Am. J. Trop. Med. Hyg., 104(3), 2021, pp. 951–958
doi:10.4269/ajtmh.20-0335

Comparison of Health-Related Quality of Life in Outpatients with Chagas and Matched Non-Chagas Chronic Heart Failure in Colombia: A Cross-Sectional Analysis

Mario J. Olivera,[1]* Johana A. Fory,[2] and Giancarlo Buitrago[3,4]

[1]*Grupo de Parasitología, Instituto Nacional de Salud, Bogotá, D.C., Colombia;* [2]*Facultad de Medicina, Universidad Militar Nueva Granada, Bogotá, D.C., Colombia;* [3]*Instituto de Investigaciones Clínicas, Facultad de Medicina, Universidad Nacional de Colombia, Bogotá, D.C., Colombia;* [4]*Hospital Universitario Nacional de Colombia, Bogotá, D.C., Colombia*

Abstract. Chagas disease represents an important cause of heart failure (HF) and affects health-related quality of life (HRQoL). The study aimed to evaluate and compare the HRQoL of patients with chagasic HF and matched non-Chagas controls to identify factors associated with HRQoL. A cross-sectional study with pair-matched controls was conducted in Colombia. From October 2018 to December 2019, a total of 84 HF patients were screened for study subjects. Four were excluded, resulting in 80 patients for the analysis, among whom 40 patients with Chagas were enrolled as cases and 40 gender- and age-matched non-Chagas patients as controls. The Kansas City Cardiomyopathy Questionnaire (KCCQ) and the Minnesota Living with Heart Failure Questionnaire (MLWHFQ) were used to measure HRQoL. Demographic, clinical, and laboratory data were obtained from each subject. Health-related quality of life scores were significantly worse among the Chagas group than among the non-Chagas group in the KCCQ domains of physical functioning and symptoms and in the MLWHFQ scale. In the multivariate analysis, the variables associated with lower HRQoL scores were living alone, obesity, having less than 12 years of education, and an increase in left ventricular diameters in the systole and diastole. Health-related quality of life in patients with chronic HF is impaired across all domains. Chagas patients showed worse HRQoL scores than non-Chagas patients. Six variables, some potentially modifiable, were independently associated with worse HRQoL.

INTRODUCTION

The quality of life (QoL) among patients with heart failure (HF) is very low compared with that among healthy people of the same age and gender, as well as with that among subjects affected by other chronic diseases.[1] People with HF experience a variety of uncomfortable signs and symptoms that severely impact their QoL, function, and longevity, in addition to imposing high costs on the healthcare system.[2–4] However, the mechanisms involved in this impairment of QoL are not well understood.

Heart failure is a final stage of several cardiovascular diseases; among them, Chagas disease represents an important cause of HF in endemic countries.[5] Interest in monitoring health-related quality of life (HRQoL) among patients with HF is growing, given the importance of being able to assess the impact of symptoms on daily life and the effect of therapy, aiming to minimize healthcare costs and decrease hospital readmissions.[1,6,7] The HRQoL concept is a very useful parameter to try to approximate the impact that HF can have on a person's daily life. This concept refers to the aspects of life that greatly influence personal experience and can prevent leading the life you want.[8]

Most of the studies that have evaluated the effect of chagasic HF on HRQoL have been carried out in Brazil[9]; however, the phenotypes of patients with chagasic HF could be different in other regions because of the discrete unit of parasite typing, immunological disturbances, comorbidities, and economic and healthcare systems. Despite the high prevalence of Chagas disease estimated in Colombia,[10] to date and to the extent that the scientific literature allows, no studies on QoL have been performed in chagasic HF in Colombia. Therefore, it is important to investigate QoL and the associated risk factors among patients with HF so that more attention can be paid to its management.

Knowledge of the HRQoL of Chagas patients could provide information for health professionals on how to evaluate and adjust the care and services offered in outpatient hospital care. Therefore, this study aimed to evaluate and compare the clinical characteristics and HRQoL profiles of patients with chagasic HF and matched non-Chagas controls. The secondary objective was to identify the factors associated with HRQoL.

METHODS

Study design and participants. A comparative cross-sectional study matched by gender and age was conducted between October 2018 and December 2019. Participants with chronic HF were selected among patients who had been screened for *Trypanosoma cruzi* (with and without Chagas disease) and who had undergone routine follow-up at the outpatient facility in the National Institute of Health of Colombia.

To be eligible for the study, outpatients with Chagas disease had to have a positive *T. cruzi* infection confirmed by two serological tests (using both ELISA and immunofluorescent antibody tests), have chronic HF of ≥ 12 months duration, have New York Heart Association (NYHA) functional class IV, and have a left ventricular ejection fraction (LVEF) ≤ 40%. In addition, they had to be aged 18 years or older and possess cognitive functions and communication skills. Participants with evidence of metastatic or recurrent cancer at the time of the study or those with a history of hospitalization in the last 2 months were excluded, as were those who had a history of psychiatric disorders or those with a recent myocardial infarction or revascularization in the last 3 months.

A comparison group was also recruited. For the participant with Chagas disease, a patient with no Chagas history matched for gender and age (± 3 years) was chosen for the

* Address correspondence to Mario J. Olivera, Grupo de Parasitología, Instituto Nacional de Salud, Avenida Calle 26 CAN 51-20, Bogotá, D.C., Colombia. E-mail: molivera@ins.gov.co

comparison group. The comparison group consisted of outpatients who had *T. cruzi* infection confirmed as negative, had chronic HF of ≥ 12 months, had NYHA class IV, and had an LVEF ≤ 40%. In addition to the age matching, these participants had to be aged 18 years or older, with no evidence of metastatic or recurrent cancer at the time of the study, without a history of hospitalization (< 2 months), and without a history of psychiatric disorders, recent myocardial infarction, or revascularization (< 3 months).

Sample size determination and procedure. The sample size calculation was based on previous works in the scientific literature that evaluated the QoL of patients with HF. It was estimated that a sample of 42 cases and 42 controls would be sufficient to detect a difference of 10.2 points in the QoL score between cases with Chagas disease and the controls, assuming a SD of up to 10.8 points, with a statistical power of 95% and a type I error of 1%. Non-probabilistic convenience sampling was used to recruit participants.

Selected patients with Chagas and the comparative group fulfilling eligibility criteria were subjected to a standardized initial consultation conducted by trained personnel. The following information was collected: 1) sociodemographic data included medical history such as age, gender, marital status, education, household, employment, income, hospitalizations, prescribed drugs, help with medication, implanted cardiac devices, heart transplantation, smoking status, and comorbidities. Patients were categorized as current smokers if they had smoked > 100 cigarettes in their lifetime and still smoked every day or some of the days.

Comorbidities were scored with the Charlson Comorbidity Index. 2) Clinical features included systolic blood pressure, diastolic blood pressure, heart rate, respiratory rest, waist circumference, hemoglobin level, weight, height, and body mass index (BMI). 3) Functional classification was assessed using the NYHA classification, from class I (no symptoms and no limitation in ordinary physical activity) to class IV (inability in physical activities with symptoms even while at rest). 4) Assessment of QoL was performed using two HRQoL assessment tools: the Minnesota Living with Heart Failure Questionnaire (MLWHFQ) and the Kansas City Cardiomyopathy Questionnaire (KCCQ).

Data collection and quality assurance. Health-related quality of life reflects the impact of the disease and its concurrent symptoms on the physical, psychological, social, and functional status perceived by the individual.[11] In assessing the HRQoL, the patients were instructed to answer the MLWHFQ and the KCCQ independently with minimal assistance from the investigators.

The MLWHFQ is a self-administered disease-specific questionnaire that measures the impact of symptoms and signs relevant to HF and its treatment on living as the person wanted to over the previous 30 days. The questionnaire includes three subscales: physical, emotional, and total HRQoL. The MLWHFQ is a 21-item instrument that uses a 6-point Likert-type scale ranging from 0 (none) to 5 (very much). A total score is obtained by summing the scores from individual questions (range 0–105), with higher scores indicating lower HRQoL.[12,13]

The KCCQ is a disease-specific health status instrument composed of 23 items. This self-administered questionnaire quantifies the domains of physical limitation, symptoms (frequency, severity, and recent change over time), self-efficacy, social limitation, and QoL limitation due to HF. Two summary scores, namely, a clinical summary score and overall summary score, can be calculated. Scores range from 0 to 100. A higher score is representative of a better health status.[14]

Data processing and analysis. The data collected through the questionnaires were recorded in Microsoft Access. To properly match Chagas and non-Chagas groups, a matched-pair analysis was performed. Each patient with Chagas was matched with a patient without Chagas.

Initially, the main sociodemographic and clinical characteristics for both the Chagas and non-Chagas groups were described. Continuous baseline characteristics were summarized using the mean ± SD or median (interquartile range) depending on the normality of the distribution of the variable. Categorical characteristics were summarized using frequencies and percentages. Normal data distribution testing was conducted using the Shapiro–Wilk test. A paired *t*-test or the Wilcoxon signed-rank test (depending on the data distribution) was used to determine the significance of the difference of means between the two groups.

Bivariate and multivariate analyses using conditional logistic regression models were carried out to assess independent predictors of HRQoL domains. Total and domain scores were categorized based on the score on each questionnaire: poor HRQoL was indicated by an MLWHFQ score > 45 and a KCCQ score < 45, and moderate/good HRQoL was indicated by an MLWHFQ score ≤ 45 and a KCCQ score ≥ 45. To avoid unstable estimates, variables with a *P*-value ≤ 0.10 in the univariate analysis were candidates for the final regression model. Crude and adjusted odds ratios (ORs) and their 95% CIs were estimated for each covariate. In all the analyses, a *P*-value less than 0.05 was used to indicate the presence of a significant association between HRQoL domains and covariates. Kansas City Cardiomyopathy Questionnaire domain scores were described using a radar graph. Statistical analyses were performed with the statistical package STATA 14 version (Stata Corp, College Station, TX).

Ethics. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and the Colombian guidelines for research with human participants. Written informed consent was obtained from all participants before enrollment in the study. The Research Ethics and Methodology Committee of the National Institute of Health, Colombia, approved this study under registration number CEMIN 29-2016.

RESULTS

Sociodemographic and clinical characteristics. Initially, 84 age-matched and gender-matched patients with HF were recruited, including 42 patients with Chagas disease and 42 patients without Chagas disease. Two patients in the Chagas group were excluded because they had a history of receiving a heart transplant. Because of this, their respective controls were also excluded. Finally, 80 patients (40 with Chagas and 40 controls) were included for further analysis. Fifty patients were men (62.5%), the ages of patients ranged from 59 to 71 years, and the mean age was 62.9 ± 2.5 years.

The ages of patients with HF and Chagas disease in this study ranged from 59 to 70 years (mean age: 62.4 years ± 2.6), whereas the ages of patients in the comparison group ranged from 61 to 71 years (mean age: 63.3 years ± 2.4). Comparisons

TABLE 1
Baseline characteristics in outpatients with chagasic heart failure compared with those with non-Chagas cardiomyopathy in Colombia

Characteristic	Patients with Chagas (*N* = 40)	Patients without Chagas (*N* = 40)	*P*-value
Demographic and medical history			
Age (years), mean ± SD	62.4 ± 2.6	63.3 ± 2.4	0.110
Gender, male, *n* (%)	25 (62.5)	25 (62.5)	1.000
Marital status, married/stable relationship, *n* (%)	29 (72.5)	22 (55.0)	0.104
Education (years) > 12, *n* (%)	15 (37.5)	25 (62.5)	0.025
Monthly income (USD), mean ± SD	216 ± 22.4	257 ± 33.2	< 0.001
Work status, *n* (% with no paid job)	30 (75.0)	22 (55.0)	0.061
Hospitalizations during the last 12 months, mean ± SD	2.6 ± 0.8	2.4 ± 0.7	0.285
Number of prescribed drugs taken daily, mean ± SD	6.7 ± 0.8	7.6 ± 0.9	< 0.001
Help with medication, *n* (%)	25 (62.5)	20 (50.0)	0.260
Received antiparasitic drug (nifurtimox/benznidazole), *n* (%)	13 (32.5)	0 (0)	< 0.001
Prior myocardial infarction, *n* (%)	18 (45.0)	10 (25.0)	0.061
Peripheral arterial disease, *n* (%)	9 (22.5)	6 (15.0)	0.390
Previous stroke, *n* (%)	7 (17.5)	5 (12.5)	0.774
Hypertension, *n* (%)	27 (67.5)	33 (82.5)	0.121
Diabetes mellitus, *n* (%)	18 (45.0)	24 (60.0)	0.179
Dyslipidemia, *n* (%)	17 (42.5)	20 (50.0)	0.501
Chronic respiratory disease, *n* (%)	10 (25.0)	12 (30.0)	0.617
Atrial fibrillation, *n* (%)	15 (37.5)	6 (15.0)	0.022
Current smokers, *n* (%)	9 (22.5)	7 (17.5)	0.572
Implantable cardioverter-defibrillator, *n* (%)	8 (20.0)	1 (2.5)	0.029
Pacemaker, *n* (%)	12 (30.0)	3 (7.5)	0.020
Clinical and supplementary tests			
Positive serology for *Trypanosoma cruzi*, *n* (%)	40 (100)	0 (0)	< 0.001
Charlson Comorbidity Index, mean ± SD	6.7 ± 2.2	7.0 ± 1.9	0.599
Body mass index (kg/m^2), mean ± SD	27.4 ± 2.7	28.3 ± 2.4	0.141
Waist (cm), mean ± SD	81.4 ± 4.0	82.3 ± 4.7	0.378
Systolic blood pressure (mm Hg), mean ± SD	105.3 ± 4.8	112.5 ± 8.6	< 0.001
Diastolic blood pressure (mm Hg), mean ± SD	70.9 ± 6.1	75.3 ± 3.6	< 0.001
Heart rate (beats/min), mean ± SD	65.1 ± 2.9	73.9 ± 1.5	< 0.001
Respiratory rate (breaths/min), mean ± SD	23.2 ± 2.3	22.3 ± 2.3	0.004
Hemoglobin (g/dL), mean ± SD	11.6 ± 0.9	12.7 ± 0.9	< 0.001
Doppler echocardiogram			
Left ventricular ejection fraction (%), mean ± SD	23.6 ± 1.4	24.4 ± 1.9	0.037
Left ventricular end-diastolic diameter (mm), mean ± SD	71.5 ± 0.6	65.6 ± 0.8	< 0.001
Left ventricular end-systolic diameter (mm), mean ± SD	62.5 ± 0.6	55.7 ± 0.7	< 0.001
Left ventricular end-diastolic volume (mL), mean ± SD	213.3 ± 14.0	204.2 ± 18.6	0.015
Left ventricular end-systolic volume (mL), mean ± SD	175.9 ± 19.7	168.7 ± 10.7	0.044
E/*e* ratio, mean ± SD	21.1 ± 2.5	20.2 ± 1.6	0.056
Apical left ventricular aneurysm, *n* (%)	7 (17.5)	0	0.012
Electrocardiogram/24-hour Holter monitoring			
Right bundle branch block, *n* (%)	19 (47.5)	3 (7.5)	< 0.001
Left bundle branch block, *n* (%)	5 (12.5)	12 (30.0)	0.056
Left anterior fascicular block, *n* (%)	16 (40.0)	7 (17.5)	0.026
Ventricular extrasystoles, *n* (%)	17 (42.5)	6 (15.0)	< 0.001
First-degree atrioventricular block, *n* (%)	7 (17.5)	4 (10.0)	0.330
Q waves, *n* (%)	9 (22.5)	4 (10.0)	0.225
QRS duration (millisecond), mean ± SD	164.7 ± 7.8	150.1 ± 6.9	< 0.001
Chest X-ray findings, *n* (%)			
Cardiomegaly	31 (77.5)	20 (50.0)	0.011
Cephalization	25 (62.5)	13 (32.5)	< 0.001
Alveolar edema	10 (25.0)	7 (17.5)	0.412
Pleural effusion	6 (15.0)	4 (10.0)	0.737
Baseline treatment, *n* (%)			
ACE inhibitors or ARB	30 (75.0)	34 (85.0)	0.264
β-Blockers	19 (45.2)	22 (55.0)	0.502
Aldosterone antagonists	24 (60.0)	26 (65.0)	0.644
Nitrates	11 (27.5)	14 (35.0)	0.469

(continued)

TABLE 1
Continued

Characteristic	Patients with Chagas (*N* = 40)	Patients without Chagas (*N* = 40)	*P*-value
Digoxin	21 (52.5)	23 (57.5)	0.653
Loop diuretics	37 (92.5)	39 (97.5)	0.305
Antiplatelet	19 (47.5)	22 (55.0)	0.502
Anticoagulants	16 (40.0)	18 (45.0)	0.651

QRS duration = the time interval from the onset to the end of the QRS complex; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker. *E/e* = mitral inflow *E* velocity to tissue Doppler *e* ratio.

between the two groups showed significant differences in the educational level ($P = 0.025$) and monthly income level ($P < 0.001$), which were higher in the comparison group. Additional sociodemographic and clinical variables are presented and compared in Table 1.

Comparison of HRQoL scores between Chagas and non-Chagas. In total, 80 patients completed the two questionnaires. Minnesota Living with Heart Failure Questionnaire and KCCQ scores of the Chagas and non-Chagas subjects are displayed in Table 2. In both questionnaires, the results showed a wide variation in the scores obtained, and significant differences between the two groups for the overall summary score and in dimensions were observed; patients in the Chagas group showed worse scores than patients without Chagas disease (all values of $P < 0.05$).

Regarding the MLWHFQ, patients with Chagas disease showed higher scores than patients without a history of Chagas (all values of $P < 0.05$). The mean (SD) total score on the MLWHFQ was 49.3 (23.2) in the non-Chagas group, whereas in the Chagas group, the mean (SD) was 58.1 (16.1). In both groups, patients showed that the physical dimension had a greater impact on daily life than the emotional dimension. In the Chagas group, the mean scores on the physical and emotional components were 26.6 ± 8.9 and 9.4 ± 2.2, respectively. By contrast, in the non-Chagas group, the score for the physical component was 23.6 ± 11.4, and the emotional component score was 8.2 ± 3.0.

Of the six dimensions measured with the KCCQ, the worst values for HRQoL were evident in the dimensions of total symptoms, physical limitation, and QoL. In addition, the best values for the HRQoL were in the dimensions of self-efficacy.

According to the KCCQ, among the two groups, the lowest mean HRQoL score for the group with Chagas disease was found in the domain of total symptoms (mean 38.6 ± 17.8), and the lowest mean HRQoL score for the non-Chagas group was found in the domain of physical limitation (mean 45.9 ± 19.2). By contrast, the highest mean HRQoL scores for both groups were observed in the self-efficacy domain (mean 56.7 ± 20.3 versus 63.4 ± 19.7). The mean clinical summary scores were 41.5 ± 11.8 and 48.7 ± 19.4 for patients with Chagas and those without Chagas, respectively.

Comparing KCCQ scores between groups, Chagas patients reported significantly lower scores in the physical limitation ($P = 0.002$), total symptoms ($P < 0.001$), social limitation ($P < 0.001$), self-efficacy ($P = 0.019$), and QoL ($P = 0.003$) domains than patients without a history of Chagas disease (Figure 1).

Predictors of HRQoL. The univariate analysis showed important associations among living alone, obesity (BMI ≥ 30), having an education of less than 12 years, smoking, dyslipidemia, having a pacemaker, having right bundle branch block, having *q* waves, having diabetes, having obstructive pulmonary disease, having pulmonary edema, the number of medications, and the increase in left ventricular diameters in the systole and diastole with low HRQoL (overall and by domain scores lower in the KCCQ and higher in the MLWHFQ).

The multivariate analysis showed a significant association between obesity and the perception of low HRQoL in both instruments, KCCQ and MLWHFQ. By contrast, living alone was significantly associated with low HRQoL in the MLWHFQ and with the KCCQ overall summary measure. Likewise, the increase in the diameter of the left ventricle in the systole was significantly associated with low HRQoL in the MLWHFQ and in the KCCQ clinical summary measure. On the other hand, the level of education and the history of diabetes were only associated with low HRQoL in the MLWHFQ. In turn, the increase in the diameter of the left ventricle in the diastole was associated with the low HRQoL reported in the KCCQ clinical summary measure (see Table 3).

DISCUSSION

In the present study, chronic HF and HRQoL in patients with Chagas disease were compared with subjects of the same gender, similar age, and with no history of Chagas disease. This is the first study to assess HRQoL in a sample of outpatients with Chagas disease and chronic HF that uses a matching pair design to reduce possible selection bias by controlling for two well-known confounders. The self-efficacy domain was found to have the best score, whereas the physical functioning and disease symptom domains had the worst scores. The variables independently associated with a low HRQoL were living alone, obesity, having less than 12 years of education, and the increase in left ventricular diameters in the systole and diastole.

In this study, two specific instruments were used to measure the HRQoL of HF, and the results show that, on average, subjects with chronic HF in both groups experience very important changes in their QoL, and the level of HRQoL is similar or even worse than that seen in cancer patients.[15–17] The mean scores in most areas of the KCCQ in the present study were significantly lower in the group of Chagas patients than in the age- and gender-matched controls without Chagas disease. These results show not only the high level of impairment of the HRQoL among patients with HF who are seen daily in clinical practice but also the differences between the populations included in clinical trials and those treated on an outpatient basis in the context of primary care.[11,18]

TABLE 2
Comparison of mean QoL scores in outpatients with chagasic heart failure and matched non-Chagas cardiomyopathy in Colombia

Scale/domain	Patients with Chagas (N = 40)	Patients without Chagas (N = 40)	P-value
Minnesota Living with Heart Failure Questionnaire	58.1 ± 16.1	49.3 ± 23.2	< 0.001
Physical	26.6 ± 8.9	23.6 ± 11.4	0.002
Emotional	9.4 ± 2.2	8.2 ± 3.0	0.022
Social	22.5 ± 8.1	17.4 ± 12.1	< 0.001
Kansas City Cardiomyopathy Questionnaire			
Physical limitation	40.8 ± 12.7	45.9 ± 19.2	0.002
Symptom score	38.6 ± 17.8	46.6 ± 21.6	< 0.001
Social limitation	42.5 ± 10.6	52.2 ± 21.8	< 0.001
Self-efficacy	56.7 ± 20.3	63.4 ± 19.7	0.019
QoL	43.4 ± 15.4	49.3 ± 21.9	0.003
Overall summary	39.6 ± 13.5	45.5 ± 18.1	0.002
Clinical summary	41.5 ± 11.8	48.7 ± 19.4	< 0.001

QoL = quality of life.

Previous studies have observed that the dimensions that assess the physical condition and the symptoms of the disease had the worst scores.[19–22] This suggests that the physical limitations and symptoms related to HF determine the HRQoL of these patients. To date, there are no published studies that have used KCCQ in patients with HF and Chagas disease. However, this instrument has been widely used in patients with HF, and the results of the present study are consistent with those that have reported greater impairment of HRQoL in patients with HF than the general population and patients with other chronic diseases.[11,14,23]

By contrast, the MLWHFQ has been used more frequently in research on Chagas disease and HRQoL.[22,24–26] In the present study, the Chagas group presented significantly worse mean MLWHFQ scores than controls without Chagas. These findings are consistent with those reported by previous studies that indicate that HRQoL is worse in patients with Chagas disease than in healthy controls when evaluated with this questionnaire[21]; this difference is more marked when patients with Chagas disease have established dilated heart disease.[26] Other research showed that patient-centered care with Chagas disease and HF increases adherence to treatment, which improves the QoL.[27] However, an important difference of the present study with those mentioned previously is that all the participants had chronic HF, in which it is more important to assess HRQoL.

Of the identified risk factors, only high body weight is considered modifiable. These results support an inverse relationship between obesity and HRQoL, which has also been documented by previous studies.[28] Although the impacts of obesity have often only been measured with respect to morbidity and mortality, the negative effects of obesity on

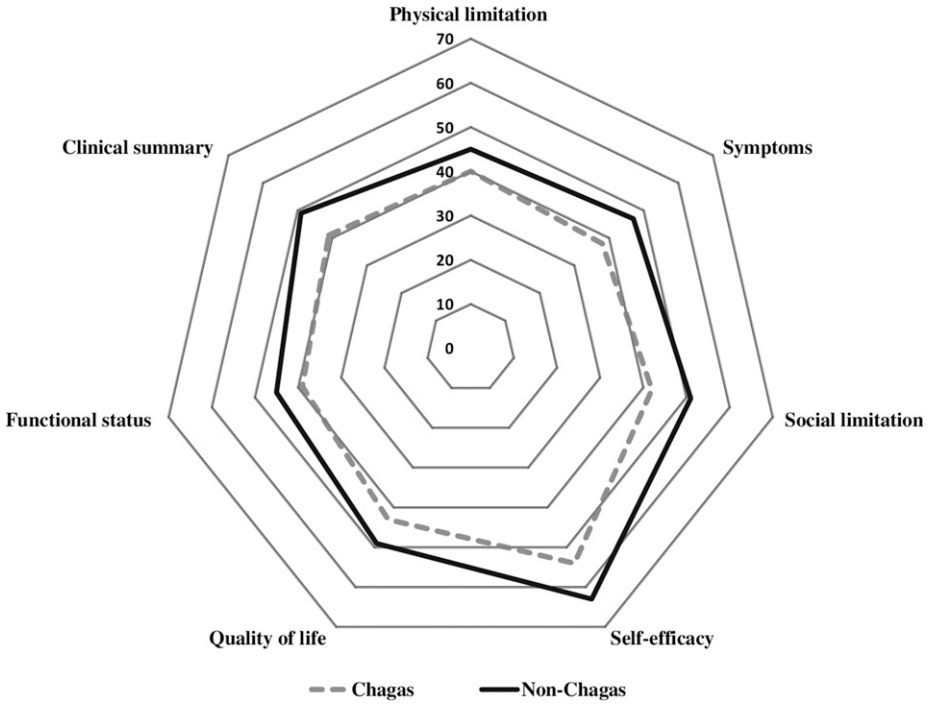

FIGURE 1. Mean scores of quality of life (QoL) for the domains of the Kansas City Cardiomyopathy Questionnaire in the Chagas and non-Chagas groups.

TABLE 3

Results of the multivariate regression analysis to assess the influence of the clinical and sociodemographic variables on the domains of the KCCQ and MLWHFQ scales

	Multivariate analysis								
	MLWHFQ			KCCQ clinical summary			KCCQ overall summary		
Covariate	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Weight (body mass index) (kg/m^2)									
< 30	Ref	–	–	Ref	–	–	Ref	–	–
≥ 30	4.4	1.1–23.2	**0.048**	6.1	1.1–29.4	**0.035**	5.9	1.2–28.4	**0.025**
Increase in left ventricular end-systolic diameter									
No	Ref	–	–	Ref	–	–	–	–	–
Yes	3.1	1.1–14.3	**0.049**	3.9	1.1–17.5	**0.036**	–	–	–
Marital status									
Married/cohabitating	Ref	–	–	–	–	–	Ref	–	–
Single/separated/divorced/widowed	3.2	1.1–15.6	**0.041**	–	–	–	4.1	1.2–17.5	**0.021**
Education (years)									
≥ 12	Ref	–	–	–	–	–	–	–	–
< 12	3.0	1.1–18.1	**0.048**	–	–	–	–	–	–
Diabetes mellitus									
No	Ref	–	–	–	–	–	–	–	–
Yes	3.5	1.1–17.4	**0.033**	–	–	–	–	–	–
Increase in left ventricular end-diastolic diameter									
No	–	–	–	Ref	–	–	–	–	–
Yes	–	–	–	3.9	1.1–19.3	**0.047**	–	–	–
E/e ratio	–	–	–	–	–	–	–	–	–
Smoking	–	–	–	–	–	–	–	–	–
Dyslipidemia	–	–	–	–	–	–	–	–	–
Pacemaker	–	–	–	–	–	–	–	–	–
Right bundle branch block	–	–	–	–	–	–	–	–	–
Q wave	–	–	–	–	–		–	–	–
Obstructive pulmonary disease	–	–	–	–	–	–	–	–	–
Pulmonary edema	–	–	–	–	–	–	–	–	–
Number of drugs	–	–	–	–	–	–	–	–	–

E/e = mitral inflow *E* velocity to tissue Doppler *e* ratio; KCCQ = Kansas City Cardiomyopathy Questionnaire; MLWHFQ = Minnesota Living with Heart Failure Questionnaire; OR = odds ratio; Ref = reference variable. Bold values are statistically significant results at $P < 0.005$.

physical, emotional, and social functionality have recently been shown to impair HRQoL. Therefore, interventions aimed at proper weight management could improve the already low HRQoL of patients with HF. Despite the apparent paradox of obesity in patients with HF, efforts to prevent and intervene in obesity must continue.[29]

A history of comorbid diabetes mellitus was associated with decreased HRQoL, and this comorbidity is present in up to half of all patients with chronic HF. The physiological consequences of diabetes are mainly based on glycemic dysregulation and include mitochondrial dysfunction, microvascular disease, and oxidative stress. These complications make diabetic people more likely to present other health problems that significantly reduce their QoL.[30]

Similar to previous studies,[21] this work has shown that single/divorced/widowed patients had a significantly lower QoL on both questionnaires than their married counterparts. It is believed that the mechanism by which marital status affects QoL is through support in activities of daily living and in the implementation of behavioral changes that promote autonomy and increase adaptability to the disease, leading to better clinical outcomes.[31] Heart failure patients who live alone are more vulnerable to social isolation, which in turn leads to poor self-care behaviors.

The relationship between years of education and HRQoL observed in this study indicates that educational disparities are important for facing adversities in different domains of the patient's HRQoL during HF. These results coincide with those reported in other studies that have shown that low educational level is associated with poor health education, lack of knowledge about HF, and its risk factors.[21,32] Furthermore, they found that many patients lacked a clear understanding of self-care. These results confirm the importance of designing educational interventions that overcome barriers to learning.

Interestingly, in this study, a significant association was observed between the increase in the diameters of the left ventricle in the systole and diastole and the deterioration of the HRQoL. However, the *E/e* ratio was not correlated with worsening of QoL. This could be because of the variability of the indexes and the small sample size in the study. It is possible that if the sample size were larger, then this index was correlated with the QoL. These results coincide with those reported in Brazil.[33] By contrast, other investigations that used the MLWHFQ found no association between the parameters of the echocardiogram and the deterioration of the HRQoL.[34]

The reasons for this unfavorable pattern in terms of HRQoL deterioration in the Chagas group are not fully understood.[35] Despite having a similar clinical presentation, some aspects related to inflammatory activity, fibrosis, and arrhythmogenic potential that predominate in heart disease of chagasic origin compared with ischemic and nonischemic cardiomyopathy could explain the impaired HRQoL and the findings of the present study.[36]

A critical situation among Chagas patients is that deworming drugs are not effective in this phase of the disease. In a recent investigation, it was shown that benznidazole therapy does not have a favorable effect on chagasic heart disease.[37] In the present study, few patients with Chagas had the opportunity to receive any antiparasitic drug (nifurtimox or benznidazole), and those who received it had adverse events, which are frequent in both drugs.[38,39]

An important finding is that less than half of Chagas patients were using beta-blockers. Previous studies in HF patients of various etiologies have confirmed the long-term beneficial effect of these drugs, producing an improvement in functional class, cardiac function, morbidity, and QoL.[40] Conversely, a high proportion of patients receiving angiotensin-converting enzyme inhibitors were observed, despite their beneficial effect on mortality, which may not lead to a significant improvement in QoL.[40]

The present study is limited in several ways. First, it has the limitations of any cross-sectional evaluation because it does not provide information on the longitudinal changes of the variable and does not allow conclusions to be drawn regarding the causal directions. Second, the participants in the present study may not be representative of all people with HF, and the included population represents a subgroup of patients with HF and systolic dysfunction, which is routinely evaluated in the outpatient setting. Thus, it is not possible to determine whether the results obtained can be extrapolated to other types of HF patient populations, such as those with a preserved ejection fraction or those who do not follow controls in hospital outpatient consultations. Third, a substantial proportion of patients in each group had a history of a previous myocardial infarction, a condition that could lead to HF instead of Chagas disease. By contrast, one of the greatest strengths was having implemented a pairing of two possible confounding factors. Another strength was using two disease-specific standardized instruments, which are internationally acceptable. Furthermore, the response rate of the questionnaires was 100%.

In conclusion, the present study quantifies the dimensions of HRQoL and identifies six characteristics, some potentially modifiable, that are independently associated with poorer QoL in patients with chronic HF in a situation of clinical stability and recruited on an outpatient basis. It shows that, on average, the HRQoL of patients with chronic HF presents a significant deterioration, which mainly affects the physical and symptomatic dimensions. It also shows that when comparing the Chagas and non-Chagas matched groups, the HRQoL, as measured by two specific questionnaires, is considerably impaired in the Chagas group. It is essential to consider the factors that affect the QoL and make periodic measurements of the QoL to identify the specific dimensions that require more attention.

Received April 22, 2020. Accepted for publication July 1, 2020.

Published online February 1, 2021.

Acknowledgment: We would like to thank the Red Chagas researchers for their support as research network.

Financial support: Funding for this evaluation was provided by the Colombian National Institute of Health.

Authors' addresses: Mario J. Olivera, Grupo de Parasitología, Instituto Nacional de Salud, Bogotá, D.C., Colombia, E-mail: molivera@ins.gov.co. Johana A. Fory, Facultad de Medicina y Ciencias de la Salud, Universidad Militar Nueva Granada, Bogotá, D.C., Colombia, E-mail: johafory@gmail.com. Giancarlo Buitrago, Instituto de Investigaciones Clínicas, Facultad de Medicina, Universidad Nacional de Colombia, Bogotá, D.C., Colombia, and Hospital Universitario Nacional de Colombia, Bogotá, D.C., Colombia, E-mail: gbuitragog@unal.edu.co.

REFERENCES

1. Zhang J, Hobkirk J, Carroll S, Pellicori P, Clark AL, Cleland JGF, 2016. Exploring quality of life in patients with and without heart failure. *Int J Cardiol 202:* 676–684.
2. Olivera MJ, Buitrago G, 2020. Economic costs of Chagas disease in Colombia in 2017: a social perspective. *Int J Infect Dis 91:* 196–201.
3. Park J, Moser DK, Griffith K, Harring JR, Johantgen M, 2019. Exploring symptom clusters in people with heart failure. *Clin Nurs Res 28:* 165–181.
4. Zhang Y, Yuan M, Gong M, Tse G, Li G, Liu T, 2018. Frailty and clinical outcomes in heart failure: a systematic review and meta-analysis. *J Am Med Dir Assoc 19:* 1003–1008.e1.
5. Olivera MJ, Villamil JFP, Gahona CCT, Hernández JMR, 2018. Barriers to diagnosis access for Chagas disease in Colombia. *J Parasitol Res 2018:* 4940796.
6. Salyer J, Flattery M, Lyon DE, 2019. Heart failure symptom clusters and quality of life. *Heart Lung 48:* 366–372.
7. Juenger J, Schellberg D, Kraemer S, Haunstetter A, Zugck C, Herzog W, Haass M, 2002. Health related quality of life in patients with congestive heart failure: comparison with other chronic diseases and relation to functional variables. *Heart 87:* 235–241.
8. Megari K, 2013. Quality of life in chronic disease patients. *Heal Psychol Res 1:* e27.
9. Sousa GR, Costa HS, Souza AC, Nunes MC, Lima MM, Rocha MO, 2015. Health-related quality of life in patients with Chagas disease: a review of the evidence. *Rev Soc Bras Med Trop 48:* 121–128.
10. Olivera MJ, Fory JA, Porras JF, Buitrago G, 2019. Prevalence of Chagas disease in Colombia: a systematic review and meta-analysis. *PLoS One 14:* e0210156.
11. Comin-Colet J, Anguita M, Formiga F, Almenar L, Crespo-Leiro MG, Manzano L, Muniz J, Chaves J, de Frutos T, Enjuanes C, 2016. Health-related quality of life of patients with chronic systolic heart failure in Spain: results of the VIDA-IC study. *Rev Esp Cardiol 69:* 256–271.
12. Rector TS, Kubo S, Cohn JN, 1987. Patients' self-assessment of their congestive heart failure, part 2: content, reliability and validity of a new measure, the Minnesota Living with Heart Failure Questionnaire. *Heart Fail 3:* 198–209.
13. Rector TS, Cohn JN, 1992. Assessment of patient outcome with the Minnesota living with heart failure questionnaire: reliability and validity during a randomized, double-blind, placebo-controlled trial of pimobendan. Pimobendan Multicenter Research Group. *Am Heart J 124:* 1017–1025.
14. Green CP, Porter CB, Bresnahan DR, Spertus JA, 2000. Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. *J Am Coll Cardiol 35:* 1245–1255.
15. Kluthcovsky ACGC, Urbanetz AA, 2015. Fatigue and quality of life in breast cancer survivors: a comparative study. *Rev Bras Ginecol Obstet 37:* 119–126.
16. Claridy MD, Ansa B, Damus F, Alema-Mensah E, Smith SA, 2018. Health-related quality of life of African-American female breast cancer survivors, survivors of other cancers, and those without cancer. *Qual Life Res 27:* 2067–2075.
17. Goswami S, Mongelli M, Peipert BJ, Helenowski I, Yount SE, Sturgeon C, 2018. Benchmarking health-related quality of life in thyroid cancer versus other cancers and United States normative data. *Surgery 164:* 986–992.
18. Cesáreo Naveiro-Rilo J, Diez-Juárez MD, Flores-Zurutuza L, Rodríguez-García MÁ, Rebollo-Gutiérrez F, Romero Blanco A, 2012. La calidad de vida en los enfermos con insuficiencia cardiaca: visión desde atención primaria de salud. *Gac Sanit 26:* 436–443.
19. Santos-Filho JCL et al., 2018. Quality of life and associated factors in patients with chronic Chagas disease. *Trop Med Int Health 23:* 1213–1222.
20. Pelegrino VM, Dantas RAS, Ciol MA, Clark AM, Rossi LA, Simoes MV, 2011. Health-related quality of life in Brazilian outpatients with Chagas and non-Chagas cardiomyopathy. *Heart Lung 40:* e25–e31.
21. Oliveira BG, Abreu MNS, Abreu CDG, Rocha MO, Ribeiro AL, 2011. Health-related quality of life in patients with Chagas disease. *Rev Soc Bras Med Trop 44:* 150–156.
22. Dourado KC, Bestetti RB, Cordeiro JA, Theodoropoulos TA, 2006. Assessment of quality of life in patients with chronic heart

failure secondary to Chagas' cardiomyopathy. *Int J Cardiol 108:* 412–413.
23. Hauptman PJ, Masoudi FA, Weintraub WS, Pina I, Jones PG, Spertus JA, 2004. Variability in the clinical status of patients with advanced heart failure. *J Card Fail 10:* 397–402.
24. Ritt LE, Carvalho AC, Feitosa GS, Pinho-Filho JA, Andrade MVS, Feitosa-Filho GS, Newby LK, Lopes RD, 2013. Cardiopulmonary exercise and 6-min walk tests as predictors of quality of life and long-term mortality among patients with heart failure due to Chagas disease. *Int J Cardiol 168:* 4584–4585.
25. Costa HS, Alves RL, da Silva SA, Alencar MC, Nunes Mdo CP, Lima MM, Rocha MO, 2014. Assessment of functional capacity in Chagas heart disease by incremental shuttle walk test and its relation to quality-of-life. *Int J Prev Med 5:* 152–158.
26. Vieira FC, de Melo Marinho PE, Brandao DC, Barbosae e Silva O, 2014. Respiratory muscle strength, the six-minute walk test and quality of life in Chagas cardiomyopathy. *Physiother Res Int 19:* 8–15.
27. Chambela MDC et al., 2020. Impact of pharmaceutical care on the quality of life of patients with heart failure due to chronic Chagas disease: randomized clinical trial. *Br J Clin Pharmacol 86:* 143–154.
28. Evangelista LS, Moser DK, Westlake C, Hamilton MA, Fonarow GC, Dracup K, 2006. Impact of obesity on quality of life and depression in patients with heart failure. *Eur J Heart Fail 8:* 750–755.
29. Horwich TB, Fonarow GC, Clark AL, 2018. Obesity and the obesity paradox in heart failure. *Prog Cardiovasc Dis 61:* 151–156.
30. Yap J et al., 2019. Association of diabetes mellitus on cardiac remodeling, quality of life, and clinical outcomes in heart failure with reduced and preserved ejection fraction. *J Am Heart Assoc 8:* e013114.
31. Kewcharoen J, Thangjui S, Kanitsoraphan C, Techorueangwiwat C, Mekraksakit P, Vutthikraivit W, 2019. The effects of marital status on outcome of heart failure population: a systematic review and meta-analysis. *Acta Cardiol* 1–9.
32. Fabbri M, Yost K, Finney Rutten LJ, Manemann SM, Boyd CM, Jensen D, Weston SA, Jiang R, Roger VL, 2018. Health literacy and outcomes in patients with heart failure: a prospective community study. *Mayo Clin Proc 93:* 9–15.
33. Santos JJA, Plewka JEA, Brofman PRS, 2009. Quality of life and clinical indicators in heart failure: a multivariate analysis. *Arq Bras Cardiol 93:* 159–166.
34. Grigioni F et al., 2003. Distance between patients' subjective perceptions and objectively evaluated disease severity in chronic heart failure. *Psychother Psychosom 72:* 166–170.
35. Costa HS, Lima MM, Figueiredo PHS, Chaves AT, Nunes MC, Rocha MO, 2019. The prognostic value of health-related quality of life in patients with Chagas heart disease. *Qual Life Res 28:* 67–72.
36. Shen L et al., 2017. Contemporary characteristics and outcomes in Chagasic heart failure compared with other nonischemic and ischemic cardiomyopathy. *Circ Heart Fail 10:* e004361.
37. Morillo CA et al., 2015. Randomized trial of benznidazole for chronic Chagas' cardiomyopathy. *N Engl J Med 373:* 1295–1306.
38. Olivera MJ, Cucunuba ZM, Alvarez CA, Nicholls RS, 2015. Safety profile of nifurtimox and treatment interruption for chronic Chagas disease in Colombian adults. *Am J Trop Med Hyg 93:* 1224–1230.
39. Olivera MJ, Cucunuba ZM, Valencia-Hernandez CA, Herazo R, Agreda-Rudenko D, Florez C, Duque S, Nicholls RS, 2017. Risk factors for treatment interruption and severe adverse effects to benznidazole in adult patients with Chagas disease. *PLoS One 12:* e0185033.
40. Coelho R, Ramos S, Prata J, Bettencourt P, Ferreira A, Cerqueira-Gomes M, 2005. Heart failure and health related quality of life. *Clin Pract Epidemol Ment Health 1:* 1–19.