

Health-related quality of life in patients with Chagas disease: a review of the evidence

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ABSTRACT

Chagas disease (ChD), a neglected tropical disease caused by infection with the parasite *Trypanosoma cruzi* (*T. cruzi*), remains a serious public health issue in Latin America and is an emerging disease in several non-endemic countries, where knowledge of the condition and experience with its clinical management are limited. Regionally, the disease is the major cause of disability secondary to tropical diseases in young adults. Health-related quality of life (HRQoL) impairment is common in patients with ChD, especially in those with Chagas dilated cardiomyopathy, the most severe manifestation of the disease, which frequently leads to heart failure. The aim of this review was to conduct a literature search for studies that have evaluated the determining factors of HRQoL in ChD patients. We included cross-sectional, case-control, cohort, and experimental studies, as well as clinical trials that evaluated the HRQoL in ChD patients aged 18 to 60 years and are presenting an explicit description of statistical analysis. Using a combination of keywords based on Descriptors in Health Sciences (DeCS) and Medical Subject Headings (MeSH) for searches in PubMed and the Scientific Electronic Library Online (SciELO), 148 studies were found. After exclusions, 12 studies were selected for analysis. Three main findings were extracted from these studies: 1) cardiac involvement is associated with a worse HRQoL in ChD patients; 2) HRQoL is associated with the patients' functional capacity; and 3) simple and inexpensive therapeutic measures are effective for improving HRQoL in ChD patients. Hence, ChD patients' functional capacity, the effectiveness of non-surgical conservative treatment, and cardiac involvement are important determining factors for the HRQoL in ChD patients.

Keywords: Chagas disease. Quality of life. Health-related quality of life. Cardiomyopathy. Determining factors.

INTRODUCTION

Chagas disease (ChD), a neglected tropical disease caused by infection with the parasite *Trypanosoma cruzi* (*T. cruzi*)⁽¹⁾⁽²⁾, remains a serious health problem issue in Latin America and is an emerging disease in several non-endemic countries, where knowledge of the condition and experience with its clinical management are limited. If ChD is not recognized and treated appropriately, patient care can be compromised. The World Health Organization (WHO) estimates that 7 to 8 million people are infected worldwide, with the majority of infections seen in Latin America where the disease is endemic⁽³⁾. Regionally, the disease is the major cause of disability secondary to tropical diseases in

young adults⁽⁴⁾. In recent decades, the epidemiological profile of the disease has changed due to new patterns of immigration and successful control in its transmission, leading to the urbanization and globalization of the disease. Cases of ChD have been increasingly detected in the US, Canada, as well as in many European and some Western Pacific countries⁽⁵⁾.

Dilated cardiomyopathy with heart failure is often a late manifestation of the chronic phase of ChD and is characterized by chronic myocarditis involving all cardiac chambers and damage to the excitation-conducting system of the intrinsic autonomic innervation⁽⁵⁾⁽⁶⁾⁽⁷⁾. This severe and frequently seen manifestation of human chronic ChD is characterized by heart failure, cardiac arrhythmia, heart blocks, thromboembolic phenomena, and sudden death⁽⁷⁾.

Despite having a similar clinical presentation, Chagas dilated cardiomyopathy has some peculiar and unique characteristics (such as more extensive inflammation and fibrosis) compared to idiopathic dilated cardiomyopathy⁽⁷⁾⁽⁸⁾⁽⁹⁾. The pathogenesis of ChD is complex, and the reason why ChD has a worse prognosis than idiopathic dilated cardiomyopathy has yet to be established.

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Impairment of the health-related quality of life (HRQoL) is common in ChD patients, especially among those presenting with dilated cardiomyopathy, which frequently leads to heart failure. However, the mechanisms involved in this HRQoL impairment are not well understood⁽¹⁰⁾. HRQoL is a broad concept derived from a school of thought within the human and biological sciences that values parameters that go beyond the control of symptoms of a disease, decrease mortality, and increased life expectancy⁽¹¹⁾. An ideal health assessment should include a measure of the person's physical health, a measure of physical, social and psychological functioning, and a measure of quality of life. Such an assessment should cover key physical, psychological, social and spiritual domains of life⁽¹²⁾. The assessment of HRQoL in ChD patients is important due to the complex interplay of biological, cultural, and socioeconomic factors that have strong medical-labor impacts and the stigmatizing nature of the disease. Therefore, the aim of this review was to conduct a literature search for studies that have evaluated the determining factors of HRQoL in ChD patients.

METHODS

This review is a summary of the evidence on the evaluation of HRQoL in ChD patients. Our inclusion criteria were: a) studies that evaluated HRQoL in ChD patients; b) cross-sectional, case-control, cohort, and experimental studies, as well as clinical trials; c) studies in ChD patients ranging from 18 to 60 years of age. We excluded duplicate articles, studies on pregnant women, those that evaluated HRQoL after surgical procedures, articles that did not fit the objective of this review, and papers that were published before the year 2000. There were no restrictions regarding the language of the papers.

We conducted the main literature search in PubMed. Secondary sources of information from the Scientific Electronic Library Online (SciELO) were also consulted. The keywords used in our search strategy were based on Descriptors in Health Sciences (DeCS) and Medical Subject Headings (MeSH) and included *Chagas*, *Chagas disease*, *Chagas heart disease*, *Chagas cardiomyopathy*, *quality of life*, and *health-related quality of life*. The keywords were matched between the two groups (Chagas heart disease and quality of life) using search operators (quotes, parentheses, *AND*, and *OR*). To verify the methodological quality of the studies, the PEDro score⁽¹³⁾ was used. The literature search was performed by two authors (GRS and HSC) between August and October 2014.

RESULTS

Using pre-established descriptors, a total of 148 studies were found (**Figure 1**). Of these, we excluded 76 because they appeared in duplicate and 29 because we determined that they did not match the objective of the study after reading the titles and abstracts. Another 31 studies were considered ineligible based on our inclusion criteria. The main reasons for exclusion were the absence of a group of patients with ChD ($n = 18$), the evaluation of HRQoL after surgical treatments ($n = 9$), review studies ($n = 2$), and studies conducted before the year 2000 ($n = 2$).

Thus, after all exclusions, 12 studies were selected for analysis. Of these, 10 were published in international journals, and 2 were published in Brazilian journals. Six cross-sectional studies evaluated HRQoL in ChD patients (**Table 1**)^{(5) (10) (14) (15) (16) (17)}, two verified the effect of non-surgical conservative treatments on HRQoL in Chagas dilated cardiomyopathy patients (**Table 2**)^{(18) (19)}, and 4 correlated HRQoL with functional capacity in ChD patients (**Table 3**)^{(20) (21) (22) (23)}. The studies found in our literature search showed heterogeneity in the patient samples: one article included patients presenting with all clinical forms of ChD (8.3%), two (16.7%) included patients with pacemakers, two (16.7%) did not mention the presence of cardiopathy, and 7 (58.3%) included patients with cardiopathy.

The instruments used for the evaluation of HRQoL include both generic and specific questionnaires. The Short-form of Health Survey (SF-36) was the most commonly used questionnaire (in 7 studies). The SF-36 is a generic questionnaire containing 36 items in 8 domains (vitality, physical functioning, bodily pain, general health, role physical, role emotional, social functioning, and mental health) and has been validated in the Brazilian Portuguese population⁽²⁴⁾. The WHO Quality of Life-BREF (WHOQOL-BREF) is another generic questionnaire that was used in two studies^{(5) (14)}. The WHOQOL-BREF is considered an important tool for health professionals in the assessment of treatment efficacy⁽²⁵⁾.

Among the specific questionnaires, the Minnesota Living with Heart Failure Questionnaire (MLWHFQ) was used in 5 studies included in this review and consists of 21 questions on functionality and disabilities related to heart failure. The MLWHFQ has also been validated in the Brazilian Portuguese population⁽²⁶⁾. For a better interpretation of the results, it is important to emphasize that the score obtained by the MLWHFQ is inversely proportional to HRQoL. Thus, higher scores represent a worse HRQoL. Another instrument, the Assessment of QUALity of life and RELated events (AQUAREL) is a specific questionnaire for evaluating HRQoL in pacemaker patients⁽²⁷⁾ and was used in one study⁽²⁸⁾.

DISCUSSION

Chagas disease is not understood by the population in the same way as it is by the scientific community⁽²⁹⁾. Regardless of the clinical presentation, ChD patients are surrounded by discrimination that affects their social, cultural, and economic relations, which may limit their quality of life^{(1) (30)}.

The main findings of the papers identified in this review can be summarized as the following 3 key points. In ChD patients, 1) cardiac involvement is associated with worse HRQoL; 2) HRQoL is associated with the patients' functional capacity; and 3) simple and inexpensive therapeutic measures are effective for improving HRQoL in ChD patients. A detailed discussion of these 3 key findings is provided below.

Health-related quality of life in patients with Chagas disease

Seven studies that evaluated the HRQoL in ChD patients who did not receive any intervention or comparison with clinical parameters were identified. Oliveira et al.⁽¹⁰⁾ evaluated

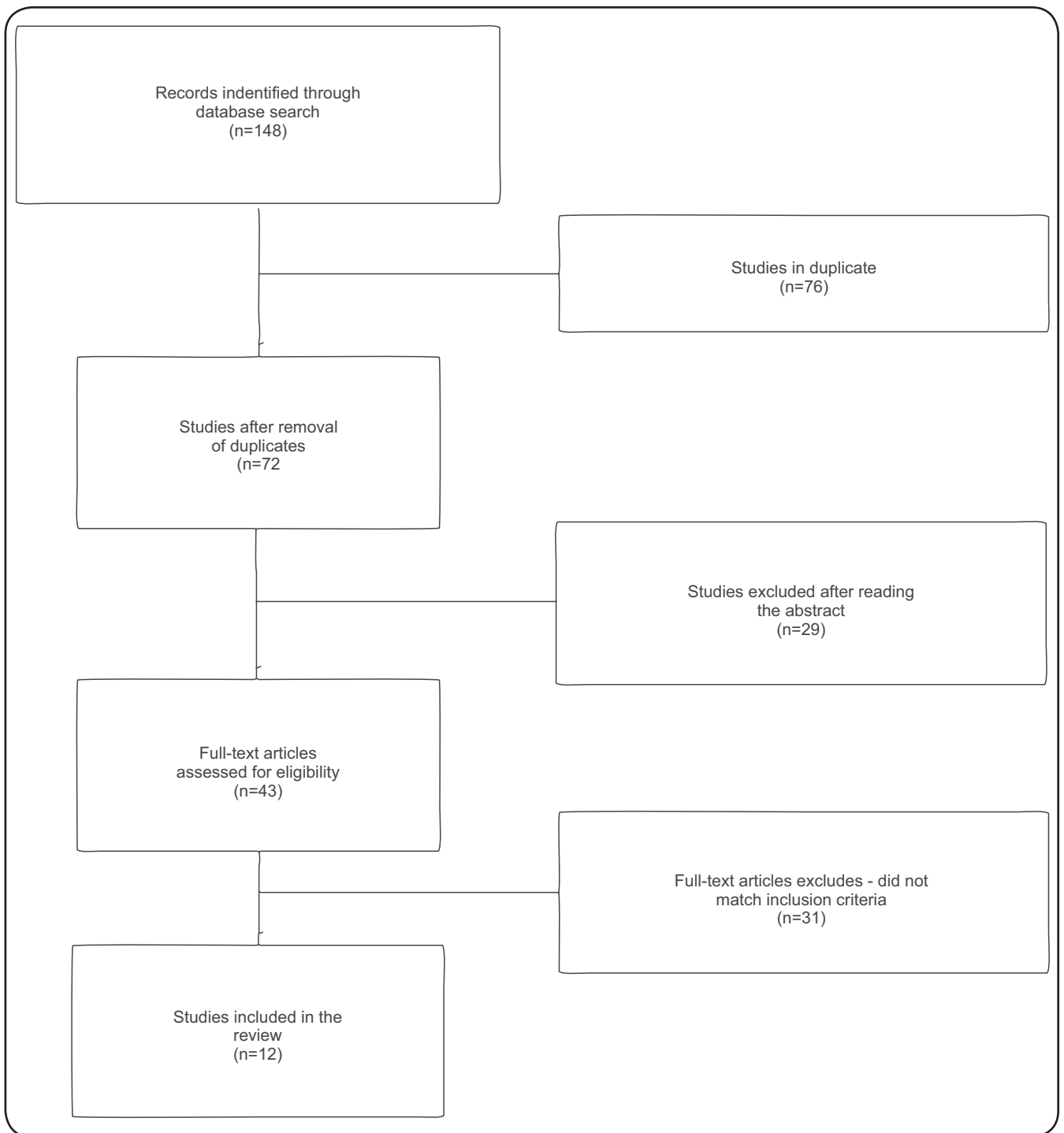


FIGURE 1 - Search results and selection of studies.

the HRQoL by using the SF-36 and MLwHFQ in ChD patients ($n = 125$) and compared their scores to those of a healthy control group ($n = 21$). The authors found that HRQoL was significantly worse in ChD patients when evaluated by the MLwHFQ ($p = 0.028$). Moreover, ChD patients had worse scores in the physical functioning ($p = 0.011$) and role emotional ($p = 0.010$) domains of the SF-36 when compared to the control group. In the authors' multivariate analysis, a worse HRQoL in ChD

patients was associated with the female sex, fewer years of education, unmarried status, worst functional class, presence of cardiovascular and gastrointestinal symptoms, comorbidities, Doppler echocardiographic abnormalities, and ventricular arrhythmia detected during Holter monitoring.

Ozaki et al.⁽¹⁴⁾ assessed the HRQoL in patients with different forms of ChD and found that patients with the digestive form had the worst HRQoL scores when evaluated by the WHOQOL

TABLE 1 - Health-related quality of life in Chagas disease patients.

Study	Sample	Objective	Instruments	PEDro Score	Results
Oliveira et al., 2008	Cardiac pacemaker patients (n = 139; 40% men) with (n = 77) and without (n = 31) ChD; unknown serology in the remaining patients (n = 31)	To compare HRQoL in pacemaker patients with and without ChD	SF-36 and SQUAREL	2/10	No differences in SF-36 components between ChD and non-ChD pacemaker patients were observed. ChD patients had worse scores in the chest discomfort (p = 0.030) and arrhythmia (p = 0.004) domains of the SQUAREL than non-ChD patients.
Oliveira et al., 2011	ChD (n = 125; 58% men) and non-ChD (n = 21; 62% men) patients	To compare HRQoL between ChD (n = 125) and non-ChD (n = 21) patients	SF-36 and MLwHFQ	2/10	ChD patients showed a worse HRQoL in the MLwHFQ (p = 0.028) and had worse scores for physical functioning (p = 0.011) and role emotional (p = 0.020) domains of the SF-36.
Ozaki et al., 2011	ChD patients presenting with different clinical manifestations (n = 110; 49% men).	To compare HRQoL among patients with clinical manifestations of ChD.	WHOQOL-BREF	2/10	Patients with the digestive form of ChD had a worse HRQoL when compared to patients with the cardiac, mixed, and indeterminate forms of the disease.
Pelegrino et al., 2011	Patients with Chagas (n = 43; 62.8% men) and non-Chagas (n = 59; 57.6% men) cardiomyopathy	To compare HRQoL between patients with Chagas (n = 43) and non-Chagas cardiomyopathy (n = 59).	SF-36	4/10	Chagas cardiomyopathy patients had a worse HRQoL in the role physical (p = 0.002) and physical functioning domains (p = 0.01) of the SF-36 when compared with patients with non-Chagas cardiomyopathy.
Souza et al., 2013	ChD disease patients with a previous diagnosis of stroke (n = 21; 57% men)	To correlate HRQoL with depressive symptoms, and functional performance stroke sequelae	WHOQOL-BREF	1/10	Depressive symptoms correlated with physical (r = -0.733; p = 0.001), psychological (r = -0.713; p = 0.012), environmental (r = -0.713; p = 0.001), and social (r = -0.659; p = 0.003) aspects of the WHOQOL-BREF. No correlation could be observed between HRQoL and functional performance (r = 0.279; p = 0.262).
Cardoso et al., 2014	Cardiac pacemaker patients (n = 92; 42% men) with and without ChD	To verify the determining factors of HRQoL	SF-36	1/10	Positive serology for <i>Trypanosoma cruzi</i> was not associated with HRQoL (statistical data not shown).

AQUAREL: assessment of quality of life and related events; ChD: Chagas disease; HRQoL: health-related quality of life; MLwHFQ: Minnesota living with heart failure questionnaire; PEDro: physiotherapy evidence database; SF-36: short-form of health survey; WHOQOL-BREF: WHO quality of life-BREF.

and reported more depressive symptoms in the Beck Depression Inventory (BDI). Other studies indicated however that the presence of cardiac involvement in the disease seemed to have a negative effect on the patients' HRQoL. Vieira et al.⁽²³⁾ compared the HRQoL between ChD patients with cardiopathy (n = 16, aged

53.5 ± 9.2 years) and those with no apparent heart disease (n = 16, aged 51.9 ± 11.9 years) using the MLwHFQ. They detected worse HRQoL values in ChD patients with cardiomyopathy for the total score of the MLwHFQ (p = 0.001) as well as for physical (p = 0.002), emotional (p = 0.031), and general factors (p < 0.001).

TABLE 2 - Effect of non-surgical treatment on health-related quality of life in Chagas dilated cardiomyopathy patients.

Study	Sample	Objective	Instruments	PEDro Score	Results
Botoni et al., 2007	Chagas dilated cardiomyopathy patients (n = 42; 71.4% men)	To verify the effect of renin-angiotensin system (RAS) inhibition on HRQoL in the overall population (n = 42) and, subsequently, the effect of carvedilol treatment on HRQoL in the experimental (n = 19) and placebo groups (n = 20)	SF-36	6/10	Improvements were found for the functional capacity (physical functioning) (p = 0.046), role physical (physical limitation) (p = 0.002), pain (bodily pain) (p = 0.021), general state (general health) (p < 0.001), and mental health (p = 0.033) domains of the SF-36 after RAS inhibition treatment. There was no improvement in any domain between the carvedilol treatment and the placebo groups.
Lima et al., 2010	Chagas dilated cardiomyopathy patients (n = 40; 57.5% men)	To verify the effect of a 12-week exercise training program on HRQoL	SF-36	6/10	The exercise training group (n = 21) showed improvements in the vitality (p = 0.013), role emotional (p = 0.012), and mental health (p = 0.031) domains of the SF-36 when compared to the inactive control group (n = 19).

HRQoL: health-related quality of life; PEDro: physiotherapy evidence database; RAS: renin-angiotensin system; SF-36: short-form of health Survey.

Regarding the cardiac form of the disease, Pelegrino et al.⁽¹⁵⁾ compared the HRQoL between patients with Chagas dilated cardiomyopathy (n = 43) and a non-ChD control group (n = 59) that was matched for age, sex, and left ventricular ejection fraction. The lowest HRQoL scores were found for the physical functioning (p = 0.01) and role physical (p = 0.002) domains of the SF-36 in patients with Chagas dilated cardiomyopathy. Moreover, even when similar degrees of systolic dysfunction were present, ChD patients were found to be in a lower functional class than the control group (p = 0.02).

The HRQoL of cardiac pacemaker patients was evaluated by two studies. One showed that the presence of ChD was not associated with SF-36 scores although the patients (n = 92, aged 65.3 ± 12.4 years) had a higher mortality rate resulting from cardiac causes (p = 0.04)⁽¹⁸⁾. Likewise, Oliveira et al.⁽²⁸⁾ showed no difference in HRQoL between ChD (n = 77) and non-ChD (n = 31) pacemaker patients in the physical (p = 0.094) and mental (p = 0.51) domains of the SF-36. However, ChD pacemaker patients had worse scores in the chest discomfort (p = 0.030) and arrhythmia (p = 0.004) domains of the SQUAREL. It can be hypothesized that the SF-36 may not be the most appropriate tool for the evaluation of HRQoL in ChD patients as it is a generic instrument.

Stroke is a serious complication of ChD that can lead to significant long-term disability. A recent study conducted

by Souza et al.⁽⁵⁾ evaluated the HRQoL in 21 ChD patients (aged 50.2 ± 13.9 years) with stroke sequelae using the WHOQOL-BREF and correlated it with depressive symptoms assessed by the BDI and functional performance by the Barthel Index (BI). They found a significant negative correlation between depressive symptoms and physical (r = -0.733, p = 0.001), psychological (r = -0.581, p = 0.012), environmental (r = -0.713, p = 0.001), and social (r = -0.659, p = 0.003) aspects of the patients' quality of life. However, functional performance was not associated with any aspects of the HRQoL. The authors suggest that the HRQoL of ChD patients after suffering a stroke is influenced to a higher degree by depressive symptoms than by the motor disability caused by the stroke sequelae.

Health-related quality of life and functional capacity in patients with Chagas heart disease

Regardless of the etiology, the main symptoms of heart failure are fatigue, dyspnea, and progressive impairment of functional capacity. All these factors contribute to a poor HRQoL⁽¹⁷⁾.

The six-minute walk test (6MWT) is a simple and inexpensive submaximal test to evaluate functional capacity⁽³¹⁾ and is widely used in ChD patients^{(20) (21) (23) (32) (33) (34)}. We identified two studies that aimed to verify the correlation between HRQoL and the distance walked in the 6MWT in ChD patients. Dourado et al.⁽²⁰⁾

TABLE 3 - Correlation between functional capacity and health-related quality of life in Chagas disease patients.

Study	Sample	Objective	Instruments	PEDro Score	Results
Dourado et al., 2006	Chagas cardiomyopathy patients (n = 61; 71% men)	To correlate HRQoL with submaximal functional capacity	MLwHFQ	1/10	HRQoL showed a correlation with submaximal functional capacity ($r = -0.4$; $p < 0.001$).
Ritt et al., 2013	Chagas cardiomyopathy patients (n = 55; 69% men)	To correlate HRQoL with functional capacity	MLwHFQ	4/10	HRQoL was associated with submaximal ($r = -0.375$; $p = 0.007$) and maximal functional capacity ($r = -0.301$; $p = 0.02$).
Costa et al., 2014	Chagas heart disease patients (n = 35; 66% men)	To correlate the functional capacity with HRQoL	SF-36 and MLwHFQ	1/10	The distance walked in the field test was associated with the MLwHFQ score ($r = -0.460$, $p = 0.006$) and with the physical functioning ($r = 0.435$; $p = 0.009$), role physical ($r = 0.447$; $p = 0.008$), and mental health ($r = 0.430$, $p = 0.011$) domains of the SF-36.
Vieira et al., 2014	ChD patients (n = 32; 56.3% men) with and without cardiopathy	To evaluate respiratory muscle strength and its association with functional capacity, QoL and rate of perceived exertion in patients with (n = 16) and without Chagas heart disease (n = 16).	MLwHFQ	2/10	Patients with Chagas heart disease presented a worse HRQoL in the overall score ($p = 0.001$), physical ($p = 0.002$), emotional ($p = 0.031$), and general health ($p < 0.001$) domains of the MLwHFQ when compared to the control group.

ChD: Chagas disease; HRQoL: health-related quality of life; MLwHFQ: Minnesota living with heart failure questionnaire; PEDro: physiotherapy evidence database; QoL: quality of life; SF-36: Short-form of health survey.

showed that the 6MWT distance was associated with the MLwHFQ score ($r = -0.4$; $p < 0.001$) in 61 patients with Chagas dilated cardiomyopathy (aged 51 ± 14 years). Similar results were found by Ritt et al.⁽²¹⁾ who showed a significant negative correlation ($r = -0.375$; $p = 0.007$) between better quality of life and higher 6MWT distance in a study involving 55 Chagas dilated cardiomyopathy patients with heart failure. The association between a submaximal functional capacity and quality of life found in these studies suggests that the evaluation of a patient's HRQoL is a useful tool for to detect any disabilities in the daily activities of ChD patients.

Another field test used to evaluate functional capacity is the Incremental Shuttle Walk Test, a symptom-limited test that was described by Singh et al.⁽³⁵⁾. The study of Costa et al.⁽²²⁾ was the first to correlate results from the Incremental Shuttle Walk Test with the HRQoL in ChD (evaluated by the SF-36 and MLwHFQ). The authors reported that the distance walked during this field test showed a significant positive correlation with MLwHFQ scores ($r = -0.460$; $p = 0.006$) and with the

physical functioning ($r = 0.435$; $p = 0.009$), role physical ($r = 0.447$; $p = 0.008$), and mental health ($r = 0.430$; $p = 0.011$) domains of the SF-36. The authors also demonstrated that the peak oxygen uptake that was assessed by cardiopulmonary exercise testing, the gold standard in the evaluation of functional capacity, only showed a statistically significant association with the physical functioning domain of the SF-36 ($r = 0.383$; $p = 0.025$). Hence, it seems that the perceived effect of ChD by the patient is more related to their daily activities than those that require intense effort.

Effect of conservative treatment strategies on the health-related quality of life in Chagas heart disease patients

In our literature search, two randomized trials that verified the effect of non-surgical treatment on the HRQoL of ChD patients were identified – one study assessed the effect of drug treatment⁽¹⁸⁾ on HRQoL, and the other one that of an exercise training program⁽¹⁹⁾.

Botoni et al.⁽¹⁸⁾ conducted a placebo-controlled study in 42 patients with Chagas dilated cardiomyopathy (aged 47.8 ± 10.4 years)

and assessed their HRQoL by the SF-36. All patients received renin-angiotensin system (RAS) inhibition therapy. Subsequently, the sample was divided into a placebo (n = 20) and a carvedilol group (n = 19). After RAS inhibition treatment, improvements of the HRQoL were seen for the physical functioning (p = 0.046), role physical (p = 0.002), bodily pain (p = 0.021), and general health (p < 0.001) domains. However, after carvedilol treatment, no improvement in the HRQoL scores were observed in the carvedilol group when compared to the placebo group in any of the SF-36 domains.

A study by Lima et al.⁽¹⁹⁾ evaluated the effect of aerobic exercise training on the HRQoL in patients with Chagas dilated cardiomyopathy (divided into a control and an experimental group) using the SF-36. After 12 weeks of exercise training, the experimental group showed improvements in the vitality (p = 0.013), role emotional (p = 0.012), and mental health (p = 0.031) domains of the SF-36 when compared to the control group. Surprisingly, significant improvements were only observed in the psychosocial domain. The authors explained this finding by the absence of functional impairment in the majority (63%) of the patients. Thus, participation in exercise programs has positive effects on ChD patients' HRQoL, likely due to interpersonal contact and care provided by the health staff.

The results of these randomized trials have great clinical meaning for the setting of ChD. Endemic areas are generally poor and with few resources. Therefore, the adoption of simple and inexpensive interventions is recommended to maximize the functionality and independence of these patients, reflecting a better HRQoL.

In conclusion, the evidence reported in the 12 selected studies suggests that the patients' functional capacity, the effectiveness of non-surgical conservative treatment, and cardiac involvement are important determining factors of the HRQoL in ChD patients.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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