

Quality of life and associated factors in patients with chronic Chagas disease

João C. L. Santos-Filho^{1,a}, Marcelo C. Vieira^{1,2,a}, Isis G. G. Xavier¹, Erica R. Maciel¹, Luiz F. Rodrigues Junior³, Eduardo O. V. Curvo¹, Iane M. Pereira¹, Marcel S. B. Quintana¹, Gilberto M. Sperandio da Silva¹, Henrique H. Veloso¹, Fernanda S. N. S. Mendes¹, Alejandro M. Hasslocher-Moreno¹, Andrea S. Sousa¹, Pedro E. A. A. do Brasil¹, Roberto M. Saraiva¹ and Mauro F. F. Mediano^{1,3}

1 *Evandro Chagas National Institute of Infectious Disease, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil*

2 *Center for Cardiology and Exercise, Aloysio de Castro State Institute of Cardiology, Rio de Janeiro, Brazil*

3 *Physical Therapy Department, National Institute of Cardiology, Rio de Janeiro, Brazil*

Abstract

OBJECTIVES To evaluate the quality of life (QoL) of patients with Chagas disease (CD) and the association between QoL domains and several clinical, socioeconomic and lifestyle characteristics of this population.

METHODS Cross-sectional observational study conducted from March 2014 to March 2017 including a total of 361 outpatients followed at Evandro Chagas National Institute of Infectious Disease, Brazil. QoL was assessed using the Portuguese shorter version of the original WHO Quality of Life questionnaire (WHOQOL-BREF). Information about clinical CD presentation, presence of comorbidities, functional class, previous benznidazole treatment, socioeconomic profile and lifestyle was also obtained.

RESULTS Environment and physical domains presented the worst QoL scores, while the social relationship domain presented the highest score. Multivariate regression analysis demonstrated that variables independently associated with QoL were functional class, sex, clinical presentation of CD, sleep duration, schooling, physical activity level, smoking, income *per capita* and residents by domicile.

CONCLUSIONS The low socioeconomic status and the physical limitations imposed by the disease presented an important impact on the QoL reduction among CD patients, especially on environment and physical domains. Strategies to improve QoL among CD patients should be tailored and consider many different variables to maximise improvements not only of patients' physical but also of their mental health.

keywords Chagas disease, quality of life, socioeconomic profile, lifestyle

Introduction

Chagas disease (CD) is an important infectious disease caused by a protozoan, *Trypanosoma cruzi*, which affects approximately 6 million people worldwide, mainly in Latin America [1]. However, the prevalence of CD has increased in non-endemic regions, such as the United States, Europe and Oceania, primarily due to migratory movements and the possibility of non-vectorial transmission [2].

The chronic phase of CD is characterised by a wide variety of symptoms ranging from the absence of specific clinical alterations despite positive serology (chronic

indeterminate presentation) to the presence of cardiac and/or digestive disturbances (cardiac and digestive presentation respectively). These symptoms, in addition to ageing, poor sociocultural conditions, the stigma of the disease and the urbanisation of recent years may influence the quality of life (QoL) of these individuals [3–5].

WHO defines QoL as “an individual's perception of their position in life in the context of culture and value systems in which they live and in relation to their personal goals, expectations, standards and concerns” [6]. Therefore, the concept of QoL is multidimensional and should include indicators of the patient's perception about the effects of disease and treatment in the physical, emotional and social domains [7]. Moreover, the survival of many more patients suffering from chronic diseases,

^aThese authors contributed equally to this work.

mainly due to improvements in their treatment, has transformed the QoL into a therapeutic target [7, 8]. However, studies examining QoL among patients with Chagas disease and its associated factors are scarce [4, 9].

Thus, the aim of the present study was to evaluate QoL of patients with CD and the association between QoL domains and several clinical, socioeconomic and lifestyle characteristics of this population.

Methods

Study design

This was an observational cross-sectional study conducted from March 2014 to March 2017. The study sample comprised outpatients followed at Evandro Chagas National Institute of Infectious Disease, a national reference centre for treatment and research in infectious and tropical diseases in Brazil. The study comprised two visits: the first one to recruit and include patients and to fill in questionnaires; and the second for clinical evaluation, cardiovascular exams and Chagas disease classification.

Patients included were of both sexes, older than 18 years and had a confirmed diagnosis of CD by two simultaneously positive serological tests (enzyme-linked immunosorbent assay and indirect immunofluorescence). Patients with any of the following conditions were excluded from the study: pregnancy, systemic diseases such as autoimmune disorders, cancer, other infectious diseases such as AIDS, chronic use of anti-inflammatory or corticosteroids, heart diseases with non-Chagas aetiology and severe cognitive impairments that precluded proper completion of the questionnaires.

Ethical considerations

All participants received information about the goals and procedures of the study and voluntarily agreed to participate by means of signing an informed consent form. The study was performed in accordance to the resolution 466/2012 of the Brazilian National Council of Health and was approved by the Institutional Ethics Committee of the Evandro Chagas National Institute of Infectious Disease (CAAE: 58273916.0.000.5262).

Sample size

The estimated sample size was based on the mean values obtained by Ozaki *et al.* [3] for each QoL domain (physical, psychological, social relationships and environment) in patients with CD. Using an estimated accuracy of 5%, assuming an $\alpha = 0.05$ and $\beta = 0.10$, and increasing the

sample size by 20% in order to account for losses and refusals, a total of 300 patients was needed to be included in the study.

Measurements

Information was collected on individual assessment sheets filled out by interviewers previously trained to perform all procedures of the study: completing the questionnaires and taking anthropometric and blood pressure measurements.

Quality of life

QoL assessment was performed using the validated Portuguese shorter version of the original WHO Quality of Life questionnaire (WHOQOL-BREF) [6, 10], a generic instrument composed of a 26-item questionnaire, of which two items relate to general QoL (overall domain) and 24 cover four QoL-related domains (physical, psychological, social relationships and environment). Each domain is assessed by question scores from 1 (none) to 5 (very much) and the mean scores show the individual's perception of each domain, where a higher score indicates a more positive perception.

Clinical presentation of CD

Classification of the clinical presentation of CD (indeterminate, cardiac, digestive and cardiodigestive) and the stage of cardiac presentation were performed by medical evaluation using clinical, electrocardiographic, echocardiographic and digestive examination data following the criteria of the Brazilian Consensus on Chagas Disease [11]. To facilitate data analysis and following a clinical rationale, patients were classified into indeterminate, cardiac without heart failure, cardiac with heart failure, digestive, cardiodigestive without heart failure and cardiodigestive with heart failure groups.

Comorbidities

Information about comorbidities (hypertension, diabetes and dyslipidaemia) was obtained from medical records, anthropometric measures and interviews. Obesity was diagnosed based on body mass index (BMI), calculated as the ratio of weight (kg) to height squared (m^2), above 30 kg/m^2 .

Socioeconomic profile

Data regarding age, sex, schooling, race, residents by domicile and income *per capita* were obtained by means of interviews. Age was categorised in <60 years old and

60 years or older. Schooling was categorised based on the number of years of formal study into <9 years, 9 to 12 years and >12 years. Race was self-reported and classified as white, black, mulatto and others. The income *per capita* was obtained by dividing the familiar income (sum of the income of each resident in the domicile divided by the number of residents) [12].

Lifestyle

Patients were asked about smoking, alcohol consumption, physical activity level and sleep duration. Smoking was as current (regular use of tobacco, regardless of how long), former (past occasional use of tobacco for at least 3 months or daily use for a period of at least 1 month) or non-smoker (currently does not use any tobacco product that emits smoke, even occasionally, even if have experienced) [13]. Alcohol consumption was categorised as none (never ingested alcohol during life), former (did not consume any amount of alcohol in the last 30 days, having ingested in the past) or current (consumed any amount of alcohol in the last 30 days).

Physical activity level was determined using the International Physical Activity Questionnaire-Short Form (IPAQ-SF), previously adapted and validated for use in the Brazilian population [14]. IPAQ is composed of eight questions about the duration and frequency of participation in vigorous, moderate, walking and sedentary activities in the last 7 days, allowing individuals to be classified into three different categories: high, moderate and low physical activity level.

Sleep duration was determined as a continuous variable by direct question and further categorised into three groups (<7 h, 7 to 9 h, and >9 h) as determined in the literature [15].

Functional class

Patients were classified according to the criteria established by the New York Heart Association (NYHA) for functional class evaluation: I – Absence of symptoms (dyspnoea) during daily activities – the limitation for efforts is similar to that expected for normal individuals; II – symptoms triggered by daily activities; III – Symptoms triggered by activities less intense than daily or small efforts; IV – symptoms at rest [16].

Benznidazole treatment

Information about previous use of benznidazole, the most common trypanocidal drug used for the treatment of CD, was obtained from medical records [11].

Data analysis

Descriptive analysis consisted of mean and standard deviation for continuous and percentage and number of observations for categorical variables. The association between variables was determined by univariate linear regression models using each QoL domain (physical, psychological, social relationships, environment and overall QoL) as the dependent variable, and clinical presentation of CD, comorbidities (hypertension, diabetes, dyslipidaemia and obesity), socioeconomic profile information (age, sex, schooling, race, residents by domicile, and income *per capita*), life style information (smoking, alcohol consumption, physical activity level and sleep duration), functional class, and benznidazole treatment as independent variables. A generalised linear model with gamma distribution and log link function that accounts for skewed and heteroscedastic residuals distribution was used to determine the variables independently associated with each QoL domain. All variables with $P < 0.20$ in the univariate model were included in the full model and only those with $P < 0.05$ were maintained in the final model.

The Research Electronic Data Capture (REDCap) web application was used for data management and the data analysis was conducted using Stata 13.0 software. Statistical significance was set at $P < 0.05$ for all analyses.

Results

Of 397 patients included in the study, 28 were excluded and 8 patients did not return for the second visit (Figure 1). The final studied population consisted of 361 individuals (mean age 60.7 ± 10.8 years) whose

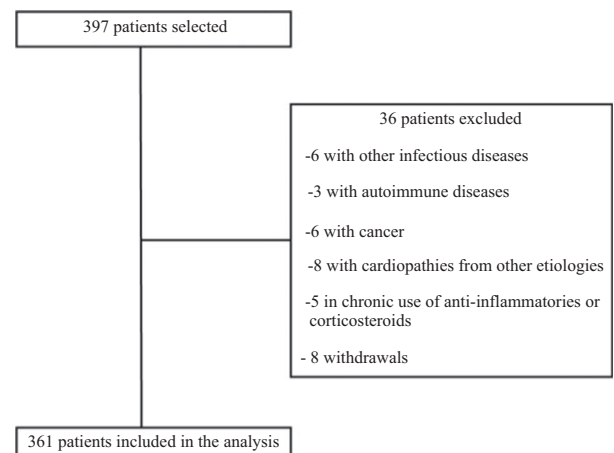


Figure 1 Study flow chart.

Table 1 Characteristics of participants included in the study

Clinical presentation of Chagas disease	Overall (<i>n</i> = 361)	Cardiac			Cardioidigestive without heart failure (<i>n</i> = 157; 43.5%)	Cardiac with heart failure (<i>n</i> = 49; 13.6%)	Digestive (<i>n</i> = 13; 3.6%)	Cardioidigestive without heart failure (<i>n</i> = 38; 10.5%)	Cardioidigestive with heart failure (<i>n</i> = 7; 1.9%)
		Indeterminate (<i>n</i> = 97; 26.9%)	Cardiac without heart failure (<i>n</i> = 157; 43.5%)	Cardiac with heart failure (<i>n</i> = 49; 13.6%)					
Age (%)									
<60 years	38.8 (140)	52.6 (51)	31.9 (50)	44.9 (22)	53.9 (7)	21.1 (8)	28.6 (2)		
≥60 years	61.2 (221)	47.4 (46)	68.1 (107)	55.1 (27)	46.1 (6)	78.9 (30)	71.4 (5)		
Sex (%)									
Male	43.8 (158)	47.4 (46)	43.3 (68)	55.1 (27)	30.8 (4)	28.9 (11)	28.6 (2)		
Female	56.3 (203)	52.6 (51)	56.7 (89)	44.9 (22)	69.2 (9)	71.1 (27)	71.4 (5)		
Schooling (%)									
<9 years	67.3 (243)	63.9 (62)	65.6 (103)	71.4 (35)	61.5 (8)	73.7 (28)	100.0 (7)		
9–12 years	18.6 (67)	16.5 (16)	18.5 (29)	18.4 (9)	30.8 (4)	23.7 (9)	0.0 (0)		
≥12 years	14.1 (51)	19.6 (19)	15.9 (25)	10.2 (5)	7.7 (1)	2.6 (1)	0.0 (0)		
Race (%)									
White	22.4 (81)	29.9 (29)	17.8 (28)	30.6 (15)	15.4 (2)	18.4 (7)	0.0 (0)		
Black	13.8 (50)	10.3 (10)	17.8 (28)	6.1 (3)	15.4 (2)	18.4 (7)	0.0 (0)		
Mulatto	59.8 (216)	57.7 (56)	59.9 (94)	57.1 (28)	69.2 (9)	57.9 (22)	100.0 (7)		
Others	3.9 (14)	2.1 (2)	4.5 (7)	6.1 (3)	0.0 (0)	5.3 (2)	0.0 (0)		
Hypertension (%)									
No	32.7 (118)	39.2 (38)	21.0 (33)	57.1 (28)	30.8 (4)	23.7 (9)	84.7 (6)		
Yes	67.3 (243)	60.8 (29)	79.0 (124)	42.9 (21)	69.2 (9)	76.3 (29)	14.3 (1)		
Diabetes Mellitus (%)									
No	78.3 (282)	72.2 (70)	82.2 (129)	81.3 (39)	76.9 (10)	73.7 (28)	85.7 (6)		
Yes	21.7 (78)	27.8 (27)	17.8 (28)	18.7 (9)	23.1 (3)	26.3 (10)	14.3 (1)		
Dyslipidaemia (%)									
No	46.5 (168)	40.2 (39)	44.6 (70)	65.3 (32)	38.5 (5)	47.4 (18)	57.1 (4)		
Yes	53.5 (193)	59.8 (58)	55.4 (87)	34.7 (17)	61.5 (8)	52.6 (20)	42.9 (3)		
Obesity (%)									
No	74.2 (268)	70.1 (68)	70.1 (110)	87.8 (43)	69.2 (9)	81.6 (31)	100.0 (7)		
Yes	25.8 (93)	29.9 (29)	29.9 (47)	12.2 (6)	30.8 (4)	18.4 (7)	0.0 (0)		
Smoking (%)									
Non-smoker	53.2 (192)	54.6 (53)	51.0 (80)	59.2 (29)	53.8 (7)	52.6 (20)	42.9 (3)		
Former	41.0 (148)	35.1 (34)	43.9 (69)	36.7 (18)	38.5 (5)	47.4 (18)	57.1 (4)		
Current	5.8 (21)	10.3 (10)	5.1 (8)	4.1 (2)	7.7 (1)	0.0 (0)	0.0 (0)		
Alcohol consumption (%)									
None	60.4 (218)	52.6 (51)	63.1 (99)	61.2 (30)	76.9 (10)	60.5 (23)	71.4 (5)		
Former	15.2 (55)	12.4 (12)	15.9 (25)	22.5 (11)	7.7 (1)	10.5 (4)	28.6 (2)		
Current	24.4 (88)	35.0 (34)	21.0 (33)	16.3 (8)	15.4 (2)	29.0 (11)	0.0 (0)		
Physical activity level (%)									
Low	25.8 (93)	18.6 (18)	24.8 (39)	32.7 (16)	23.1 (3)	36.8 (14)	42.9 (3)		
Moderate	47.9 (173)	48.4 (47)	46.5 (73)	51.0 (25)	53.8 (7)	47.4 (18)	42.9 (3)		

J. C. L. Santos-Filho *et al.* **Quality of life in chronic Chagas disease****Table 1** (Continued)

Clinical presentation of Chagas disease	Overall (<i>n</i> = 361)	Indeterminate (<i>n</i> = 97; 26.9%)	Cardiac without heart failure (<i>n</i> = 157; 43.5%)	Cardiac with heart failure (<i>n</i> = 49; 13.6%)	Digestive (<i>n</i> = 13; 3.6%)	Cardio digestive without heart failure (<i>n</i> = 38; 10.5%)	Cardio digestive with heart failure (<i>n</i> = 7; 1.9%)
High NYHA functional class (%)	26.3 (95)	33.0 (32)	28.7 (45)	16.3 (8)	23.1 (3)	15.8 (6)	14.3 (1)
I	67.6 (244)	87.6 (85)	69.4 (109)	20.4 (10)	92.3 (12)	73.7 (28)	0.0 (0)
II	23.0 (83)	10.3 (10)	23.6 (37)	53.1 (26)	7.7 (1)	21.0 (8)	14.3 (1)
III and IV	9.4 (34)	2.1 (2)	7.0 (11)	26.5 (13)	0.0 (0)	5.3 (2)	85.7 (6)
Residents by domicile (persons)	2.8 (1.45)	2.9 (1.55)	2.9 (1.53)	2.9 (1.20)	2.5 (1.4)	2.5 (1.3)	2.0 (0.6)
Income per capita (per R\$1000.00)	925.6 (923.5)	961.0 (772.7)	936.7 (817.1)	778.7 (477.7)	685.7 (358.2)	1099.6 (1867.2)	713.6 (329.9)
BMI (kg/m ²)	27.2 (4.9)	28.2 (4.5)	27.8 (5.0)	25.1 (4.2)	26.6 (5.5)	26.0 (5.1)	24.4 (4.4)
SBP (mmHg)	133.2 (21.9)	137.2 (18.1)	137.6 (20.1)	111.6 (20.8)	129.3 (22.0)	138.1 (21.1)	110.7 (21.9)
DBP (mmHg)	76.5 (12.3)	79.9 (10.5)	78.1 (10.8)	65.8 (12.6)	77.0 (12.9)	76.8 (13.3)	65.9 (14.8)
Left ventricular ejection fraction (%)	57.9 (13.9)	68.4 (5.5)	58.5 (9.9)	34.8 (10.5)	64.7 (5.4)	60.9 (8.1)	31.5 (5.6)
Left ventricular end-diastolic diameter (cm)	5.5 (0.8)	5.1 (0.5)	5.5 (0.7)	6.7 (0.6)	5.0 (0.4)	5.3 (0.6)	7.0 (1.0)
Left ventricular end-systolic diameter (cm)	3.7 (1.2)	2.9 (0.5)	3.5 (0.9)	5.6 (0.7)	3.0 (0.5)	3.4 (0.7)	6.1 (0.9)
Left ventricular end-diastolic volume (ml/m ²)	68.6 (30.8)	51.2 (10.9)	64.9 (20.5)	118.4 (36.8)	52.5 (9.7)	60.3 (15.4)	116.3 (48.0)
Left ventricular end-systolic volume (ml/m ²)	30.4 (27.0)	16.4 (5.2)	23.8 (12.8)	79.6 (34.1)	18.6 (5.2)	24.1 (9.9)	80.8 (37.4)
Presence of aneurysm							
No	84.5 (305)	99.0 (96)	80.9 (127)	75.5 (37)	100.0 (13)	71.1 (27)	71.4 (5)
Yes	15.5 (56)	1.0 (1)	19.1 (30)	24.5 (12)	0.0 (0)	28.9 (11)	28.6 (2)
Conduction abnormalities							
None	50.7 (183)	89.7 (87)	31.8 (50)	40.8 (20)	92.3 (12)	34.2 (13)	14.3 (1)
Unifascicular block	26.0 (94)	10.3 (10)	33.8 (53)	28.6 (14)	7.7 (1)	36.8 (14)	28.6 (2)
Bifascicular block	22.4 (81)	0.0 (0)	34.4 (54)	26.5 (13)	0.0 (0)	29.0 (11)	42.9 (3)
Trifascicular block	0.9 (3)	0.0 (0)	0.0 (0)	4.1 (2)	0.0 (0)	0.0 (0)	14.3 (1)
Sleep duration (%)							
<7 h	49.0 (177)	44.3 (43)	37.6 (59)	38.8 (19)	69.2 (9)	39.5 (15)	28.6 (2)
7–9 h	40.7 (147)	49.5 (48)	53.5 (84)	44.9 (22)	23.1 (3)	44.7 (17)	42.9 (3)
≥9 h	10.3 (37)	6.2 (6)	8.9 (14)	16.3 (8)	7.7 (1)	15.8 (6)	28.6 (2)
Benznidazole treatment							
No	91.1 (329)	91.7 (89)	90.5 (142)	89.8 (44)	84.6 (11)	100.0 (38)	71.4 (5)
Yes	8.9 (32)	8.3 (8)	9.5 (15)	10.2 (5)	15.4 (2)	0.0 (0)	28.6 (2)
Quality of life (WHOQOL-BREF)							
Physical domain	59.5 (17.2)	66.2 (16.6)	59.0 (16.2)	50.8 (16.8)	58.8 (20.4)	58.3 (15.2)	45.9 (17.1)
Psychological domain	66.5 (15.4)	71.4 (15.3)	65.5 (15.2)	63.3 (15.2)	66.0 (13.0)	64.9 (14.3)	53.0 (15.2)
Social relationship domain	68.9 (14.8)	71.3 (13.3)	67.0 (14.4)	67.5 (18.9)	76.9 (12.3)	70.4 (13.9)	64.3 (13.4)
Environment domain	57.2 (13.6)	60.1 (13.6)	56.4 (13.0)	56.8 (13.1)	53.8 (14.6)	57.9 (15.1)	41.5 (7.4)
Overall	63.1 (16.9)	66.0 (15.3)	63.2 (16.5)	60.5 (19.8)	61.5 (16.5)	60.5 (17.8)	57.1 (18.9)

Data are expressed as percentage (number of observation) for categorical and mean (standard deviation) for continuous variables. BMI, body mass index; DBP, diastolic blood pressure; NYHA, New York Heart Association; SBP, systolic blood pressure.

characteristics are presented in Table 1 (overall and stratified by CD clinical presentation). Most were women, aged 60 years or older, educated for <9 years, self-reported as mulatto and were classified as NYHA functional class I. The most prevalent CD clinical presentation was cardiac, followed by indeterminate and cardiogestive (Table 1). Prevalence of comorbidities was 67% for hypertension, 22% for diabetes mellitus and 54% for dyslipidaemia.

The domains that presented the worst QoL scores were environment and physical domains and the domain that presented the higher score was social relationships. Intermediate values were achieved in the psychological and overall domains (Table 1).

Univariate analysis demonstrated an important association between female sex, schooling, race, clinical presentation of CD, obesity, smoking, alcohol consumption, physical activity level, functional class, income *per capita* and sleep duration with physical domain. Age, sex, schooling, race, clinical presentation of CD, hypertension, obesity, alcohol consumption, physical activity level, functional class, residents by domicile, income *per capita* and sleep duration were associated with the psychological domain. The variables schooling, smoking, alcohol consumption, physical activity level, functional class, residents by domicile and clinical presentation of CD showed association with social relationship domain. Sex, schooling, race, clinical presentation of CD, smoking, physical activity level, functional class, residents by domicile, income *per capita* and sleep duration were associated with the environment domain. The variables that showed association with the overall quality of life domain in the univariate analysis were sex, schooling, clinical

presentation of CD, obesity, alcohol consumption, physical activity level, functional class, residents by domicile and income *per capita*.

Table 2 presents the results of multivariate regression analysis for physical health domain. Female sex presented a negative association with QoL, while those with higher education had higher QoL scores for the physical health domain. Physical activity level showed a positive correlation, indicating that the most active individuals presented better QoL in this domain. Functional class presented a progressive negative association with QoL in the physical domain, demonstrating that symptom worsening was associated with a worse QoL perception. A negative association between sleeping <7 h per night and QoL in the physical domain was also observed. Multivariate regression analysis revealed that female sex and functional class were negatively associated with QoL in the psychological domain (Table 3). Regarding social relationship domain, the only variable that presented a significant association after multivariate regression analysis was CD clinical presentation, specifically cardiac without heart failure (Table 4).

Multivariate regression analysis for environment domain (Table 5) showed that clinical presentation of CD, smoking, functional class, residents by domicile, income *per capita* and sleep duration were associated with QoL perception in this domain. Cardiogestive was the only clinical presentation that influenced QoL in the aforementioned domain. Smokers presented worse perception of QoL than non-smokers. Functional class and sleeping <7 h per night also had a negative association with environment domain. Number of residents by domicile presented positive association with this domain of QoL, as did income *per capita*. The variables associated with the overall quality of life domain were sex and functional class (Table 6), both presenting negative association with the QoL perception.

Table 2 Multivariate regression using physical health domain as dependent variable

Variable	B	CI 95%	P-value
Sex (female)	-0.1	-0.1 to -0.03	<0.001
Schooling			
9–12 years	+0.04	-0.03 to 0.1	0.28
≥12 years	+0.1	+0.01 to +0.1	0.02
Physical activity level			
Moderate	+0.06	-0.001 to +0.1	0.05
High	+0.1	+0.05 to +0.2	0.001
Functional class (NYHA)			
II	-0.2	-0.3 to -0.1	<0.001
III and IV	-0.4	-0.5 to -0.3	<0.001
Sleep duration			
<7 h	-0.1	-0.1 to -0.03	0.003
≥9 h	-0.02	-0.1 to +0.1	0.63

NYHA, New York Heart Association.

Discussion

The identification of which QoL domains are most affected in patients with CD is of paramount importance

Table 3 Multivariate regression using psychological domain as dependent variable

Variable	B	CI 95%	P-value
Sex (female)	-0.1	-0.2 to -0.1	<0.001
Functional class (NYHA)			
II	-0.1	-0.2 to -0.1	<0.001
III and IV	-0.2	-0.3 to -0.1	<0.001

NYHA, New York Heart Association.

Table 4 Multivariate regression using social relationship domain as dependent variable

Variable	β	CI 95%	P-value
Clinical presentation of Chagas disease			
Cardiac without heart failure	-0.1	-0.1 to -0.01	0.02
Cardiac with heart failure	-0.05	-0.1 to 0.02	0.15
Digestive	+0.1	-0.05 to -0.2	0.23
Cardiodigestive without heart failure	-0.01	-0.1 to +0.07	0.75
Cardiodigestive with heart failure	-0.1	-0.3 to +0.06	0.22

to the development of tailored strategies to improve physical and mental health. In this context, our study is the first to examine the influence of several clinical, socio-economic and lifestyle characteristics on different QoL domains among patients with CD.

In accordance with previous studies, we observed that the social relationship domain had the best score, while physical and environment domains had the worst [3, 17]. Variables independently associated with QoL were functional class, sex, clinical presentation of CD, sleep duration, schooling, physical activity level, smoking, income *per capita* and residents by domicile.

Functional class was the variable most often negatively associated with QoL (physical, psychological, environment, and overall quality of life domains). In all those

domains, there was a worsening perception of QoL in patients with poorer functional classes. Oliveira *et al.* [18] and Pelegrino *et al.* [19] also found an association between poor functional class and lower QoL for both physical and psychological domains in patients with CD. A recent narrative review by Sousa *et al.* [20] also supports our findings as they concluded that QoL is associated with functional capacity in individuals with CD.

In our study, women had a worse perception of QoL for physical, psychological and overall quality of life domains. Laguardia *et al.* [21], when standardising scores obtained from the Brazilian SF-36 version, also found worse QoL scores among women. In addition, Oliveira *et al.* [18] also showed that women had a worse QoL for mental summary, emotional role and physical functioning domains of SF-36 instrument. Social, psychological and hormonal factors may explain the worse QoL scores observed among women [22]. Many studies have demonstrated a greater prevalence of depressive symptoms among women, which also is extremely important in the perception of QoL [23, 24].

In the present study, CD clinical presentation was associated with QoL only in social and environment domains. Cardiac presentation without heart failure was associated with the worst QoL in the social domain while cardiodigestive presentation with heart failure and digestive presentation were associated with the lowest environment scores (the latter only with borderline significance; $P = 0.069$). A study conducted by Gontijo *et al.* [17] found a significant association between cardiac

Table 5 Multivariate regression using environment domain as dependent variable

Variable	B	CI 95%	P-value
Clinical presentation of Chagas disease			
Cardiac without heart failure	-0.04	-0.1 to +0.2	0.21
Cardiac with heart failure	+0.04	-0.04 to +0.1	0.35
Digestive	-0.1	-0.2 to +0.01	0.07
Cardiodigestive without heart failure	-0.03	-0.1 to +0.06	0.54
Cardiodigestive with heart failure	-0.2	-0.4 to -0.06	0.01
Smoking			
Former	-0.02	-0.07 to +0.3	0.39
Current	-0.1	-0.2 to -0.05	0.003
Functional class (NYHA)			
II	-0.2	-0.2 to -0.1	<0.001
III and IV	-0.1	-0.2 to -0.01	0.03
Residents by domicile (persons)	+0.02	+0.005 to +0.04	0.01
Income <i>per capita</i> (per R\$1000.00)	+0.00001	+0.0003 to +0.0008	<0.001
Sleep duration			
<7 h	-0.08	-0.1 to -0.03	<0.001
≥ 9 h	-0.07	-0.1 to +0.007	0.07

NYHA, New York Heart Association.

Table 6 Multivariate regression using overall quality of life domain as dependent variable

Variable	B	CI 95%	P-value
Sex (female)	−0.06	−0.1 to −0.005	0.03
Functional class (NYHA)			
II	−0.1	−0.2 to −0.07	<0.001
III and IV	−0.2	−0.3 to −0.1	<0.001

NYHA, New York Heart Association.

presentation and lower scores in the psychological domain. However, in the study by Ozaki *et al.* [3], patients with digestive presentation presented the lowest scores in all QoL domains. Similarly to our study, Oliveira *et al.* [18] found that cardiovascular symptoms (functional class) strongly impact all QoL domains, while gastrointestinal symptoms were only related to the physical functioning domain. A recent narrative review found that cardiac involvement is associated with a worse perception of QoL in patients with CD [20].

Our results did not demonstrate any influence of clinical presentations on physical domains. In the case of cardiac presentation, this unexpected result could be attributed to the inclusion of the functional capacity variable in the multivariate model, since functional capacity presents a straight association with several different facets evaluated in physical domain such as fatigue, mobility, activities of daily living and work capacity. Therefore, cardiac-related symptoms are probably more important to impact physical-related QoL, regardless of the clinical presentation. In addition, the proportion of patients classified with digestive presentation in our study is very small, which limits the analysis of the influence of the digestive presentation on QoL.

Sleep duration was another important variable associated with QoL. In our study, sleeping less than seven hours or more than nine hours per night were negatively associated with QoL in the physical health and environment domains. In fact, other studies found that short or long sleep periods are associated with adverse clinical outcomes [15, 25] and lower QoL [25, 26]. Inadequate sleep patterns inhibit sufficient rest and cause a greater fatigue in performing daily activities and a poor QoL in the physical health domain [27]. Defective housing conditions can negatively influence sleep and could be responsible for the low QoL scores in the environment domain [28, 29].

Physical activity level was positively associated with the perception of QoL in the physical health domain in patients with CD, as also described by others in the general population [30]. However, Oliveira *et al.* [18] found

no influence of physical activity levels on QoL in CD patients. Those results could be related to the very low physical activity level of patients included in their study [18]. Therefore, we can suggest that physically active individuals could maintain sufficient levels of mobility and independence that positively influenced the perception of QoL in this domain. Thus, physical activity programs for patients with CD should be encouraged whenever individuals do not present medical restrictions [9, 31, 32].

Schooling was another variable positively associated with QoL in the physical health domain. The population with CD is predominantly illiterate or with a low level of schooling [3, 19, 33], which restricts their access to higher paying jobs [34] and health services [35]. In line with our findings, lower schooling levels have been associated with poorer perception of QoL in both the Brazilian general population [35, 36] and patients with CD [18].

The last three variables that influenced the perception of QoL were smoking, income *per capita* and residents by domicile, all of them associated with environment domain. The negative association between smoking and QoL perception in the environment domain may be related to socioeconomic issues, since smoking prevalence and cigarette consumption are higher among populations with low socioeconomic status [37].

The total income available at home is the result of multiplying the income per capita by the number of residents in the domicile, variables that presented a positive association with QoL in the environment domain. Therefore, an increase in household income would be expected to provide a better perception of QoL [6].

Our study has some limitations. The sample consisted of patients regularly followed at our outpatient clinic, which may explain the higher proportion of patients with the cardiac presentation of the disease than in the general population of patients with CD where patients with the indeterminate presentation should predominate. The small number of patients with digestive and cardiodigestive presentations limited the study of the association of those CD presentations with QoL domains. In addition, the high-quality health care provided by our institution, a national reference centre for treatment of infectious disease, may have a positive influence on the response provided by patients when answering research questionnaires. This could limit the applicability of our results to general CD population. Since our sample presented a high percentage of patients ageing ≥ 60 years, a specific instrument to evaluate QoL among older patients, such as WHOQOL-OLD questionnaire, could have been included in the study. We also did not assess depression,

an important confounding factor for QoL in the general population [38] and in individuals with CD [3].

Conclusion

The low socioeconomic status and the physical limitations imposed by Chagas disease significantly impact the QoL reduction of CD patients, especially in environment and physical domains. The most important variables independently associated with QoL were functional class, sex, clinical presentation of CD, sleep duration, schooling, physical activity level, smoking, income *per capita* and residents by domicile. In this context, strategies to improve QoL among CD patients should take into account all of these variables in order to maximise improvements not only of patients' physical but also of their mental health.

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References

- World Health Organization. Chagas disease in Latin America: an epidemiological update based on 2010 estimates. *Wkly Epidemiol Rec* 2015; **90**: 33–43.
- Schmunis GA, Yadon ZE. Chagas disease: a Latin American health problem becoming a world health problem. *Acta Trop* 2010; **115**: 14–21.
- Ozaki Y, Guariento ME, de Almeida EA. Quality of life and depressive symptoms in Chagas disease patients. *Qual Life Res* 2011; **20**: 133–138.
- Junqueira Junior LF. Challenges for improving quality of life in Chagas disease. *Rev Soc Bras Med Trop* 2015; **48**: 117–120.
- Chambela MC, Mediano MFF, Ferreira RR *et al.* Correlation of 6-min walk test with left ventricular function and quality of life in heart failure due to Chagas disease. *Trop Med Int Health* 2017; **22**: 1314–1321.
- The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychol Med* 1998; **28**: 551–558.
- Alonso J. The measurement of health related-quality of life in clinical research and practice. *Gac Sanit* 2000; **14**: 163–167.
- Seidl EM, Zannon CM. Quality of life and health: conceptual and methodological issues. *Cad Saude Publica* 2004; **20**: 580–588.
- Mediano MFF, Mendes FSNS, Pinto VLM *et al.* Cardiac rehabilitation program in patients with Chagas heart failure: a single-arm pilot study. *Rev Soc Bras Med Trop* 2016; **49**: 319–328.
- Fleck MP, Louzada S, Xavier M *et al.* Application of the Portuguese version of the abbreviated instrument of quality life WHOQOL-bref. *Rev Saude Publica* 2000; **34**: 178–183.
- Dias JCP, Ramos AN Jr, Gontijo ED *et al.* II Consenso Brasileiro em Doença de Chagas, 2015. *Epidemiol Serv Saude* 2016; **25**: 7–86.
- Instituto Brasileiro de Geografia e Estatística. Censo Demográfico 2010. Características da população e dos domicílios. Resultados do universo. Rio de Janeiro: IBGE; 2011.
- Instituto Brasileiro de Geografia e Estatística. Pesquisa Nacional por Amostra de Domicílios. Pesquisa Especial de Tabagismo-PETab. Rio de Janeiro: IBGE; 2009.
- Craig CL, Marshall AL, Sjöström M *et al.* International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003; **35**: 1381–1395.
- Grandner MA, Hale L, Moore M *et al.* Mortality associated with short sleep duration: the evidence, the possible mechanisms, and the future. *Sleep Med Rev* 2010; **14**: 191–203.
- Bocchi EA, Braga FG, Ferreira SM *et al.* III Brazilian guidelines on chronic heart failure. *Arq Bras Cardiol* 2009; **93**: 3–70.
- Gontijo ED, Guimarães TN, Magnani C, Paixão GM, Dupin S, Paixão LM. Qualidade de vida dos portadores de doença de Chagas. *Rev Med Minas Gerais* 2009; **19**: 281–285.
- Oliveira BG, Abreu MN, Abreu CD *et al.* Health-related quality of life in patients with Chagas disease. *Rev Soc Bras Med Trop* 2011; **44**: 150–156.
- Pelegrino VM, Dantas RA, Ciol MA, Clark AM, Rossi LA, Simões MV. Health-related quality of life in Brazilian outpatients with Chagas and non-Chagas cardiomyopathy. *Heart Lung* 2011; **40**: e25–e31.
- Souza GR, Costa HS, Souza AC, Nunes MC, Lima MM, Rocha MO. Health-related quality of life in patients with Chagas disease: a review of the evidence. *Rev Soc Bras Med Trop* 2015; **48**: 121–128.
- Laguardia J, Campos MR, Travassos C, Najar AL, Anjos LA, Vasconcellos MM. Brazilian normative data for the Short Form 36 questionnaire, version 2. *Rev Bras Epidemiol* 2013; **16**: 889–897.
- Gijsberts CM, Agostoni P, Hofer IE *et al.* Gender differences in health-related quality of life in patients undergoing coronary angiography. *Open Heart* 2015; **2**: e000231.
- Rocha NS, Schuch FB, Fleck MP. Gender differences in perception of quality of life in adults with and without chronic health conditions: the role of depressive symptoms. *J Health Psychol* 2014; **19**: 721–729.
- Albert PR. Why is depression more prevalent in women? *J Psychiatry Neurosci* 2015; **40**: 219–221.
- Loprinzi PD, Joyner C. Meeting sleep guidelines is associated with better health-related quality of life and reduced premature all-cause mortality risk. *Am J Health Promot* 2018; **32**: 68–71.

J. C. L. Santos-Filho *et al.* **Quality of life in chronic Chagas disease**

26. Faubel R, Lopez-Garcia E, Guallar-Castillón P *et al.* Sleep duration and health-related quality of life among older adults: a population-based cohort in Spain. *Sleep* 2009; **32**: 1059–1068.
27. Edinger JD, Bonnet MH, Bootzin RR *et al.* Derivation of research diagnostic criteria for insomnia: report of an American Academy of Sleep Medicine Work Group. *Sleep* 2004; **27**: 1567–1596.
28. Hirotsu C, Bittencourt L, Garbuio S, Andersen ML, Tufik S. Sleep complaints in the Brazilian population: impact of socioeconomic factors. *Sleep Sci* 2014; **7**: 135–142.
29. Grandner MA, Williams NJ, Knutson KL, Roberts D, Jean-Louis G. Sleep disparity, race/ethnicity, and socioeconomic position. *Sleep Med* 2016; **18**: 7–18.
30. Bize R, Johnson JA, Plotnikoff RC. Physical activity level and health-related quality of life in the general adult population: a systematic review. *Prev Med* 2007; **45**: 401–415.
31. Bocchi EA. Exercise training in Chagas' cardiomyopathy: trials are welcome for this neglected heart disease. *Eur J Heart Fail* 2010; **12**: 782–784.
32. Mediano MFF, Mendes FSNS, Pinto VLM, Silva PSD, Hasslocher-Moreno AM, Sousa AS. Reassessment of quality of life domains in patients with compensated Chagas heart failure after participating in a cardiac rehabilitation program. *Rev Soc Bras Med Trop* 2017; **50**: 404–407.
33. Magnani C, Oliveira BG, Gontijo ED. Representations, myths, and behaviors among Chagas disease patients with pacemakers. *Cad Saude Publica* 2007; **23**: 1624–1632.
34. Mota DCGA, Benevides-Pereira AMT, Araújo SM. Estresse e resiliência em doença de Chagas. *Aletheia* 2006; **24**: 57–68.
35. Maciel NM, De Conti MHS, Simeão SFAP, Genebra CVDS, Corrente JE, De Vitta A. Sociodemographic factors, level of physical activity and health-related quality of life in adults from the north-east of São Paulo, Brazil: a cross-sectional population study. *BMJ Open* 2018; **8**: e017804.
36. Campolina AG, Pinheiro MM, Ciconelli RM, Ferraz MB. Quality of life among the Brazilian adult population using the generic SF-8 questionnaire. *Cad Saude Publica* 2011; **27**: 1121–1131.
37. Hiscock R, Bauld L, Amos A, Fidler JA, Munafò M. Socioeconomic status and smoking: a review. *Ann N Y Acad Sci* 2012; **1248**: 107–123.
38. Kolovos S, Kleiboer A, Cuijpers P. Effect of psychotherapy for depression on quality of life: meta-analysis. *Br J Psychiatry* 2016; **209**: 460–468.

Corresponding Author Mauro F. F. Mediano, Evandro Chagas National Institute of Infectious Disease, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil. E-mails: mauro.mediano@ini.fiocruz.br or mffmediano@gmail.com