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The prognostic value of health-related quality of life in patients with Chagas heart disease

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Abstract

Purpose To verify the prognostic value of health-related quality of life (HRQoL) and the differences in HRQoL and clinical variables between groups of Chagas heart disease (CHD) patients with and without cardiovascular adverse events.

Methods Seventy-five CHD patients were evaluated by echocardiography, maximal exercise testing, and Short-form of Health Survey (SF-36) Questionnaire. Patients were followed during 6 years. In the statistical analysis, uni- and multivariate Cox regression were performed to verify the accuracy of the HRQoL in predicting cardiovascular events.

Results After the follow-up period (41 ± 12 months), 20 patients (27%) had adverse events. Those with poor outcome had lower left ventricular ejection fraction (LVEF) ($p = 0.002$), higher left ventricular end-diastolic diameter (LVDd) ($p = 0.019$), and worse scores in general health perceptions ($p = 0.047$), social role functioning ($p = 0.026$), and mental component summary ($p = 0.043$) of SF-36. Patients with lower LVEF ($p = 0.003$), higher LVDd ($p = 0.022$), worse HRQoL in the general heath perceptions domain ($p = 0.022$), and mental component summary ($p = 0.031$) were associated with worse prognosis. In the multivariate Cox regression, LVEF (HR 0.94, 95% CI from 0.90 to 0.98, $p = 0.007$) and mental component summary (HR 0.98, 95% CI from 0.94 to 1.00, $p = 0.047$) remained as independent predictors of adverse events in CHD patients.

Conclusion The assessment of HRQoL, especially the mental component, should be taken into account to provide an accurate prognosis in addition to other well-established predictors of poor outcomes in CHD patients.

Keywords Chagas disease · Chagas heart disease · Health-related quality of life · Prognosis

Introduction

Chagas disease is a neglected parasitic infection transmitted primarily through parasite-laden secretions from hematophagous triatomine insects [1, 2]. The disease was firstly described in 1909 by the physician Carlos Chagas [3]. More than a century after its discovery, Chagas disease remains a major public health problem in Brazil and Latin America [4, 5] and emerges in non-endemic countries [6–8] due to globalization and immigration.

Among the clinical forms, Chagas heart disease (CHD), especially Chagas cardiomyopathy, is the most severe, with high potential for morbidity and mortality [9]. During the progression of the disease, patients may evolve with cardiac dilation and global ventricular dysfunction, heart failure, complex arrhythmias, thromboembolism, and sudden cardiac death [4, 9, 10], which leads to a worsening of the health-related quality of life (HRQoL).

In addition to severe pathophysiological damage, the disease can be stigmatizing, affects individuals at their most productive age, and leads to a major medical-welfare and labor impact [11]. In patients with Chagas disease, the presence of depressive symptoms is a common finding [12] and it was expected that patients with CHD should have worse HRQoL when compared to the general population.

Previous studies [11, 13] showed that the worse HRQoL of patients with Chagas disease is related to sex (worse in

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female patients), cardiovascular complaints, poor functional classification, and higher percentage of patients with artificial pacemakers. Furthermore, a recent review [14] summarized that HRQoL correlates with variables of clinical significance in patients with CHD, such as functional capacity and New York Heart Association (NYHA) functional class [15].

Despite the important clinical meaning of HRQoL in patients with Chagas disease, its prognostic value remains unknown, although it has already been demonstrated in patients with heart failure [16–19]. Therefore, the present study was addressed to verify the differences in HRQoL, and clinical variables in CHD patients with and without adverse cardiovascular event after 6 years of follow-up and to determine the prognostic value of HRQoL in the CHD patients.

Patients and methods

A prospective study with patients with CHD was followed up at scheduled clinic visits from an Outpatient Reference Center for Chagas Disease. The research was approved by the Institutional Ethics Committee and all patients gave their written informed consent before participating in study.

At least two positive serologic tests for antibodies against *Trypanosoma cruzi* were required for the diagnosis of Chagas disease. To be included in the study, patients should also have clinical, electrocardiographic, or echocardiographic findings compatible with CHD [5]. Exclusion criteria were the presence of systemic or heart disease by any other causes or comorbidities and the inability to perform exercise testing.

At the baseline, patients underwent echocardiography, symptom-limited exercise testing, and a health-related quality of life questionnaire.

Echocardiography was performed according to recommendations of the American Society of Echocardiography [20]. Left ventricular ejection fraction (LVEF) was obtained by modified Simpson's rule. Early diastolic velocity (e′) at the medial border of the mitral annulus was obtained and the ratio between peak mitral E and e′ (E/e′) was calculated.

The symptom-limited exercise test was performed on a treadmill (Digistress Pulsar, Micromed, Brazil) using a standard Bruce protocol [21]. The maximal exercise capacity was defined by peak oxygen uptake (VO_{2peak}), expressed in mL kg min, and calculated indirectly by the formula $VO_{2peak} = 2.33$ (time in min) + 9.48 [22]. The ratio between heart rate achieved during the test and maximum heart rate (HRmax = 220 minus the patient age) were used as %HR achieved. The heart rate recovery was defined as the difference between the peak heart rate achieved during the test and the heart rate after 1 min of passive recovery [23].

HRQoL was assessed by the Short-form of Health Survey (SF-36), the most used questionnaire to assess the quality of life in patients with Chagas disease [14]. The questionnaire was previously translated for the Brazilian Portuguese language [24].

The SF-36 contains 36 items in eight domains (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health). The main result is the score obtained in each domain, from 0 to 100 (worst and best, respectively). Subsequently, all domains can be summarized into two main components: the physical component summary and the mental component summary.

Follow-up period

Follow-up started after the baseline evaluations and was conducted by scripted telephone interviews every 4 months for 6 years, between March 2010 and February 2016. The endpoint was adverse cardiovascular outcome, defined as cardiac death, heart transplantation, or ischemic event.

Statistical analysis

Data were analyzed with SPSS software (Chicago, Illinois). The descriptive analysis was shown as mean and standard deviation, median, and interquartile range or absolute number and percentage.

Differences between groups with and without adverse cardiovascular events were verified by Independent *T* test, Chi square, and Mann–Whitney, with significance levels set at 0.05.

To verify the prognostic role of HRQoL domains in predicting adverse cardiovascular events, the uni- and multivariate Cox regression analyses were used. In the multivariate analysis, the variables that showed a p value < 0.1 in the univariate analysis were included.

Results

Baseline characteristics of the sample

A total of 75 CHD patients were evaluated and the baseline characteristics are shown in Table 1.

HRQoL and adverse cardiovascular outcome

At the final follow-up (41 ± 12 months), 20 patients (27%) had adverse cardiovascular events. Twelve patients died, seven had a cerebrovascular event, and one had undergone cardiac transplantation. Patients with events had lower LVEF ($p = 0.002$), higher LVDd ($p = 0.019$), and worse HRQoL in

Table 1 Baseline characteristics of the sample ($n=75$)

Variables	Value
Age (years)	48.4 ± 8.0
Male sex (%)	46 (61)
NYHA functional class (%)	
I	45 (60)
II	24 (32)
III	6 (8)
Medication, *n* (%)	
Amiodarone	60 (80)
β-blockers	19 (25)
ACE inhibitor	75 (100)
Diuretics	64 (85)
Digitalis	09 (12)
Anticoagulants	13 (17)
Exercise testing	
VO_{2peak} (mL kg min)	27.9 ± 7.5
HRR (bpm)	20.0 (15.0–31.0)
%HR achieved	79.1 ± 12.7
Echocardiography	
LVEF (%)	41.0 (35.0–53.5)
LVDd (mm)	60.2 ± 9.6
E/e′ ratio	10.9 ± 4.3
SF-36 domains	
Physical functioning	75 (60–90)
Physical role functioning	75 (50–100)
Bodily pain	62 (51–100)
General health perceptions	55 (43–72)
Vitality	65 (50–75)
Social role functioning	87 (62–100)
Emotional role functioning	100 (33–100)
Mental health	64 (48–82)
SF-36 summaries	
Physical component summary	47 (41–53)
Mental component summary	44 (31–56)

Data presented as mean and standard deviation (mean ± SD), median (MD), and interquartile range (25–75%) or absolute number (percentage)

NYHA New York Heart Association functional class, *6MWT* 6-minute walk test, *VO_{2peak}* peak oxygen uptake, *HRR* heart rate recovery, %HR achieved percentage of maximum heart rate achieved at exercise test, *LVEF* left ventricular ejection fraction, *LVDd* left ventricular end-diastolic diameter, *E/e′ ratio* ratio of the early diastolic transmitral flow velocity to early diastolic mitral annular velocity, *SF-36* short-form of the health-related quality of life questionnaire

general health perceptions ($p=0.047$) and social role functioning ($p=0.026$) domain compared to event-free group. Differences among variables are shown in Table 2.

The univariate Cox analysis showed that lower LVEF, higher LVDd, lower value in the general heath perceptions domain, and mental component summary were associated with worse prognosis at the end of follow-up (Table 3). In the final multivariate Cox regression model, only LVEF (HR 0.94, 95% CI from 0.90 to 0.98, $p=0.007$) and mental component summary (HR 0.98, 95% CI from 0.94 to 1.00, $p=0.047$) remained as independent predictors of adverse cardiovascular outcome in CHD patients.

Discussion

Despite the clinical importance of HRQoL assessment, no other study addressed the patient's perception of health as a possible prognostic factor in CHD. So, from our point of view, this is the first study that demonstrated the impact of the HRQoL on the prognosis of patients with CHD. The main findings of the present study were that (1) CHD patients with adverse cardiovascular events had lower LVEF, higher LVDd, and worse scores in general health perceptions, social role functioning, and mental component summary of SF-36, and (2) LVEF and mental component summary were independent predictors of poor outcomes in CHD patients.

After the follow-up period, the echocardiographic variables of systolic function and the evaluation of HRQoL in some domains, especially the psychosocial aspects, were worse in the group with cardiovascular event. In fact, lower values of LVEF and increased LVDd represent the systolic dysfunction and left ventricular dilation, well-established markers of organic-functional impairment, and poor prognosis [10, 25, 26]. On the other hand, lower values in the psychosocial factors domains may represent the patient's perception about the presence and progression of cardiovascular symptoms, social isolation, fear of death, and the strong stigma of the disease.

Another important finding was the similarity between the groups with and without adverse events in exercise capacity and in the physical aspects of HRQoL. In our sample, physical function was not a predictor of worse prognosis. However, our sample comprised patients with predominantly preserved functional class, most of them in grade I of NYHA classification (without limitations during ordinary physical activity) [15].

Finally, it was demonstrated that the mental component of HRQoL, along with LVEF, is an independent predictor of prognosis in CHD patients. It is possible that the association between worsening mental component and the presence of left ventricular systolic dysfunction may suggest, even intuitively, the clinical progression of the disease by the patient's perception.

Many studies [16–19, 27, 28] have reported the efficacy of predicting adverse events in patients with heart failure by quality of life questionnaires. However, the comparison between the data was made difficult by the application of many different questionnaires, most of

Table 2 Differences in demographic data, functional status, echocardiographic parameters, and HRQoL between CHD patients with and without adverse cardiovascular events

Variables	Without adverse event ($n=55$)	With adverse event ($n=20$)	p value
Follow-up period (months)	61 ± 7	25 ± 14	**< 0.001**
Age, years	47.9 ± 8.0	49.5 ± 8.2	0.461
Male sex, *n* (%)	35 (64)	11 (55)	0.497
NYHA functional class, *n* (%)			
I	33 (60)	12 (60)	0.826
II	17 (31)	7 (35)	
III	05 (09)	1 (05)	
Echocardiography			
LVEF, %	44.0 (36.0–60.7)	35.0 (27.0–42.0)	**0.002**
LVDd, mm	58.8 ± 10.2	64.5 ± 5.7	**0.019**
E/e′ ratio	10.8 ± 3.9	11.0 ± 5.4	0.893
Exercise testing			
VO_{2peak}, mL kg min	29.5 ± 6.8	27.9 ± 7.7	0.808
%HR achieved	80 ± 13	78 ± 11	0.426
HRR, bpm	20 (15–30)	18 (9–33)	0.428
HRQoL domains			
Physical functioning	75 (60–90)	70 (65–80)	0.339
Physical role functioning	62 (34–83)	60 (50–75)	0.965
Bodily pain	62 (51–100)	62 (52–100)	0.480
General health perceptions	56 (47–77)	47 (37–62)	**0.047**
Vitality	65 (45–75)	63 (50–78)	0.520
Social role functioning	88 (63–100)	63 (50–88)	**0.026**
Emotional role functioning	100 (33–100)	67 (33–100)	0.527
Mental health	64 (47–84)	68 (48–76)	0.588
HRQoL summaries			
Physical component summary	49 (40–53)	46 (43–53)	0.886
Mental component summary	44 (31–58)	33 (24–41)	**0.043**

Data presented as mean and standard deviation (mean ± SD), median (MD), and interquartile range (25–75%) or absolute number (percentage)

p values highlighted in bold are statistically significant ($p < 0.05$)

them specific for heart failure. A systematic review with meta-analysis [29] identified five specific questionnaires used in patients with heart failure. We applied a generic questionnaire in the assessment of HRQoL because not all the patients in the sample had typical signs and symptoms of heart failure, although all of them presented electrocardiographic and echocardiographic findings of CHD.

Despite the limitations, such as the use of a generic questionnaire and the small number of events, we herein demonstrated that simple questionnaires to evaluate patients' perceptions about their health can provide important prognostic information. Furthermore, a patient-derived measure that predicts outcome is potentially useful in the setting of Chagas disease, since many patients often come from resource-limited areas with scarce health services.

Conclusion

The mental component of HRQoL is an independent predictor of poor outcome in patients with CHD. The worsening of the mental component seems to indicate the possibility of disease progression and should be taken into account in establishing the patient's prognosis.

Table 3 Univariate cox analysis for cardiovascular adverse events at follow-up

Variables	Univariate cox analysis		
	HR	95% CI	*p* value
Age	1.02	0.97–1.08	0.395
Sex	1.29	0.53–3.12	0.569
NYHA class	0.92	0.46–1.84	0.823
LVEF	0.94	0.90–0.98	**0.003**
LVDd	1.05	1.01–1.10	**0.022**
E/e′ ratio	1.01	0.91–1.12	0.837
VO_{2peak}	1.01	0.95–1.07	0.834
HRR	0.99	0.95–1.03	0.702
%HR achieved	0.99	0.95–1.02	0.496
Physical functioning	0.99	0.98–1.00	0.566
Physical role functioning	1.00	0.99–1.00	0.954
Bodily pain	1.00	0.99–1.00	0.364
General health perceptions	0.97	0.94–0.99	**0.022**
Vitality	0.99	0.96–1.00	0.371
Social role functioning	0.99	0.98–1.00	0.085
Emotional role functioning	1.00	0.99–1.00	0.740
Mental health	1.00	0.98–1.00	0.652
Physical component	1.00	0.96–1.00	0.876
Mental component	1.00	0.96–1.00	**0.031**

p values highlighted in bold are statistically significant ($p < 0.05$)

HR hazard ratio, *95% CI* 95% confidence interval

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Compliance with ethical standards

Conflict of interest All authors declare no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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