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ORIGINAL RESEARCH ARTICLE

The use of the CALL Risk Score for predicting mortality in Brazilian heart failure patients

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Abstract

Aims This study aimed to develop and validate a simple method for predicting long-term all-cause mortality in ambulatory patients with chronic heart failure (CHF) residing in an area where Chagas disease is endemic, which will be important not only for patients living in Latin America but also to those living in developed non-endemic countries.

Methods and results A total of 677 patients with a wide spectrum of aetiologies for left ventricular systolic dysfunction and receiving optimized evidence-based treatment for CHF were prospectively followed for approximately 11 years. We established a risk score using Cox proportional hazard regression models. After multivariable analysis, four variables were independently associated with mortality and included in the CALL Risk Score: Chagas cardiomyopathy aetiology alone [hazard ratio, 3.36; 95% confidence interval (CI), 2.61–4.33; $P < 0.001$], age ≥60 years (hazard ratio, 1.36; 95% CI, 1.06–1.74; $P = 0.016$), left anterior fascicular block (hazard ratio, 1.64; 95% CI, 1.27–2.11; $P < 0.001$), and left ventricular ejection fraction <40% (hazard ratio, 1.73; 95% CI, 1.30–2.28; $P < 0.001$). The internal validation considered the bootstrapping, a resampling technique recommended for prediction model development. Hence, we established a scoring system attributing weights according to each risk factor: 3 points for Chagas cardiomyopathy alone, 1 point for age ≥60 years, and 2 points each for left anterior fascicular block and left ventricular ejection fraction <40%. Three risk groups were identified: low risk (score ≤2 points), intermediate risk (score of 3 to 5 points), and high risk (score ≥6 points). High-risk patients had more than two-fold increase in mortality (26.9 events/100 patient-years) compared with intermediate-risk patients (10.1 events/100 patient-years) and almost seven-fold increase compared with low-risk patients (4.3 events/100 patient-years). The CALL Risk Score data sets from the development and internal validation cohorts both displayed suitable discrimination c-index of 0.689 (95% CI, 0.688–0.690; $P < 0.001$) and 0.687 (95% CI, 0.686–0.688; $P < 0.001$), respectively, and satisfactory calibration [Greenwood–Nam–D'Agostino test (8) = 7.867; $P = 0.447$] and [Greenwood–Nam–D'Agostino test (8) = 10.08; $P = 0.273$], respectively.

Conclusions The CALL Risk Score represents a simple and validated method with a limited number of non-invasive variables that successfully predicts long-term all-cause mortality in a real-world cohort of patients with CHF. Patients with CHF stratified as high risk according to the CALL Risk Score should be monitored and aggressively managed, including those with CHF secondary to Chagas disease.

Keywords Chronic heart failure; Chagas cardiomyopathy; Prognosis; Mortality

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Introduction

Chronic heart failure (CHF) is a leading cause of morbidity and mortality worldwide. It is a major public health problem with an increasing incidence and prevalence of the disease.[1–3] The likelihood of survival may vary significantly among patients with different aetiologies and subsets of patients with CHF. In this context, CHF secondary to Chagas cardiomyopathy has a poorer prognosis than other aetiologies,[4–6] mainly in Latin America countries where the disease is endemic.[3,7,8]

The prognostics indexes that are currently employed in clinical practice have some limitations. They rely on either peak oxygen consumption or invasive measurements, are designed to assess patients with severe CHF in need of a heart transplant,[9–11] and were validated during hospitalization for acute decompensated heart failure.[12–14] Furthermore, most of these models have not included a substantial proportion of individuals receiving contemporary evidence-based treatments. Finally, a few models include patients with Chagas cardiomyopathy, the leading cause of CHF aetiology in areas where the disease is endemic.

The purpose of this investigation was to develop and validate a multivariate risk model for predicting long-term all-cause mortality in an independent, outpatient population with CHF residing in an endemic area for Chagas disease, who were not enrolled in a clinical trial, using variables that are easily obtainable (demographic, standard laboratory tests, 12-lead resting electrocardiogram, and 2D echocardiography data) in clinical practice.

Materials and methods

Study population

At presentation, the history of all patients was recorded, and then the patients underwent a physical examination, standard laboratory tests, 12-lead electrocardiogram, and 2D transthoracic echocardiogram. Chagas disease was investigated in all patients with suggestive epidemiology and confirmed by two positive serological tests for Chagas (haemagglutination and indirect immunofluorescence staining) according to the recommendations of the World Health Organization.[15] Chagas-hypertensive and Chagas-ischaemic aetiologies were determined for individuals that had Chagas disease and, concomitantly, systemic arterial hypertension (diagnosis based on guidelines at that time) and coronary artery disease (confirmed by coronary angiography), respectively; in other words, they had both potential aetiologies for CHF. Patients with isolated aetiologies (Chagas, hypertensive, or ischaemic) were evaluated apart from previous groups. Individuals with a clinical diagnosis of CHF and a left ventricular ejection fraction (LVEF) $<$55% on 2D echocardiography were screened for this study. Patients with heart valve disease or concomitant conditions that potentially cause heart disease were excluded.

We used the entire data set for the development cohort, considering all eligible patients (convenience sample) routinely followed from 02 January 2000 to 30 December 2010 at Cardiomyopathy Outpatient Service, Hospital de Base, São José do Rio Preto Medical School, a public referral centre for severe CHF management in the northwest of São Paulo, Brazil. The information about the medical therapies used to treat CHF was retrieved from a prospectively collected database of patients. All patients received evidence-based treatment for CHF, according to the international guidelines at the time. Thus, treatment with angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), mineralocorticoid receptor antagonist, and beta-blockers at targeted or maximal tolerated doses was considered for all patients. Patients usually visited the outpatient service every 4 months, and a senior heart failure expert (R. B. B.) monitored the treatment administered. Patients were followed until the study closed; they were also censored at heart transplantation or death.

For the internal validation, we used the bootstrapping, a resampling technique recommended for prediction model development. The methodology of this investigation is consistent with the TRIPOD[16] checklist for prediction model development and validation.

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/)[17] and approved by the local Human Research Ethics Committee of São José do Rio Preto Medical School (CAAE - 02716112.6.0000.5415). The need for individual informed consent was waived, as this study was a retrospective analysis of prospectively collected data used for routine care, and a breach of privacy or anonymity did not occur.

Data collection

The demographic data, New York Heart Association (NYHA) functional class, heart rate, systemic arterial pressure, medical history, results from standard laboratory tests, 12-lead resting electrocardiogram, and information from cardiac electronic implantable devices were retrieved from the patients' medical records. The available definitions and data collection approaches were constant throughout the study.

Outcome

The primary outcome was the long-term [median (25th to 75th) of 1303 days (631–2116 days)] all-cause mortality based on a review of hospital records or confirmed by telephone contacts with patients' relatives. No loss to follow-up was observed in our investigation.

Statistical analysis

Development cohort, internal validation, and creation of risk groups

Descriptive statistics of the sample were calculated using absolute numbers and percentages for categorical data and

means and standard deviations for continuous variables with a normal distribution. The *t*-test (or the non-parametric Wilcoxon test when data were not normally distributed) was used to compare continuous variables, and the chi-square test (or Fisher's exact test, when expected frequencies were lower than 5) was used to compare categorical variables. We did not use any method for data imputation.

Cox proportional hazard regression models were used for univariable analysis to identify risk factors related to all-cause mortality in our cohort. Variables that were significant at a level of 0.05 in the univariable analysis were considered potentially independent variables for the multivariable analysis. Multivariable Cox proportional hazard regression model was developed for all-cause mortality in the global cohort, prospectively followed for approximately 11 years. Variables significant at the 0.05 level in the multivariable analyses using a stepwise method were identified as predictive factors. Further, as an internal validation of the model, a total of 10 000 bootstrap samples with replacement were drawn from the original sample. Once the final multivariable model was constructed and validated, a severity risk score was developed by assigning a weight to each risk factor category based on the β parameter from the multivariable Cox proportional hazards regression. The score was calculated as a sum of the weights of each of the risk factors, with a higher score corresponding to a higher likelihood of death within almost 11 years. Three severity risk groups (low risk, intermediate risk, and high risk) were created, based on the score, according to optimal cut-off points.[18] The predictive performance of the model was assessed by calculating the concordance (c-index), as shown by Steyerberg.[19] In order to assess the ability of the models to match predicted and observed mortality rates, the Greenwood–Nam–D'Agostino method was used. Finally, using the Kaplan–Meier estimator, survival predictions for each risk group were evaluated, and differences between risk groups were assessed by the log-rank test. Further, Kaplan–Meier curves were plotted for each risk group according to the CALL Risk Score.

The statistical analysis was performed by experts in statistics who were blinded to the outcomes, aiming to minimize selection and data interpretation bias, using a suitable software. All tests were two-sided with a *P*-value considered significant at <0.05 and were performed using R software, version 3.6.0 (http://www.r-project.org/).

Results

Development cohort

The CALL study included 677 ambulatory patients (67.7% male) with CHF, aged 48–67 years (mean 57 ± 14 years). Most patients (66.5%) presented with NYHA functional classes I or II at study entry. A Chagas aetiology of CHF was present in 34.6% of individuals, followed by hypertensive (19.2%), Chagas-hypertensive (15.7%), idiopathic dilated cardiomyopathy (14.8%), ischaemic (11.7%), and Chagas-ischaemic (4.0%) aetiology. The mean LVEF was 35.1 ± 10.5% (range 27.9–43.2%), and most patients (64.7%) presented an LVEF $<40\%$. Approximately 29.2% of patients had atrial fibrillation, 31.9% had a left anterior fascicular block (LAFB), 34.7% had a pacemaker, and 8.4% had an implantable cardioverter defibrillator (*Table 1*). Among the laboratory tests, anaemia (haemoglobin level <12 g/dL for women and <13 g/dL for men) and a

Table 1 Baseline characteristics of the development cohort

Variables	Development cohort ($N = 677$) Median (25th to 75th) or *N* (%)
Demographic and clinical characteristics	
Age (years)	58 (48–67)
Age ≥60 (years)	306 (45.2)
Male	458 (67.7)
Chagas cardiomyopathy alone	234 (34.6)
Chagas-ischaemic association	28 (4.1)
Chagas-hypertensive association	106 (15.7)
Hypertensive cardiomyopathy alone	130 (19.2)
Idiopathic dilated cardiomyopathy	100 (14.8)
Ischaemic cardiomyopathy alone	79 (11.7)
NYHA functional class I	259 (38.3)
NYHA functional class II	191 (28.2)
NYHA functional class III	139 (20.5)
NYHA functional class IV	88 (13.0)
Heart rate (beats/min)	71 (64–80)
Systolic blood pressure (mmHg)	110 (100–130)
Diastolic blood pressure (mmHg)	75 (70–80)
Diabetes mellitus	118 (17.4)
Implantable cardioverter defibrillator	57 (8.4)
Pacemaker	235 (34.7)
Laboratory variables	
Haemoglobin (g/dL)	13.3 (12.2–14.2)
Sodium (mg/dL)	141 (138–144)
Potassium (mg/dL)	4.4 (4.1–4.8)
Creatinine (mg/dL)	1.2 (1.0–1.4)
CKD-EPI (mL/min/1.73 m^2)	63.0 (50.0–78.0)
CKD-EPI <60 mL/min/1.73 m^2	307 (45.3)
Electrocardiographic variables	
Atrial fibrillation	198 (29.2)
Left bundle branch block	231 (34.1)
Right bundle branch block	178 (26.3)
Left anterior fascicular block	216 (31.9)
Low voltage of QRS	58 (8.6)
Ventricular premature contraction	339 (50.1)
Echocardiographic variables	
Left ventricular end-diastolic diameter (mm)	64 (59–71)
Left ventricular systolic diameter (mm)	54 (47–61)
Right ventricular diameter (mm)	23 (19–28)
Wall motion abnormalities	213 (31.5)
Left ventricular ejection fraction (%)	35.3 (27.9–42.8)
Left ventricular ejection fraction $<40\%$	438 (64.7)

CKD-EPI, estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology Collaboration; *N*, number of individuals; NYHA, New York Heart Association.

glomerular filtration rate <60 mL/min/1.73 m^2 (according to Chronic Kidney Disease Epidemiology Collaboration) were observed in 25.7% and 45.3% of patients, respectively.

This cohort received maximal tolerated daily doses of medications, according to the recommendations of the guideline during long-term follow-up, with a mean daily dose (mg/day) of enalapril (17.3 ± 8.5), captopril (97.0 ± 44.3), ramipril (8.4 ± 2.6), losartan (51.5 ± 24.4), carvedilol (33.2 ± 19.7), metoprolol succinate (139.0 ± 69.9), spironolactone (29.3 ± 19.0), furosemide (84.4 ± 58.4), amiodarone (223.0 ± 88.8), and digoxin (0.186 ± 0.067). The mean daily dose of losartan was relatively low because the study HEAAL, which showed a beneficial effect on morbidity and mortality for patients taking 150 mg of losartan daily, was published at approximately the close of the study.[20] The rates for beta-blockers, ACEIs or ARBs, and spironolactone usage were 71.0%, 96.5%, and 68.5%, respectively.

Patients in the development cohort for the CALL study presented with 73.0%, 23.8%, and 6.9% rates of hospitalization due to acute decompensated heart failure, cardiogenic shock (systolic blood pressure ≤90 mmHg associated to clinical signs of peripheral vasoconstriction, as oliguria, cyanosis, and diaphoresis), and the need for a heart transplant, respectively. During follow-up (1459 ± 1031 days), 253 (37.4%) patients with CHF died.

In our investigation, factors that were significant at $P < 0.05$ in the univariate analysis using Cox regression (Chagas cardiomyopathy alone, age ≥60 years, LAFB, LVEF <40%, systolic blood pressure, diastolic blood pressure, and right bundle branch block) were included in the model, using a stepwise backward elimination method. The final multivariate model, for which c-index was 0.689 [95% confidence interval (CI), 0.688–0.690; $P < 0.001$] and yielded good calibration [Greenwood–Nam–D'Agostino test (8) = 7.867; $P = 0.447$] in the development cohort, identified only four independent predictors of long-term all-cause mortality (*Table 2*). These factors are a Chagas cardiomyopathy aetiology alone (hazard ratio, 3.36; 95% CI, 2.61–4.33; $P < 0.001$), age ≥60 years (hazard ratio, 1.36; 95% CI, 1.06–1.74; $P = 0.016$), LAFB (hazard ratio, 1.64; 95% CI, 1.27–2.11; $P < 0.001$), and LVEF <40% (hazard ratio, 1.73; 95% CI, 1.30–2.28; $P < 0.001$).

An important strength of our investigation was that the CALL Risk Score exhibited consistent performance in predicting all-cause mortality over time, as evidenced by c-index and Greenwood-Nam-D'Agostino tests, confirming its good predictive and calibration properties at other time points of follow-up (*Table 3*).

Internal validation

The analysis of the validation considered the bootstrapping, a resampling technique recommended to evaluate the performance and optimism of the developed model. In this context, using a suitable statistical software, a total of 10 000 bootstrap samples with replacement were drawn from the original sample. This procedure was replicated 10 000 times, and, as the size of each sample is chosen randomly, we obtained an average size of 429 individuals for the validation cohort. After this assessment, we confirmed that the model exhibited similar performance in terms of calibration [Greenwood–Nam–D'Agostino test (8) = 10.08; $P = 0.273$] and discrimination characteristics [c-index of 0.687 (95% CI, 0.686–0.688; $P < 0.001$)].

The CALL Risk Score predicted long-term all-cause mortality in patients with CHF and stratified the risk into three categories (low risk, intermediate risk, or high risk). Two hundred fifty-nine patients (38.3%) were included in the low-risk subgroup, showing an average long-term mortality rate of 21.2%. The intermediate-risk subgroup included 294 individuals (43.4%) with a mortality rate of approximately 37.4%, and the high-risk subgroup included 124 patients (18.3%) and showed a long-term all-cause mortality rate of 71.0%. High-risk patients had more than two-fold increase in mortality (26.9 events/100 patient-years) compared with intermediate-risk patients (10.1 events/100 patient-years) and almost seven-fold increase compared with low-risk patients (4.3 events/100 patient-years). *Table 4* shows the differences in survival probabilities between risk groups according

Table 2 Univariate and multivariate analysis of prognostic factors associated with all-cause mortality by Cox regression analysis in the development cohort (*N* = 677 individuals)

Parameters	*N* (%) or median (25th to 75th)	Univariate			Multivariate		
		HR	95% CI	*P*-value	HR	95% CI	*P*-value
Chagas cardiomyopathy alone	234 (34.6)	3.63	2.83–4.67	<0.001	3.36	2.61–4.32	<0.001
Age ≥60 years	306 (45.2)	1.29	1.01–1.65	0.045	1.36	1.06–1.74	0.016
Left anterior fascicular block	216 (31.9)	2.01	1.57–2.59	<0.001	1.64	1.27–2.11	<0.001
Left ventricular ejection fraction <40%	438 (64.7)	1.86	1.41–2.45	<0.001	1.72	1.30–2.28	<0.001
Systolic blood pressure (mmHg)	110 (100–130)	0.98	0.97–0.99	<0.001	0.99	0.98–1.00	0.068
Diastolic blood pressure (mmHg)	75 (70–80)	0.97	0.96–0.98	<0.001	1.00	0.98–1.01	0.545
Right bundle branch block	178 (26.3)	1.61	1.41–2.45	<0.001	0.89	0.65–1.22	0.480

CI, confidence interval; HR, hazard ratio; *N*, number of individuals.

Table 3 Predictive and calibration properties of the CALL Risk Score over time

	Discrimination (concordance index)			Calibration (Greenwood-Nam-D'Agostino test)		
Follow-up	c-index	*95* (%) CI	*P*-value	Degrees of freedom	Chi-square	P-value
1 year	0.759	0.757–0.761	P < 0.001	7	3.710	0.813
2 year	0.745	0.744–0.746	P < 0.001	8	0.829	0.999
3 year	0.737	0.736–0.738	P < 0.001	8	2.790	0.947
5 year	0.708	0.707–0.709	P < 0.001	8	6.740	0.565
Long-term	0.689	0.688–0.690	P < 0.001	8	7.867	0.447

CI=confidence interval.

Table 4 Differences in survival probabilities among risk groups according to the CALL Risk Score during the complete follow-up

	Development cohort		
	Total *N* (%)	Survival probability	*P*-value
Risk groups			
Low risk (≤2 points)	259 (38.3)	0.71 (0.63–0.79)	
Intermediate risk (3 to 5 points)	294 (43.4)	0.44 (0.36–0.54)	<0.001
High risk (≥6 points)	124 (18.3)	0.08 (0.03–0.22)	

N, number of individuals.

to the CALL Risk Score during the complete follow-up. Additionally, mortality rates according to the risk groups over time are shown in Supporting Information, *Table S1*.

The simplest method to estimate the risk score for long-term all-cause mortality in ambulatory patients with CHF consists of adding 3 points for Chagas cardiomyopathy aetiology alone, 1 point for age ≥60 years, and 2 points each for LAFB and LVEF <40% (*Table 5*).

The Kaplan–Meier survival curves for complete follow-up of patients with CHF according to risk stratifications (low risk, intermediate risk, and high risk) provided by the CALL Risk Score are shown in *Figure 1*. Additionally, the corresponding cumulative survival graphs for (A) 12 months, (B) 24 months, (C) 36 months, and (D) 60 months of follow-up are shown in Supporting Information, *Figure S1*.

Discussion

In the present study, we enrolled a large population of ambulatory patients with CHF presenting with a wide spectrum of aetiologies and left ventricular systolic dysfunction. Importantly, half of the population was composed of patients with Chagas cardiomyopathy, which reflects the daily clinical practice in an area where Chagas disease is endemic. One novel finding of this investigation is that we developed and validated the CALL Risk Score, a simple risk model based on commonly obtained and non-invasive variables for predicting long-term all-cause mortality in patients with CHF.

Table 5 Long-term all-cause mortality risk expressed as a point-based scoring system with the acronym CALL Risk Score

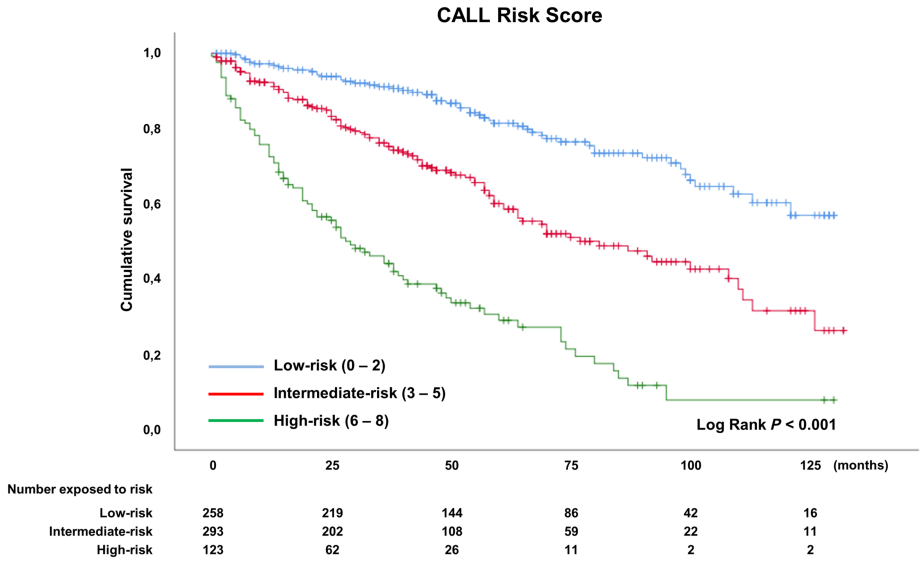
Risk factor	Score
Chagas cardiomyopathy alone	3
Age ≥60 years	1
Left anterior fascicular block	2
Left ventricular ejection fraction <40%	2

Another interesting finding was the presence of systemic arterial hypertension as the second cause of systolic CHF and the association of Chagas disease with systemic arterial hypertension as the third cause of systolic CHF in our cohort. These features characterize an epidemiological profile that is completely different from the profiles observed in areas where Chagas disease is not endemic.

The CALL Risk Score accurately discriminated three groups of risks for patients with CHF and represents an interesting tool for the early, reliable, and easily assessment of prognosis in ambulatory clinical practice. Therefore, our study is of interest not only to physicians working in areas where Chagas cardiomyopathy is endemic but also to physicians working in North America and Europe because immigrants with this condition from endemic areas are frequently found.[8,21] In this regard, it should be pointed out that about 5% Chagas disease patients are found to have CHF and about 10% of patients with dilated cardiomyopathy have Chagas disease as aetiology of such a condition in non-endemic countries.[22,23]

Importantly, our internal validation considered the bootstrapping method, a resampling technique recommended as a prerequisite for prediction model, aiming to improve on what the regression model can offer and also to prevent overfittings.[16,24] Moreover, our investigation included patients with the full range of aetiologies, such as Chagas cardiomyopathy, hypertensive, idiopathic, ischaemic heart disease, and the association of Chagas disease with hypertensive or ischaemic heart disease. The heart failure symptoms ranged from NYHA functional classes I to IV, and the LVEF at the study

FIGURE 1 Long-term survival probabilities for the development cohort of patients with chronic heart failure according to risk stratifications (low risk, intermediate risk, and high risk) provided by the CALL Risk Score.



entry ranged from 27.9% to 42.8%. In this context, our validation valued a significant number of patients at intermediate risk and high risk in whom the risk prediction might be more challenging,[25] representing the population in whom validation results may be most widely applicable.

Our prediction model yielded a c-index of 0.689 and appropriate value for the Greenwood–Nam–D'Agostino test ($P = 0.447$) in the development cohort, constructed by Cox regression, as recommended for long-term prognostic assessments of outcomes.[16] Notably, the calibration (the agreement between observed and predicted risks obtained from the Greenwood–Nam–D'Agostino test) is also very important in prognostic settings, because the main purpose is to predict the future risk of the target population,[26] as observed for the CALL Risk Score. On the other hand, the discrimination (which is useful for separating people with a disease from those without it, e.g. using c-indexes) is an important issue for diagnostic and prognostic settings.[27]

Based on the CALL Risk Score, Chagas cardiomyopathy alone, age ≥60 years, LAFB, and LVEF <40% had independent predictive power. Our risk model highlighted Chagas cardiomyopathy alone and the presence of LAFB in a 12-lead resting electrocardiogram, which are frequently observed in patients with this condition, as independent predictors of all-cause mortality, suggesting the negative correlation between Chagas aetiology and the prognosis of patients with CHF.[4,6,28,29]

In our study, reduced LVEF was an independent predictor of outcome, similarly to the MUSIC Risk Score[30] and the Seattle Heart Failure Model.[25] However, despite that, the aetiology of Chagas disease was itself a strong predictor of all-cause mortality in patients with CHF.[4–6] In this context, our results support the hypothesis that notwithstanding the younger age, severity of systolic dysfunction, and comprehensive use of contemporary evidence-based treatments for CHF, patients with Chagas cardiomyopathy alone continue to have a worse prognosis, overlapping other aetiologies.[31] This finding might explain why other aetiologies had reduced predictive powers for long-term global mortality and were not featured in the CALL Risk Score.

Furthermore, our investigation did not identify the NYHA functional class as risk predictor in patients with CHF. Additionally, the NYHA functional class has some limitations,[32] and patients' self-assessed symptoms and their classifications are occasionally inconsistent.[33] The NYHA functional class is difficult to establish among patients with limited physical activity, co-morbidities, or an advanced age, circumstances that are very common among patients with CHF. Therefore, this parameter was excluded from the MUSIC Risk Score.[30] We did not define our finding as a study limitation, because we were able to develop a model that was exclusively based on objective variables.

Renal dysfunction was not an independent predictor of all-cause mortality in our series, similar to the HFSS study.[9] Higher rates of ACEIs/ARBs usage in our study may have influenced our results, because blockade of the renin–angiotensin–aldosterone system protects both the cardiovascular and renal systems.[34] This fact justifies the potential discrepancy with previous models[9,35–37] that did not include a substantial number of individuals with optimized medical therapy according to current guidelines,[1–3] and/or hospitalized patients,[12–14] and have been developed using participants from clinical trials,[25,38] limiting their use in daily clinical practice. In contrast, our study was performed in an ambulatory population that was treated according to

international guidelines at the time. This approach at least partially accounts for the disparity among data from our real-world cohort and previous studies.

Although previous investigations have shown a significant effect of Chagas disease on the global mortality of patients with CHF,[4–6,39] the effect of the aetiology of Chagas cardiomyopathy on all-cause mortality has never been previously reported in a model similar to the one used in the present study, which employed proper calibration and validation. Therefore, despite the limited scientific evidence available regarding the treatment of heart failure secondary to Chagas disease, based on the findings from our study, we can suggest that patients with Chagas cardiomyopathy presenting with CHF must also be closely monitored and aggressively treated considering the overlap of two conditions for poorer prognosis, heart failure by itself and Chagas disease.

Early prognostication of poor outcomes in patients with CHF remains an unsolved challenge. The ability to predict an individual's risk in daily clinical practice requires the addition of the points for the predictors observed in a particular patient to calculate the long-term mortality risk score. Moreover, adequate stratification will assist clinicians with making decisions and may permit a better allocation of resources. Indeed, this possibility may lead to a faster adjustment of the treatments and the ability to predict the management of these most severe patients in specialized CHF units, whereas most low-risk patients with CHF would require less intensive follow-up. Then the CALL Risk Score represents a simple tool for daily clinical practice in areas where Chagas cardiomyopathy is endemic and in non-endemic countries, aiming to improve the standardization of care and decision-making.

Previous studies have developed models to predict outcome in patients with chronic Chagas disease,[40,41] and the HFSS has been applied to patients specifically with Chagas disease heart failure as well.[42] In this context, it should be emphasized that our study does not deal with prognostication in a cohort of patients with chronic Chagas disease, but with a cohort of patients with CHF, including those with chronic Chagas disease. Therefore, the models mentioned earlier do not apply to our cohort.

Study limitations

Our investigation has some limitations. The CALL Risk Score was derived from a cohort of patients with CHF who were prospectively followed in a single centre and may not be generalizable to a wider population. Its benefit in patients with diastolic heart failure is uncertain, because this score was only derived and validated in patients with systolic CHF. Given the current economic restraints in Brazil to provide implantable cardioverter defibrillator treatment to all patients in need, only severely ill patients may have received implants for secondary prevention. In this context, the possible bias in patient selection should be considered. On the other hand, among the strengths of the study, the model was developed based on a large ambulatory cohort with a wide spectrum of CHF aetiologies and left ventricular systolic dysfunction, mainly patients with Chagas cardiomyopathy, as observed in daily clinical practice in areas where Chagas cardiomyopathy is endemic. Furthermore, the model showed good and consistent performance for predicting mortality over time in patients with CHF and stratified the risk into three categories (low risk, intermediate risk, or high risk). In addition, the CALL Risk Score was validated using the bootstrapping technique, a suitable and recommended method for prediction model development, including a real-world population. Finally, we report a typical cohort of patients with CHF who were treated in an area where Chagas cardiomyopathy is endemic, which may help physicians treating this condition in areas where Chagas cardiomyopathy is not endemic. Further studies are needed to externally validate the CALL Risk Score to confirm its value as a generalizable clinical prediction tool for different cohorts of patients with CHF.

Conclusions

In summary, the CALL Risk Score predicts the survival of ambulatory patients with CHF using easily obtained non-invasive variables and confirms the negative effect of Chagas aetiology on the CHF prognosis. The model provides an accurate identification of a subgroup of high-risk patients who should be closely managed.

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Conflict of interest

None declared.

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Data availability

The data sets generated and/or analysed during the current study are not publicly available due to the use of potentially identifying postal codes in the deprivation analysis, as

approved by the local Human Research Ethics Committee, but they are available upon reasonable request.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Mortality rates according to the risk groups over time.

Figure S1. *The cumulative survival graphs of patients with CHF according to risk stratifications (low-, intermediate-, and high-risk) provided by the CALL Risk Score at (A) 12-months, (B) 24-months, (C) 36-months, and (D) 60-months.*

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