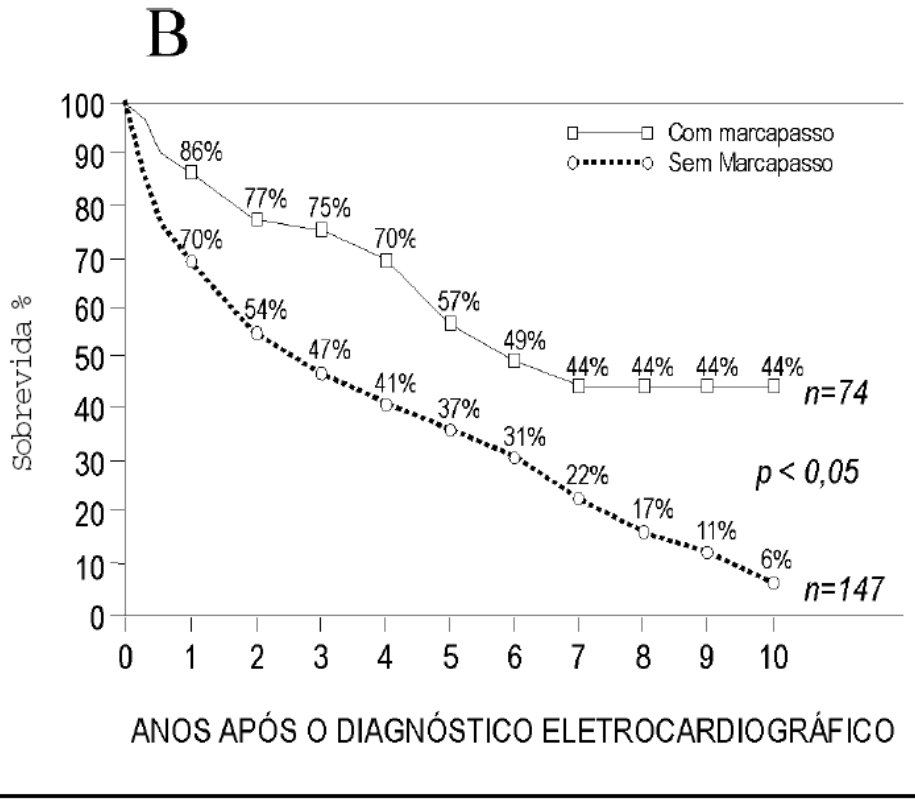

MIOCÁRDIO ANORMAL - ESTÁVEL
(inflamação, fibrose, dilatação, lesão de ponta)
EV's
Falência hemodinâmica
Hipoxemia, acidose
Distúrbios eletrolíticos
Disfunção autonômica
Estimulação simpática
Antiarrítmicos
Alterações agudas nos canais de membrana, receptores e efetores celulares e bombas iônicas, causando anormalidades eletrofisiológicas
MIOCÁRDIO ANORMAL - INSTÁVEL
FV


Risco anual de morte súbita (%)
25
20
15
10
5
1
0
CCC + Recup. Parada Cardíaca
CCC + TVS espontânea
CCC + TVNS + Indução TVS
CCC + TVNS + ↓ FE
CCC + ↓ FE
CCC + TVNS
CCC
Todo e qualquer chagásico
20
15
10
5
0
10.000
20.000
30.000
Nº de chagásicos (milhões)
Nº de mortes súbitas (ano)


A
Amiodarona, isolada ou em associação
Sem droga, quinidina ou procainamida
Sobrevida %
87%
79%
75%
65%
60%
60%
60%
59%
n=34
57%
25%
22%
22%
14%
10%
7%
7%
n=42
p < 0,01
0 1 2 3 4 5 6 7 8
ANOS APÓS O DIAGNÓSTICO ELETROCARDIOGRÁFICO


B
Com marcapasso
Sem Marcapasso
Sobrevida %
86%
77%
75%
70%
57%
49%
44%
44%
44%
44%
n=74
70%
54%
47%
41%
37%
31%
22%
17%
11%
6%
n=147
p < 0,05
0 1 2 3 4 5 6 7 8 9 10
ANOS APÓS O DIAGNÓSTICO ELETROCARDIOGRÁFICO

Garzon e Lorga 2000

- 987 pacientes
- Acompanhados por 7+- 5 anos
- 368 óbitos (39% morte súbita)
  - A maioria nos primeiros 5 anos (73%)
  - Quase todos em 10 anos (92%)
- Fatores de risco independentes
  - ECG anormal
  - Cardiomegalia
  - TV de qualuqer forma
  - FE deprimida

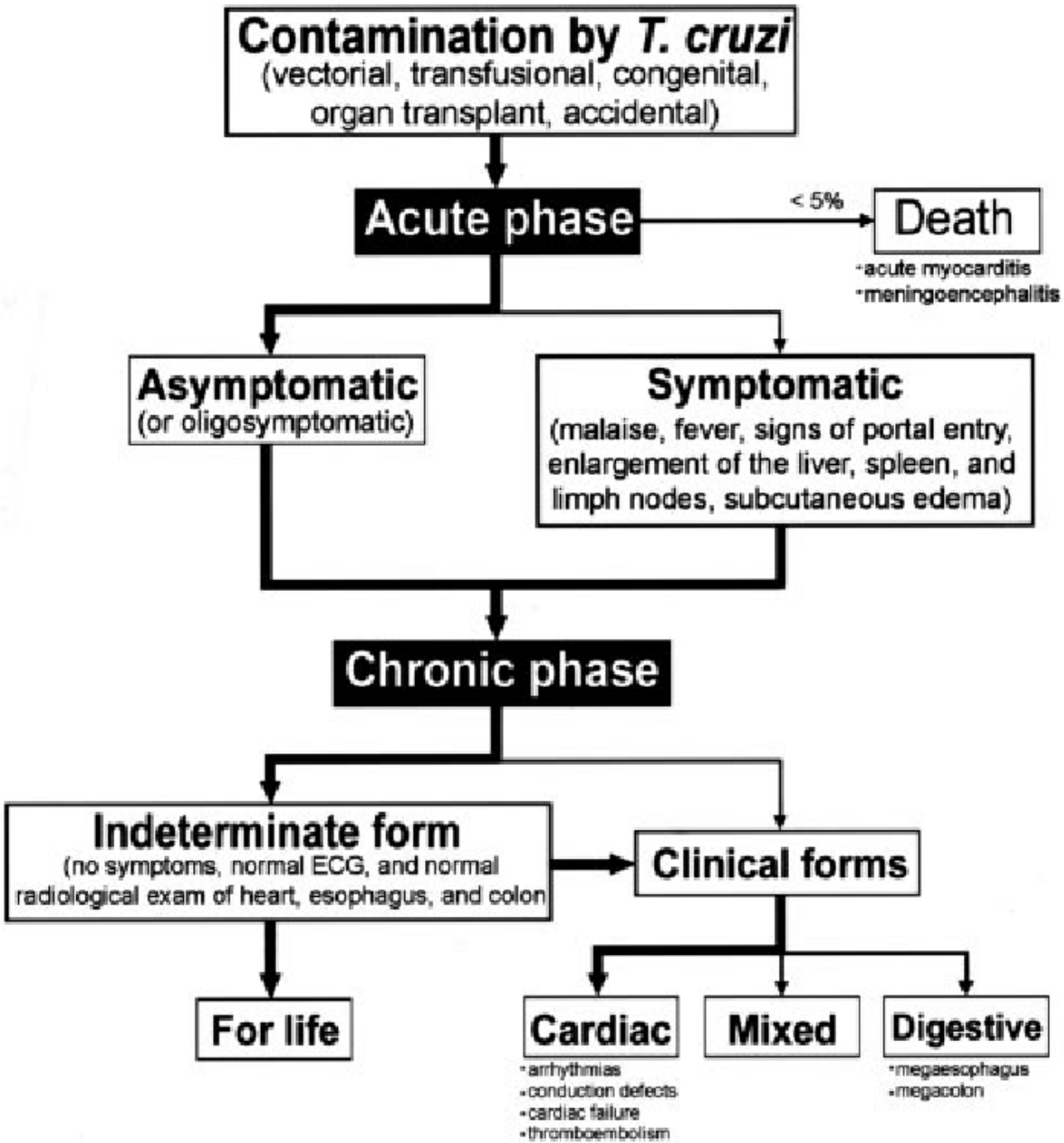

Contamination by T. cruzi
(vectorial, transfusional, congenital, organ transplant, accidental)
Acute phase
< 5%
Death
•acute myocarditis
•meningoencephalitis
Asymptomatic
(or oligosymptomatic)
Symptomatic
(malaise, fever, signs of portal entry, enlargement of the liver, spleen, and limph nodes, subcutaneous edema)
Chronic phase
Indeterminate form
(no symptoms, normal ECG, and normal radiological exam of heart, esophagus, and colon
Clinical forms
For life
Cardiac
•arrhythmias
•conduction defects
•cardiac failure
•thromboembolism
Mixed
Digestive
•megaesophagus
•megacolon

TABLE 1

Multivariate Cox Proportional-Hazards Analysis of Risk of Death in Chagas Disease Patients with Cardiac Disease

	Prevalence (n = 136)	Hazard Ratio (95% CI)	P Value	β Regression Coefficient
LVEF < 0.50	34 (25%)	4.8 (0.9–24.4)	0.053	1.6
Ventricular tachycardia at stress testing or at 24-h Holter	41 (30%)	9.5 (1.1–80.3)	0.040	2.2
Filtered QRS > 150 ms	26 (19%)	3.8 (1.0–14.7)	0.050	1.3

Multivariate Cox Proportional-Hazards Analysis of Risk of Death in Chagas Disease Patients Substituting the Filtered QRS > 150 ms for the ECG QRS > 133 ms

	Prevalence (n = 178)	Hazard Ratio (95% CI)	P Value	Coefficient β Regression
LVEF < 0.50	36 (20%)	7.7 (1.5–39.7)	0.014	2.0
Ventricular tachycardia at stress testing or at 24-h Holter	46 (26%)	5.1 (1.0–26.2)	0.050	1.6
QRS > 133 ms	30 (17%)	4.4 (1.3–14.8)	0.016	1.5

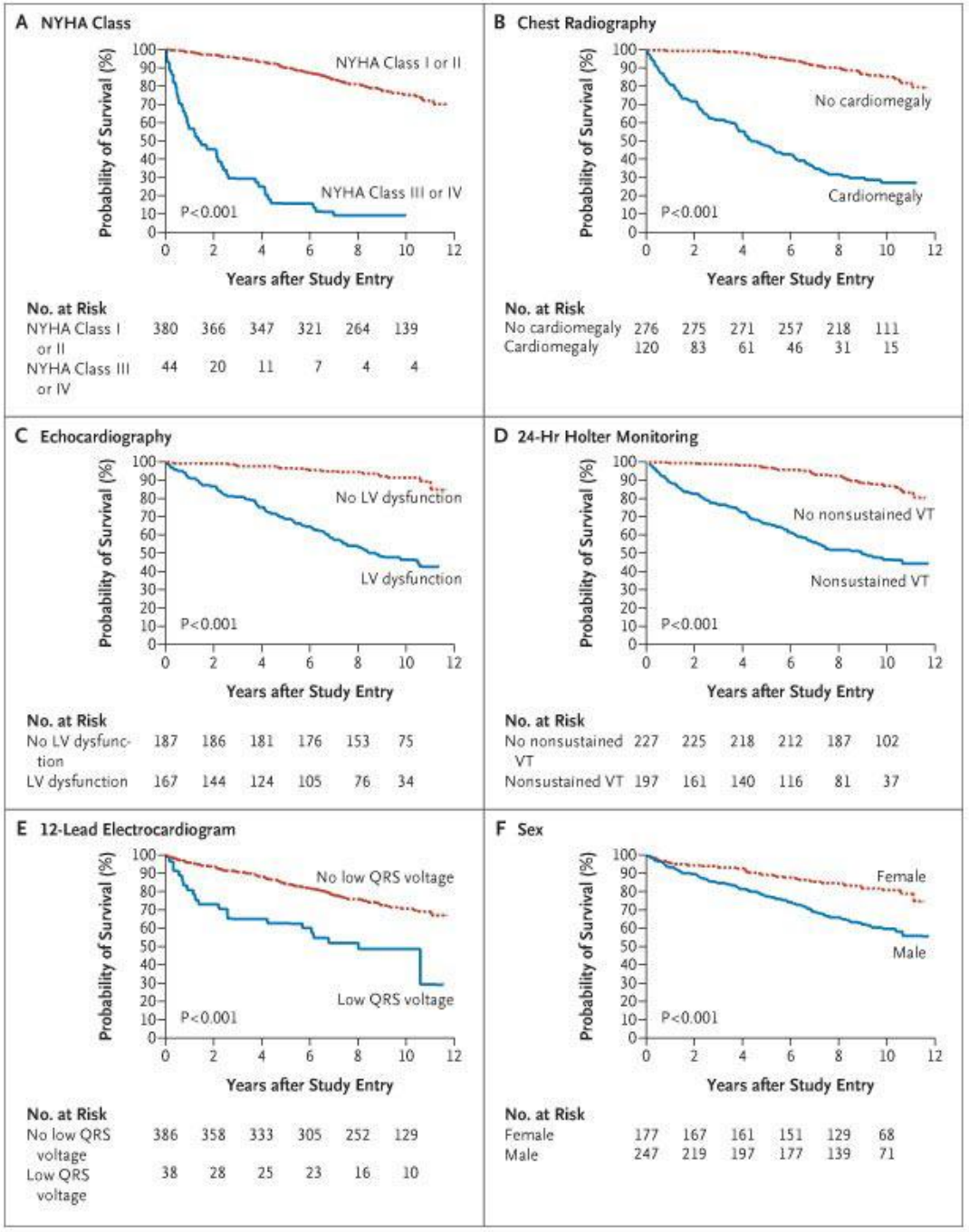


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Table 3. Risk of Death at 5 and 10 Years in the Development and Validation Cohorts, According to Risk Category.*

Risk Category	Development Cohort (N=331)			Validation Cohort (N=153)		
	No. (%)	Death at 5 Yr	Death at 10 Yr	No. (%)	Death at 5 Yr	Death at 10 Yr
		% (95% CI)			% (95% CI)	
Low	203 (61.3)	2 (0–5)	10 (5–14)	100 (65.4)	0	9 (2–16)
Intermediate	62 (18.7)	18 (8–28)	44 (31–57)	30 (19.6)	15 (1–28)	37 (16–59)
High	66 (19.9)	63 (51–75)	84 (74–93)	23 (15.0)	53 (31–75)	85 (63–100)
		difference in probability of death†			*difference in probability of death†*	
		0.61	0.74		0.53	0.76
C statistic (95% CI)‡		0.84 (0.79–0.89)			0.81 (0.72–0.90)	

* The risk category was calculated by adding the points for each of the following risk factors: male sex (2 points), low QRS voltage on the electrocardiogram (2 points), nonsustained ventricular tachycardia on 24-hour Holter monitoring (3 points), segmental or global wall-motion abnormality on the echocardiogram (3 points), cardiomegaly on chest radiography (5 points), and NYHA class III or IV (5 points). The prognostic index was categorized in three groups: low risk (0 to 6 points), intermediate risk (7 to 11 points), and high risk (12 to 20 points). CI denotes confidence interval.

† The difference in the probability of death between the high- and the low-risk groups was calculated by the formula $(P_{high} - P_{low}) \div 100$.

‡ The C statistic for overall score is reported.

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Table 2. Multivariate Cox Proportional-Hazards Analysis of the Development Cohort and Scoring System.*

Risk Factor	Prevalence (N=331)	Hazard Ratio (95% CI)	P Value	β Regression Coefficient	Points†
NYHA class III or IV — no. (%)	33 (10.0)	4.05 (2.46–6.67)	<0.001	1.40	5
Cardiomegaly — no. (%)	89 (26.9)	3.43 (2.06–5.72)	<0.001	1.23	5
Segmental or global WMA — no. (%)	155 (46.8)	2.46 (1.26–4.79)	0.008	0.90	3
Nonsustained VT — no. (%)	160 (48.3)	2.15 (1.28–3.62)	0.004	0.77	3
Low QRS voltage — no. (%)	28 (8.5)	1.87 (1.03–3.37)	0.039	0.62	2
Male sex — no. (%)	200 (60.4)	1.72 (1.06–2.81)	0.030	0.54	2

* Because data for some variables were missing for some patients, the final sample used in the multivariate analysis consisted of 331 patients, 98 of whom died. CI denotes confidence interval, WMA wall-motion abnormality, and VT ventricular tachycardia.

† Assignment of points to risk factors was based on a linear transformation of the corresponding β regression coefficient. The coefficient of each variable was divided by 0.54 (the lowest β value, corresponding to male sex), multiplied by a constant (2), and rounded to the nearest integer.

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Table 1. Population Characteristics of the Development Cohort and Crude Association of Potential Prognostic Determinants with Death.*

Characteristic	All Patients (N=424)	Survivors (N=294)	Nonsurvivors (N=130)	P Value†	Hazard Ratio (95% CI)‡
Demographic and clinical					
No. of patients with data	424	294	130		
Age — yr	47±11	46±11	51±11	<0.001	NA
Age >48 yr — no. (%)	205 (48.3)	124 (42.2)	81 (62.3)	<0.001	2.06 (1.45–2.93)
Male sex — no. (%)	247 (58.3)	151 (51.4)	96 (73.8)	<0.001	2.33 (1.57–3.44)
Palpitations — no. (%)	126 (29.7)	93 (31.6)	33 (25.4)	0.19	0.75 (0.51–1.18)
Syncope — no. (%)	27 (6.4)	14 (4.8)	13 (10.0)	0.04	2.06 (1.16–3.66)
NYHA class III or IV — no. (%)	44 (10.4)	4 (1.4)	40 (30.8)	<0.001	13.92 (9.36–20.70)
Electrocardiographic					
No. of patients with data	424	294	130		
Isolated RBBB — no. (%)	79 (18.6)	62 (21.1)	17 (13.1)	0.05	0.60 (0.36–0.99)
Isolated LAFB — no. (%)	56 (13.2)	41 (13.9)	15 (11.5)	0.60	0.85 (0.49–1.45)
RBBB plus LAFB — no. (%)	103 (24.3)	75 (25.5)	28 (21.5)	0.44	0.85 (0.56–1.30)
LBBB — no. (%)	30 (7.1)	11 (3.7)	19 (14.6)	<0.001	3.07 (1.88–5.01)
PVCs — no. (%)	158 (37.3)	103 (35.0)	55 (42.3)	0.15	1.28 (0.91–1.82)
Q waves — no. (%)	28 (6.6)	10 (3.4)	18 (13.8)	<0.001	3.72 (2.25–6.14)
ST-T changes — no. (%)	118 (27.8)	70 (23.8)	48 (36.9)	0.005	1.73 (1.21–2.47)
1st or 2nd degree AV block — no. (%)	38 (9.0)	19 (6.5)	19 (14.6)	0.007	2.00 (1.31–3.06)
Low QRS voltage — no. (%)	38 (9.0)	17 (5.8)	21 (16.2)	0.001	2.57 (1.61–4.10)
Atrial fibrillation or flutter — no. (%)	13 (3.1)	2 (0.7)	11 (8.5)	<0.001	5.43 (2.91–10.13)
Radiologic					
No. of patients with data	396	273	123		
Cardiomegaly — no. (%)	120 (30.3)	37 (13.6)	83 (67.5)	<0.001	9.22 (6.29–13.51)
Pulmonary congestion — no. (%)	23 (5.8)	1 (0.4)	22 (17.9)	<0.001	10.70 (6.58–17.38)
Echocardiographic					
No. of patients with data	354	251	103		
Increased LVEDD — no. (%)	133 (37.6)§	55 (21.9)	78 (75.7)	<0.001	7.97 (5.07–12.54)
Segmental or global WMA — no. (%)	167 (47.2)¶	80 (31.9)	87 (84.5)	<0.001	8.53 (5.00–14.56)
Apical aneurysm — no. (%)	37 (10.5)	25 (10.0)	12 (11.7)	0.64	1.09 (0.60–2.00)
Intracavitary thrombus — no. (%)	7 (2.0)	3 (1.2)	4 (3.9)	0.20	2.34 (0.86–6.35)
24-Hr Holter monitoring					
No. of patients with data	424	294	130		
Frequent PVCs — no. (%)‖	191 (45.0)	106 (36.1)	85 (65.4)	<0.001	2.95 (2.05–4.23)
Nonsustained VT — no. (%)**	197 (46.5)††	97 (33.0)	100 (76.9)	<0.001	5.74 (3.81–8.66)
Heart-rate variability					
No. of patients with data	374	262	112		
SDNN <100 msec — no. (%)	83 (22.2)	46 (17.6)	37 (33.0)	0.001	1.93 (1.30–2.86)

* Plus–minus values are means ±SD. NA denotes not applicable, RBBB right bundle-branch block, LAFB left anterior fascicular block, LBBB left bundle-branch block, PVCs premature ventricular complexes, AV atrioventricular, LVEDD left ventricular end-diastolic diameter, WMA wall-motion abnormality, VT ventricular tachycardia, and SDNN standard deviation of normal-to-normal RR intervals.

† P values are for the comparison of survivors with patients who died and were calculated by the unpaired t-test for mean age and by the chi-square test or Fisher's exact test, as appropriate, for the other variables.

‡ Hazard ratios with corresponding 95 percent confidence intervals (CIs) were calculated by univariate Cox regression analysis and are for the comparison of survivors with patients who died.

§ Increased LVEDD was mild in 47 percent, moderate in 31 percent, and severe in 22 percent of patients. According to observations from our laboratory, mildly, moderately, and severely increased LVEDDs correspond to values of 55 through 65 mm, 66 through 75 mm, and greater than 75 mm, respectively.

¶ WMA was exclusively regional in 14 percent, mildly global in 29 percent, moderately global in 19 percent, and severely global in 38 percent of patients. According to observations from our laboratory, mildly, moderately, and severely depressed ejection fractions correspond to values of 0.55 through 0.45, 0.44 through 0.30, and less than 0.30, respectively.

‖ Frequent PVCs were defined as more than 1000 PVCs per 24 hours.

** Ventricular tachycardia was defined by a heart rate of more than 100 beats per minute.

†† Patients who had nonsustained VT on a treadmill exercise test were also included.

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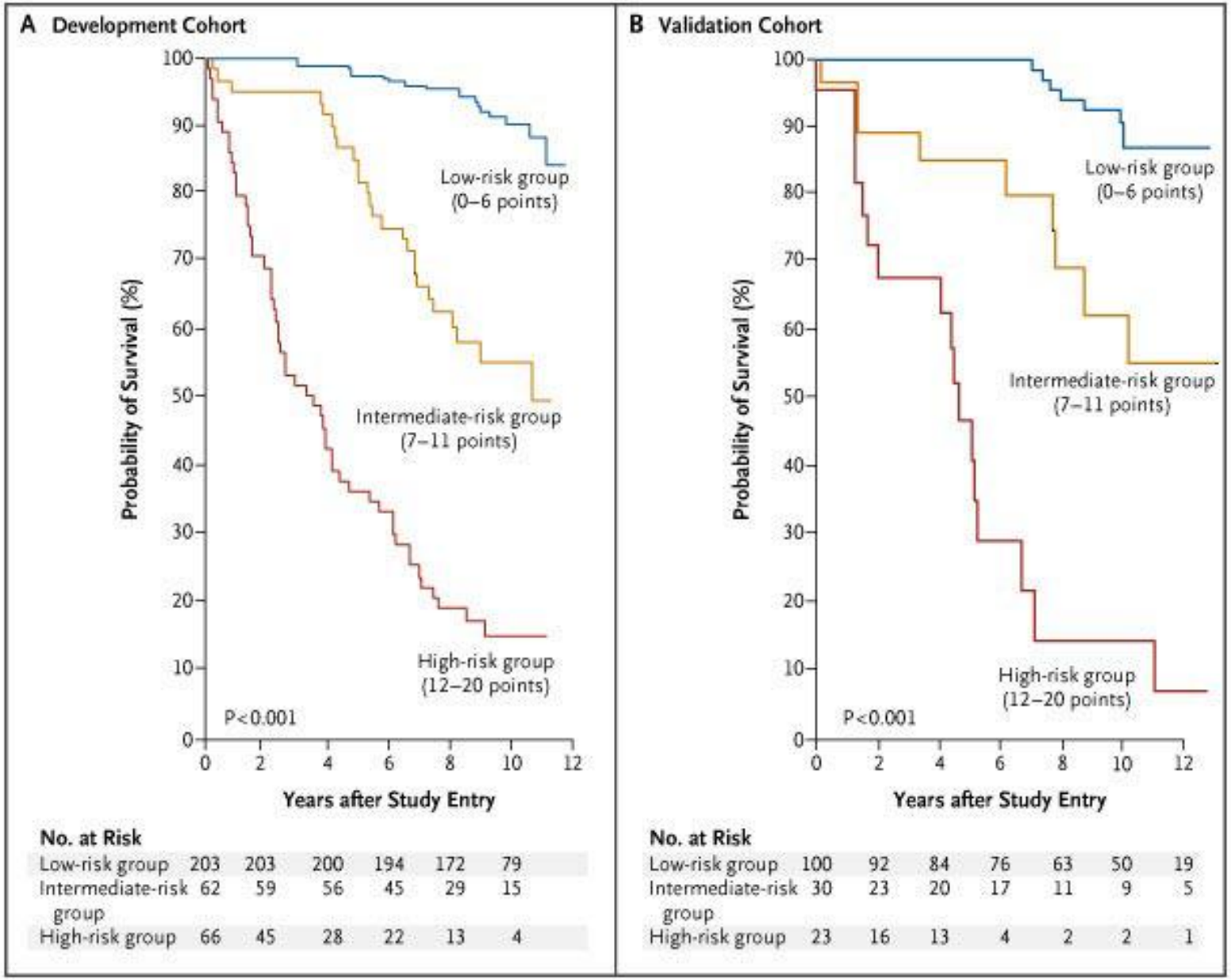

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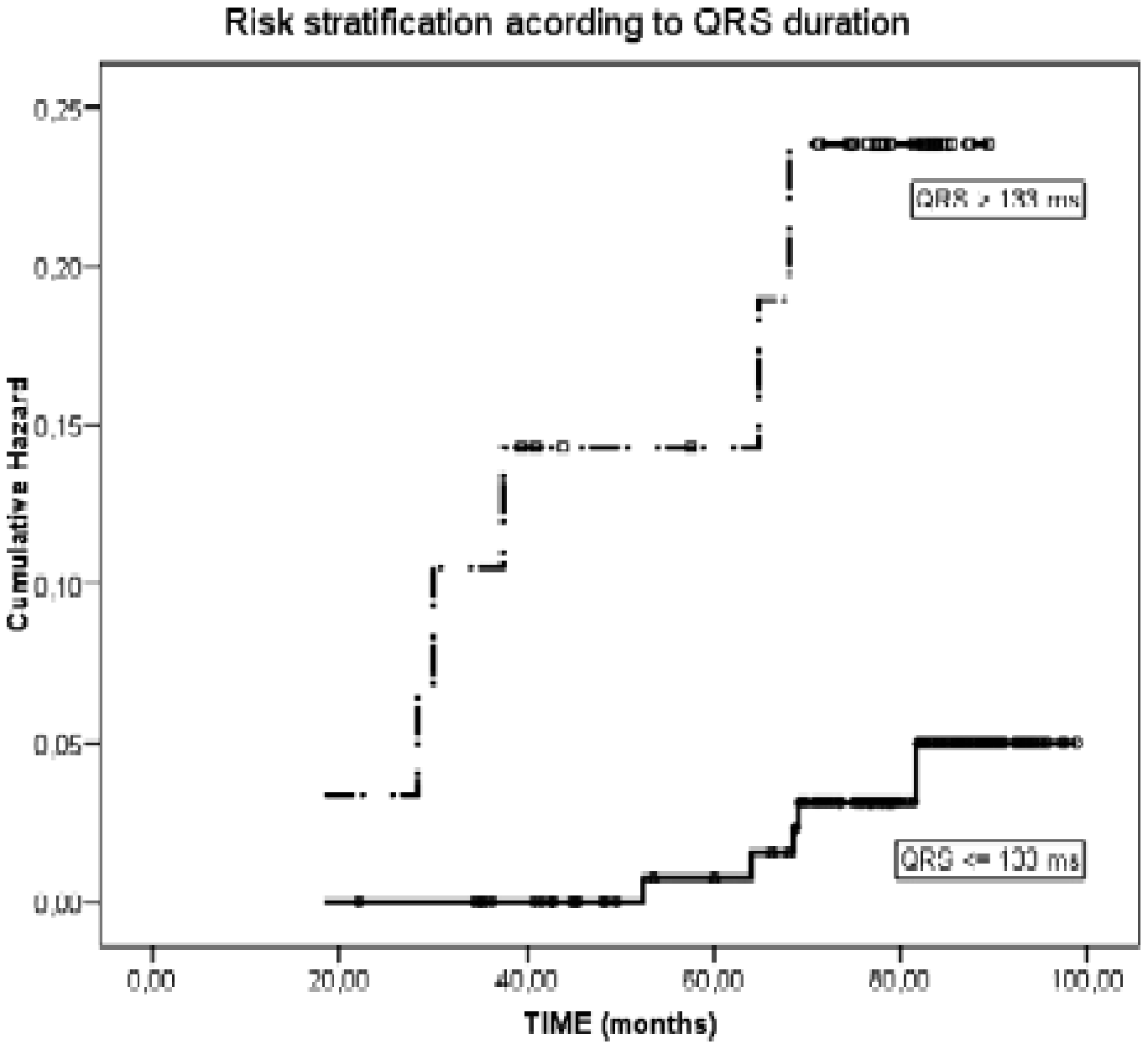
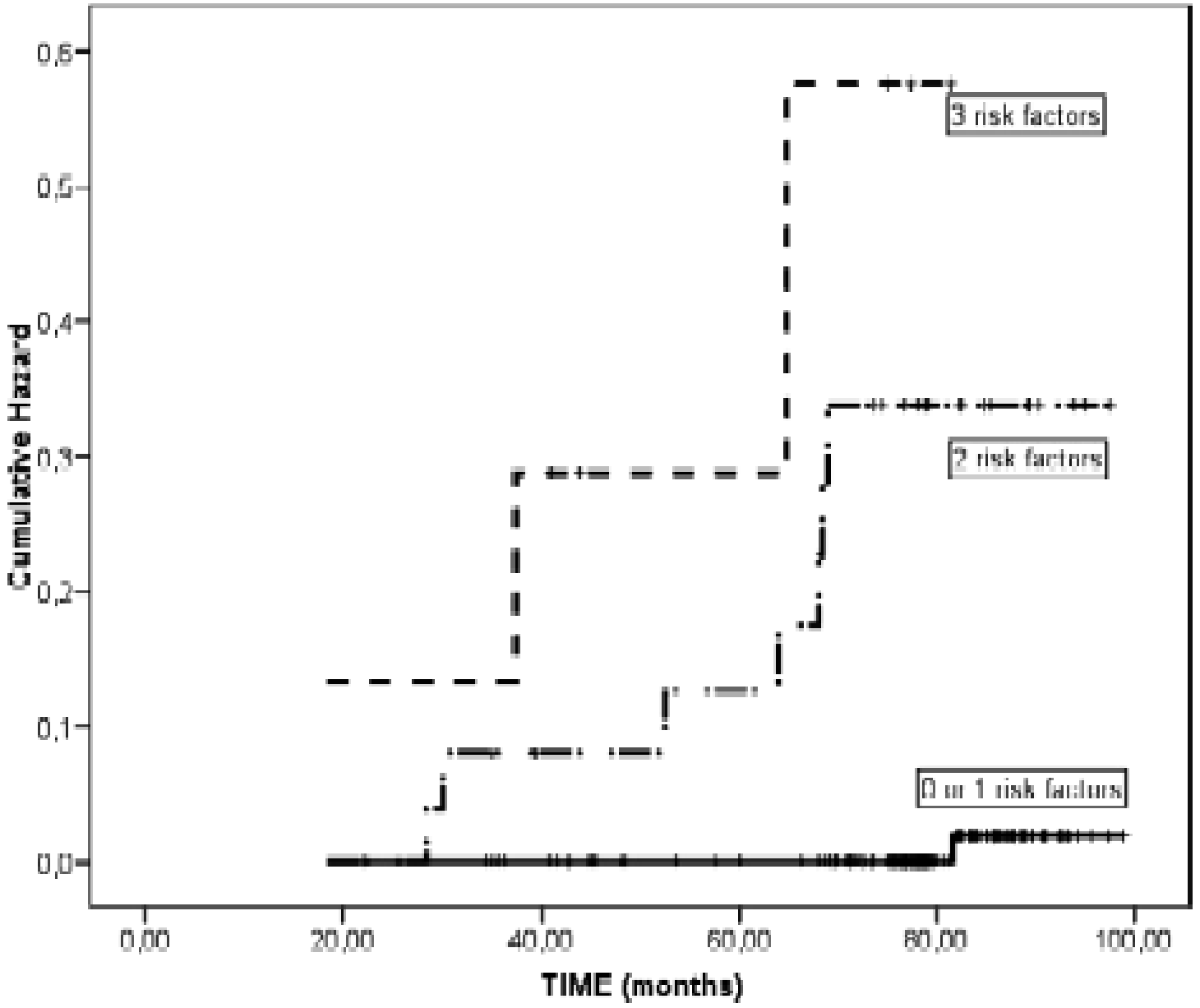

Risk stratification acording to QRS duration
Cumulative Hazard
0,25
0,20
0,15
0,10
0,05
0,00
QRS > 139 ms
QRS <= 139 ms
0,00
20,00
40,00
60,00
80,00
100,00
TIME (months)

Risk stratification using QRS duration, LVEF and NSVT



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Quadro I - Causas de óbito em diferentes subgrupos populacionais da doença de Chagas

Autores	Nº de P	Características da população estudada*	Seguimento	Nº de óbitos relacionados à DC	Causas de óbito n(%)			
					MS	ICC	AVC	Outras
Prata, 1959[17]	169	- População hospitalar - Pacientes com IC descompensada	NR	82	31(38)	43(53)	-	8†(9)
Lima & Rassi, 1962[18]	642	- Pacientes de clínica particular - 100% com ECG anormal (61% com EV's) - 47% com AC normal e 53% com AC aumentada (RX)	NR	57	40(70)	13(23)	4(7)	-
Porto, 1964[19]	503	- Pacientes de consultório (área endêmica) - ECG normal em 39% das vezes e anormal em 61% das vezes	Até 5-6 anos	96‖	36(38)	53(55)	-	7‡(7)
Brasil, 1965[20]	86	- Pacientes de clínica particular - 50% sem cardiopatia aparente (forma subclínica) e 50% com cardiopatia	10 anos	25¶¶	18(72)	6(24)	1(4)	-
Baruffa, 1974[21]	172	- População de área endêmica (Rio Grande do Sul) - 23% na forma indeterminada;22% na forma digestiva; 31% na forma cardíaca e 24% na forma cardiodigestiva	NR	18	10(56)	8(44)	-	-
Macedo, 1976[22]	840	- População de área endêmica - Inquérito clínico epidemiológico	4 anos	24	9(38)	14(58)	-	1§(4)
Pugliese et al, 1976[23]	160	- Pacientes com IC descompensada - Revisão de prontuários médicos	Até 2,5 anos	96	10(10)	63(66)	1(1)	22‖(23)
Dias, 1982[24]	268	- Pacientes com fase aguda conhecida	27 anos	19	10(53)	5(26)	3(16)	1¶(5)
Espinosa et al, 1985[25]	104	- Pacientes ambulatoriais - 29% com ECG normal; 39% com ECG anormal, sem ICC e 32% com ECG anormal e ICC severa	4,9 anos	36##	15(42)	16(44)	5(14)	-
Coura et al, 1985[26]	*235*	- População de campo - Chagásicos crônicos	Até 10 anos	41	31(76)	9(22)	1(2)	-
Santana, 1987[27]	76	- Pacientes ambulatoriais (CF I ou II) - 19,5% com ECG normal e 81,5% com ECG anormal - 57% com AC normal e 43 % com AC aumentada (RX)	5,2 anos	14***	10(71)	3(21)	1(7)	-
Acquatella et al, 1987[28]	755	- Pacientes ambulatoriais - 48% com ECG normal, 12% *borderline* e 40% anormal - 79% assint., 13% sintomas leves/mod. e 8% ICC severa	2,3 anos	48†††	19(40)	19(40)	4(8)	6#(12)
Carrasco et al, 1994[29]	185	- Pacientes com ECG anormal, sem sinais de ICC	6,4 anos	33	12(36)	6(18)	3**(9)	-
	104	- Pacientes com ECG anormal + ICC	2,3 anos	67	14(21)	52(78)	1(1)	-
Silva, 1997[30]	78	- Pacientes de ambulatório ou enfermaria com TVNS ao H - 85% em CF I ou II e 15% em CF III ou IV	4,6 anos	21‡‡‡	16(76)	2(9,5)	1(5)	2††(9,5)
Garzon, 1998[31]	987	- Pacientes de ambulatório ou enfermaria submetidos a estudo hemodinâmico	7 anos	331	169(51)	147(44)	-	15‡‡(5)
Rassi Jr., 1999[32]	444	- Pacientes de ambulatório (população não-selecionada)	9,1 anos	111	74(67)	23(21)	-	14§§(12)

Abreviações: **AC**, área cardíaca; **AVC**, acidente vascular cerebral; **CF**, classe funcional; **DC**, Doença de Chagas; **ECG**, eletrocardiograma; **EV's**, extrassístoles ventriculares; **H**, Holter; **IC**, insuficiência cardíaca; **ICC**, insuficiência cardíaca congestiva; **mod**, moderados; **MS**, morte súbita; **NR**, não referido; **P**, pacientes; **RX**, raios x de tórax; **TVNS**, taquicardia ventricular não-sustentada. *No momento da inclusão dos pacientes no estudo. †causas não especificadas. ‡causas extracardíacas. §complicação de megacólon. ‖1 Stokes-Adams, 7 choques e 14 embolias pulmonares; ¶complicação de megacólon. #causas desconhecidas. **tromboembolismo pulmonar. ††1 tromboembolismo mesentérico e 1 pró-arritmia. ‡‡tromboembolismo. §§outras causas CV.

‖ Aproximadamente 11% dos óbitos ocorreram em pacientes com ECG normal e 89% naqueles com ECG anormal.

¶¶ 20% dos óbitos ocorreram nos pacientes sem cardiopatia aparente e 80% naqueles com cardiopatia.

22% dos óbitos ocorreram nos pacientes com ECG anormal, sem ICC e 78% naqueles com ECG anormal e ICC severa.

*** Todos os óbitos ocorreram nos pacientes com ECG anormal; 93% dos óbitos nos pacientes com AC aumentada e 86% naqueles em CF II.

††† 15% dos óbitos ocorreram nos pacientes assintomáticos, 25% nos pacientes com sintomas leves/moderados e 60% naqueles com ICC severa.

‡‡‡ Aproximadamente 2/3 dos óbitos ocorreram nos pacientes em classe funcional I/II e 1/3 naqueles em CF III/IV.

Quadro II - Preditores de morte súbita na cardiopatia chagásica crônica. TE teste regométrico; DNS disfunção do nó sinusial; BAVs bloqueios atrioventriculares; FV fibrilação ventricular; EVP estimulação ventricular programada

Preditores Maiores:

- Disfunção ventricular
- Taquicardia ventricular não sustentada* ao Holter/TE
- Taquiarritmias ventriculares sustentadas
- Recuperados de parada cardiorrespiratória
- Bradiarritmias severas (DNS, BAVs avançados)
- Síncope

Preditores Menores:

- Potenciais tardios (ECGAR)
- Pré-síncope

Variáveis sem valor prognóstico:

- Extra-sistolia ventricular isolada (Holter)
- BCRD isolado
- Indução de TV polimórfiva ou de FV à EVP

Variáveis a serem investigadas:

- Variabilidade da FC
- Dispersão do QT

*acompanhada de disfunção ventricular