Research Square

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Dizziness and quality of life in Chagas disease patients with cardiac implantable electronic devices

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Abstract

Purpose Residual symptoms, particularly dizziness, persist in many recipients of cardiac implantable electronic devices (CIED). We compared dizziness and quality of life in CIED patients with and without chronic Chagas cardiomyopathy (CCC).

Methods Cross-sectional study of consecutive CIED outpatients. The primary outcome was the presence of dizziness on systematic clinical assessment; the Dizziness Handicap Inventory measured burden. Quality of life was assessed with the Short Form-36 Health Survey (SF-36). Analyses used Firth penalized logistic and multiple linear regression, plus mediation analysis.

Results Of 100 patients (mean age 68.2 years, 59% women), 36 had CCC. The CCC group had lower ejection fraction ($p = 0.039$), worse functional class ($p = 0.024$), and more non-sustained ventricular tachycardia (50.0% vs 4.7%; $p < 0.001$). Dizziness was more frequent in CCC (83.3% vs 51.6%; $p = 0.002$) and remained independent after adjustment (odds ratio 3.96; 95% confidence interval 1.46–10.78; $p = 0.007$). Global SF-36 and its components were similar between groups, but dizziness was associated with lower global (45.6 vs 50.1; $p = 0.026$) and physical component (42.7 vs 50.0; $p = 0.002$) scores; mediation analysis showed a significant indirect effect of CCC on quality of life through dizziness. No drug class or comorbidity was associated with dizziness.

Conclusion CIED recipients with CCC report dizziness more often than other etiologies, independently of structural and arrhythmic burden and of medication, and dizziness is associated with worse physical quality of life. The variables evaluated did not identify the mechanism, supporting systematic assessment of dizziness in follow-up.

Introduction

Chagas disease remains an important cause of cardiomyopathy, conduction disturbances, and arrhythmias in Latin America, frequently leading to the implantation of cardiac implantable electronic devices (CIED). Although these devices reduce arrhythmic events and treat bradyarrhythmias, symptoms often persist during outpatient follow-up and cannot always be explained by the electrical substrate that prompted implantation alone [1].

Among these symptoms, dizziness deserves particular attention. It is a heterogeneous manifestation, frequently described as unsteadiness, presyncope, or a nonspecific sensation of malaise, with potential functional and emotional repercussions [2]. In Chagas cardiomyopathy, this complaint may acquire additional relevance because of the diffuse autonomic impairment, the hemodynamic changes, and the myocardial dysfunction that characterize the disease [3].

Although syncope is a classic manifestation in this population, its presence alone probably does not adequately reflect the overall symptom burden. Systematic assessment of dizziness may offer a more comprehensive view of the clinical experience of these patients.

In addition, quality of life in CIED recipients is rarely represented by a single global score [4]. The SF-36 (Short Form-36 Health Survey) allows different dimensions of health perception to be assessed, including physical limitations, social impact, pain, and mental health. Domain-level analysis may therefore identify specific patterns of impairment that are not captured by the aggregate components.

The present study therefore aimed to evaluate the association between Chagas disease, dizziness burden, and quality of life measured by the SF-36 in patients with cardiac implantable electronic devices.

Methods

Study population

This was a cross-sectional observational study of consecutive outpatients with a cardiac implantable electronic device followed at the outpatient cardiac device clinic of the Federal University of São Paulo (UNIFESP), São Paulo, Brazil. Patients were identified from a previously structured database; individuals recorded as deceased were excluded. Chronic Chagas cardiomyopathy was defined by two positive serological tests for *Trypanosoma cruzi* using different methods, together with electrocardiographic and/or echocardiographic abnormalities compatible with Chagas heart disease. Assessment was performed exclusively in the post-implantation phase, because the aim of the study was to characterize residual symptom burden and quality of life during outpatient follow-up, and not to evaluate the therapeutic effect of the device itself on dizziness. As all patients already had a functioning device in place, the comparison was made between etiologies (Chagas versus non-Chagas) under equivalent electrical therapy, rather than between the periods before and after implantation. The study was conducted in accordance with current ethical standards and was approved by the institutional research ethics committee (CAAE 69911423.6.0000.5505).

Assessment of dizziness

The primary outcome of dizziness was defined in binary form (presence or absence), based on systematic clinical assessment during outpatient follow-up. As a secondary measure of severity, dizziness burden was quantified with the Dizziness Handicap Inventory (DHI), a validated self-administered questionnaire that quantifies the self-perceived handicap resulting from dizziness [5]. The instrument comprises 25 items distributed across three domains — physical, emotional, and functional — with each item scored as “yes” (4 points), “sometimes” (2 points), or “no” (0 points), yielding a total score from 0 to 100; higher values indicate greater functional impact of dizziness. The version validated for Brazilian Portuguese was used [6]. The 25 items of the instrument are available in the Supplementary Material (Appendix 1). According to the severity classification proposed by Whitney et al. [7], the handicap resulting from dizziness is categorized as mild (0–30), moderate (31–60), or severe (61–100).

Assessment of quality of life

Quality of life was assessed with the SF-36 (Medical Outcomes Study 36-Item Short-Form Health Survey), a generic, multidimensional instrument widely used to measure self-reported health perception [8]. It comprises 36 items grouped into eight domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The version validated for Brazilian Portuguese was used [9], and its items are available in the Supplementary Material (Appendix 2). For each domain, the corresponding items were summed into a raw score, subsequently converted to a 0–100 scale by linear transformation, according to the formula: [(raw score obtained − lowest possible score) ÷ possible score range] × 100. On this scale, higher values indicate better health perception. The global score was calculated as the arithmetic mean of the eight domains. The physical component was defined as the mean of the physical functioning, role-physical, bodily pain, and general health domains, and the mental component as the mean of the vitality, social functioning, role-emotional, and mental health domains. Individual domains were additionally analyzed in an exploratory fashion.

Clinical variables

Chagas disease was defined as a binary variable. Syncope was considered on the basis of a documented clinical history. Age, body mass index, syncope, device type, left ventricular ejection fraction, diabetes mellitus, beta-blocker use, and polypharmacy (defined as the concurrent use of five or more drug classes) were included as covariates in the adjusted models.

Statistical analysis

The normality of continuous variables was assessed with the Shapiro-Wilk test, complemented by graphical inspection. Normally distributed variables were expressed as mean ± standard deviation and compared with the Welch t test; variables without a normal distribution were expressed as median and interquartile range and compared with the Mann-Whitney test. Categorical variables were expressed as absolute and relative frequencies and compared with the Pearson chi-square test or the Fisher exact test, as appropriate. The primary outcome of dizziness (present/absent) was analyzed by logistic regression; because of the number of events, Firth penalized logistic regression was adopted, with a parsimonious model adjusted for age and left ventricular ejection fraction, and results were expressed as odds ratio (OR) and 95% confidence interval (CI). For the quality-of-life outcomes (global SF-36 score, physical component, and mental component), multiple linear regression models were constructed with adjustment for age, body mass index, syncope, device type, left ventricular ejection fraction, diabetes mellitus, beta-blocker use, and polypharmacy; model adequacy was verified by residual analysis. The total Dizziness Handicap Inventory score was analyzed as a secondary measure of severity. In addition, the association between functional class and the general health domain was assessed by linear regression adjusted for age and sex. In an exploratory fashion, the association between the presence of dizziness and pharmacological variables (angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, beta-blocker, calcium channel blocker, loop diuretic, thiazide diuretic, aldosterone antagonist, and amiodarone) and comorbidities (atrial fibrillation and chronic kidney disease) was assessed by univariable Firth logistic regression, without correction for multiple testing. The hypothesis that the

association between Chagas disease and quality of life would be mediated by dizziness was assessed by mediation analysis, with estimation of the natural indirect and direct effects — the binary mediator modeled by Firth penalized logistic regression and the continuous outcome by linear regression, both adjusted for age and left ventricular ejection fraction — and confidence intervals obtained by bootstrapping with 5,000 resamples. Results were expressed as β coefficient, 95% CI, and p value. A two-sided significance level of 5% was adopted. All analyses were performed with R version 4.6.1 (R Foundation for Statistical Computing, Vienna, Austria), using the logistf package for the Firth penalized models.

Sample size

No a priori sample size calculation was performed, as the study used a convenience sample comprising all consecutive eligible patients registered in the database during the study period. Patients with a cardiac implantable electronic device in outpatient follow-up were considered eligible, and individuals recorded as deceased were excluded, resulting in 100 patients. In a sensitivity analysis, the available sample (36 patients with Chagas disease and 64 without the disease) provided 80% power to detect, at a two-sided significance level of 5%, a standardized between-group difference of moderate magnitude (Cohen d ≈ 0.58). For the primary outcome of dizziness (present versus absent; 83.3% versus 51.6%), the estimated statistical power was approximately 92%.

Results

One hundred patients with a cardiac implantable electronic device were included, of whom 36 (36%) had Chagas disease and 64 (64%) did not. Among the 64 non-Chagas patients, 14 (21.9%) had ischemic cardiomyopathy and the remainder had non-ischemic etiologies. Age was similar between groups (70.5 ± 12.2 versus 66.9 ± 16.8 years; p = 0.215), as was the prevalence of syncope (19.4% versus 20.3%; p = 1.000). Body mass index was lower in Chagas patients (20.2 ± 3.6 versus 22.3 ± 3.9 kg/m²; p = 0.009), as was left ventricular ejection fraction (median 52% [40–64] versus 60% [50–68]; p = 0.039). The distribution of NYHA functional class differed between groups (p = 0.024), with a predominance of NYHA II among Chagas patients and of NYHA I among non-Chagas patients; no patient was in NYHA IV. The clinical characteristics of the sample are presented in Table 1. The distribution of devices and their respective indications is presented in Table 2.

The frequency of dizziness was markedly higher among Chagas patients: 83.3% in the Chagas group versus 51.6% in non-Chagas patients (p = 0.002; Table 1). As a secondary measure of severity, the Dizziness Handicap Inventory score was numerically higher in the Chagas group (median 17 [8–64] versus 14 [8–18]; p = 0.079; Mann-Whitney test). The distribution by severity categories showed greater impairment in Chagas patients: moderate-to-severe dizziness (DHI ≥ 31) was present in 36.1% versus 4.7% (p < 0.001), mainly at the expense of the severe category (30.6% versus 1.6%). These findings reinforce, in terms of severity, the same direction observed for the primary outcome.

In contrast with this greater symptom burden, the global SF-36 score and its physical and mental components were similar between groups. In the exploratory analysis of individual domains, Chagas patients had worse performance in the bodily pain domain ($p < 0.001$) and a higher score in the role-emotional domain ($p = 0.016$), with no significant difference in the remaining domains (Table 3). Given the absence of patients in NYHA class IV, the relationship between functional status and quality of life was assessed by grouping patients into NYHA III versus NYHA I/II. Patients in NYHA III had a worse score in the general health domain (44.6 ± 11.0 versus 51.6 ± 10.7; $p = 0.039$), an association that persisted after adjustment for age and sex ($\beta = -7.69$; 95% CI −14.13 to −1.26; $p = 0.020$; Figure 1).

Among patients who underwent head-up tilt testing (24 Chagas and 29 non-Chagas), the frequency of a positive tilt test was similar between groups (37.5% versus 48.3%; $p = 0.579$), as was reproduction of habitual dizziness (33.3% versus 48.3%; $p = 0.401$). No differences were observed in the distribution of autonomic response patterns, including orthostatic hypotension, delayed orthostatic hypotension, vasovagal response, cardioinhibitory response, mixed response, orthostatic intolerance, and carotid sinus hypersensitivity (Table 4).

Multivariable analysis

In the Firth logistic regression adjusted for age and left ventricular ejection fraction, Chagas disease remained independently associated with the presence of dizziness (OR 3.96; 95% CI 1.46 to 10.78; $p = 0.007$). There was no independent association between Chagas disease and the global SF-36 score or its physical and mental components (Table 5). The presence of dizziness, in turn, was associated with worse quality of life, with a lower global SF-36 score (45.6 versus 50.1; $p = 0.026$) and, above all, a lower physical component score (42.7 versus 50.0; $p = 0.002$). In the mediation analysis, Chagas disease exerted a significant indirect effect on quality of life, operating through dizziness, both on the global SF-36 score (indirect effect −1.72; 95% CI −3.67 to −0.33) and on the physical component (−2.32; 95% CI −4.59 to −0.60); the direct and total effects were not significant. In an exploratory analysis of potential determinants of dizziness, none of the pharmacological classes evaluated and none of the comorbidities analyzed (atrial fibrillation and chronic kidney disease) showed an association with the presence of dizziness (all $p > 0.10$). As a secondary measure of severity, an exploratory association was observed between the DHI score and the response to head-up tilt testing ($p = 0.025$), detailed in the Discussion.

Seeking to identify possible mechanistic correlates for the higher frequency of dizziness observed in Chagas patients, we compared echocardiographic parameters and Holter recordings performed during the same follow-up period (Table 6). Structurally, Chagas patients had a thinner left ventricular posterior wall (median 9 mm versus 10 mm; $p = 0.006$), with a similar trend for the interventricular septum ($p = 0.059$), a pattern consistent with the dilated and hypokinetic pathophysiology of Chagas cardiomyopathy, in contrast with the predominantly hypertrophic profile observed in non-Chagas patients. On Holter monitoring, Chagas patients had lower mean (64.7 ± 9.8 versus 72.6 ± 11.5 bpm; $p = 0.002$) and maximum (109 ± 32 versus 125 ± 27 bpm; $p = 0.027$) heart rates, a higher burden of premature ventricular complexes (median 660 versus 87 complexes; $p = 0.044$), and a markedly higher frequency of

non-sustained ventricular tachycardia (50.0% versus 4.7%; $p < 0.001$). Heart rate variability, assessed by SDNN, was numerically reduced in Chagas patients without reaching statistical significance (104 ± 51 versus 122 ± 46 ms; $p = 0.143$). This more pronounced electrocardiographic pattern occurred despite the lower prevalence of ischemic etiology among Chagas patients, already shown in Table 1.

Discussion

The main findings of this study can be summarized in five observations. First, patients with Chagas disease and a cardiac implantable electronic device had greater structural impairment, characterized by lower ejection fraction and worse functional class. Second, they had greater electrical impairment, evidenced by lower mean heart rate, a higher burden of premature ventricular complexes, and a higher frequency of non-sustained ventricular tachycardia. Third, these patients had a higher frequency of dizziness. Fourth, despite this more severe structural and electrical phenotype, these abnormalities did not explain the intensity of symptoms. Finally, the set of cardiac and autonomic variables evaluated did not identify the mechanism responsible for the higher frequency of dizziness; in an exploratory analysis of severity, a possible association with the response to head-up tilt testing was observed, suggesting an autonomic contribution that remains to be confirmed.

The greater structural and arrhythmic impairment observed in Chagas patients is consistent with the natural history of Chagas cardiomyopathy. Chronic inflammation, diffuse myocardial fibrosis, and involvement of the conduction system promote ventricular remodeling, systolic dysfunction, and a high burden of ventricular arrhythmias, accounting for the greater need for cardiac devices in this population. Classic and contemporary studies consistently demonstrate that Chagas cardiomyopathy presents greater electrical complexity and a worse prognosis when compared with other etiologies of heart failure [3, 10–12].

However, one of the most relevant aspects of this study was to demonstrate that this greater cardiac impairment did not explain the higher frequency of dizziness. Despite the lower ejection fraction, the higher burden of ventricular arrhythmias, and the higher frequency of non-sustained ventricular tachycardia, none of these variables showed an independent association with symptoms. Likewise, pharmacological classes frequently related to dizziness, such as beta-blockers, calcium channel blockers, diuretics, and amiodarone, also did not remain associated after multivariable adjustment. These findings suggest that persistent dizziness in the Chagas patient does not simply represent a marker of greater cardiac severity, but probably reflects another pathophysiological component of the disease.

The most plausible hypothesis is the participation of autonomic dysfunction. Involvement of the autonomic nervous system is one of the earliest and best established features of Chagas disease and may occur independently of the degree of ventricular dysfunction. Changes in vagal modulation, reduced baroreflex sensitivity, lower chronotropic reserve, and orthostatic intolerance have been widely described in this population [3, 13–15]. These mechanisms compromise cardiovascular adaptation to postural

changes and may produce unsteadiness, presyncope, and persistent dizziness, even in the absence of significant arrhythmias or device failure.

In our analysis, the response to head-up tilt testing was not associated with the presence of dizziness, assessed as the primary outcome. However, in an exploratory analysis of severity, patients with higher Dizziness Handicap Inventory scores had a higher frequency of an abnormal response to the test ($p = 0.025$), suggesting that autonomic dysfunction may relate more to the intensity than to the simple presence of the symptom. This hypothesis-generating observation indicates that the investigation of dizziness in this population may benefit from systematic assessment of the orthostatic hemodynamic response, information that is not provided by the methods traditionally used in the follow-up of CIED recipients.

This observation carries relevant clinical implications. In Chagas patients who remain symptomatic despite adequate device function and the absence of arrhythmias accounting for the symptoms, investigation of orthostatic hypotension, a vasodepressor response, or orthostatic intolerance may directly modify clinical management. Identifying these phenotypes makes it possible to optimize hydration, review doses of diuretics and vasodilators, provide postural guidance, and implement specific strategies for symptom prevention — approaches that would hardly be considered if dizziness were attributed exclusively to structural cardiac impairment.

Although Chagas patients had a higher frequency of dizziness, this difference did not translate into a worse global SF-36 score, which nevertheless does not mean an absence of impact. In the mediation analysis, the effect of Chagas disease on quality of life proved to be partly indirect, operating through the higher frequency of dizziness: the indirect effect was significant both on the global score (−1.72; 95% CI −3.67 to −0.33) and, more markedly, on the physical component (−2.32; 95% CI −4.59 to −0.60). This negative indirect effect was counterbalanced by a non-significant direct effect of opposite sign, so that the total effect of etiology on global health perception was close to null. A generic global score therefore tends to dilute specific and opposing influences from each domain: dizziness, more frequent in the Chagas patient, is associated with worse physical quality of life, while other dimensions remain relatively preserved. Previous studies have shown heterogeneous results regarding the impact of Chagas disease on quality of life, with functional class being one of the most consistent determinants of global health perception [16–21]. Our findings add that specific symptoms, such as dizziness, exert a measurable impact on defined domains of quality of life, even though this is barely apparent in the global score. Given its cross-sectional and exploratory nature, this mediation analysis should be interpreted as hypothesis-generating.

Limitations

This study has limitations. Its cross-sectional design precludes causal inference, and the mediation analysis, although formally estimated, rests on assumptions that cannot be verified with data collected at a single time point. The convenience sample from a single center limits generalizability, and no a priori sample size calculation was performed. Dizziness was ascertained as a binary clinical variable, which

does not distinguish between its different phenotypes. Head-up tilt testing was available in only 53 patients and Holter data in a subset of the sample, which reduces power for these comparisons. The exploratory analyses of individual SF-36 domains and of pharmacological determinants were performed without correction for multiple testing and should be interpreted accordingly. Finally, device interrogation data and time since implantation were not incorporated into the models, and residual confounding cannot be excluded.

Taken together, the findings demonstrate that Chagas patients with a cardiac implantable electronic device present a more severe phenotype from structural, electrical, and symptomatic standpoints, with a higher frequency of dizziness and repercussions on quality of life. However, the greater cardiac impairment, drug use, and the autonomic variables evaluated did not, in isolation, explain the higher frequency of dizziness. An exploratory analysis of severity suggested a possible autonomic contribution, a hypothesis that warrants targeted investigation. Systematic assessment of dizziness — and the incorporation of autonomic evaluation into follow-up — may therefore complement the conventional investigation based on echocardiography, Holter monitoring, and device interrogation.

Conclusion

Patients with Chagas disease and a cardiac implantable electronic device have a higher frequency of dizziness, independently of structural and arrhythmic impairment and of drug use, with repercussions on quality of life. The cardiac and autonomic variables evaluated did not identify the mechanism responsible for this greater symptom burden. An exploratory analysis of severity, based on the Dizziness Handicap Inventory, suggested a possible contribution of the autonomic response, reinforcing the need for targeted investigation of dizziness as a clinically relevant and potentially modifiable symptom in the follow-up of this population.

Abbreviations

AV, atrioventricular; BMI, body mass index; CCC, chronic Chagas cardiomyopathy; CI, confidence interval; CIED, cardiac implantable electronic device; CRT, cardiac resynchronization therapy; DHI, Dizziness Handicap Inventory; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; LVEF, left ventricular ejection fraction; NSVT, non-sustained ventricular tachycardia; NYHA, New York Heart Association; OR, odds ratio; PM, pacemaker; PVC, premature ventricular complex; SDNN, standard deviation of normal-to-normal RR intervals; SF-36, Short Form-36 Health Survey; SND, sinus node dysfunction.

Declarations

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Author contributions. All authors contributed to the study conception and design. The specific contributions were as follows:

Pedro Henrique Correia Filgueiras: conception and design, data collection, data analysis and interpretation, statistical analysis, drafting of the article, and final approval.

Rhanniel Theodorus Helhyas Oliveira Shilva Gomes Villar: data collection, statistical analysis, critical revision of the article, and final approval.

Carlos Arthur Hansel Diniz da Costa: statistical analysis, drafting of the article, and final approval.

Alexandre Costa Souza: critical revision of the article and final approval.

Bárbara Oliveira da Eira: conception and design, critical revision of the article, and final approval.

Claudio Cirenza: critical revision of the article and final approval.

Angelo Amato Vincenzo de Paola: conception and design, critical revision of the article, and final approval.

Ethics approval. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Research Ethics Committee of the Federal University of São Paulo (UNIFESP) (CAAE 69911423.6.0000.5505).

Consent to participate. Written informed consent was obtained from all individual participants included in the study.

Consent to publish. Not applicable. The manuscript does not contain data from any individual person in a form that would permit identification.

Data availability. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Patient and public involvement. Patients or members of the public were not involved in the design, conduct, reporting, or dissemination of this study.

Clinical trial registration. Not applicable. This is an observational cross-sectional study and was not registered as a clinical trial.

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Tables

Tables are available in the Supplementary Files section.

Figures

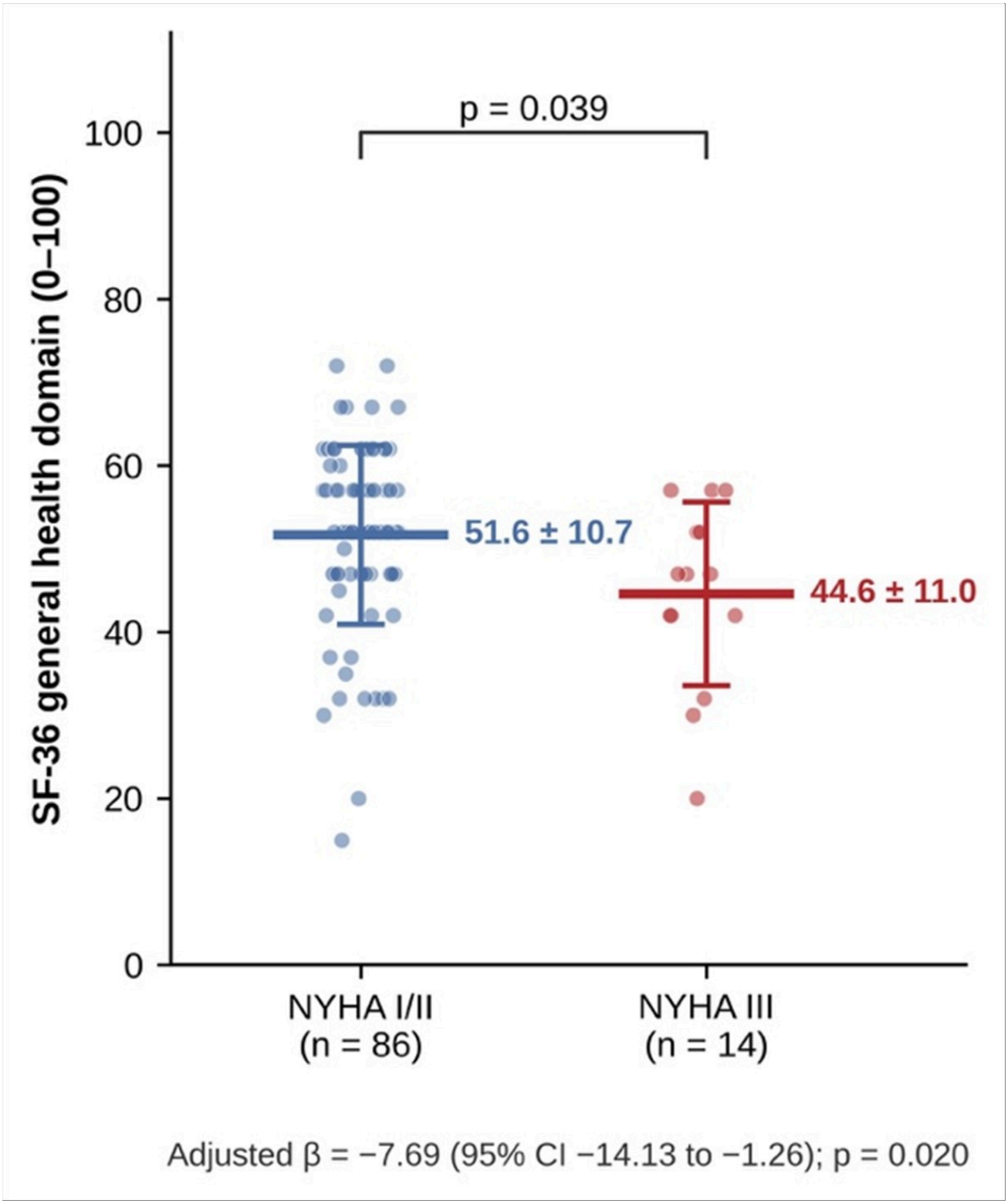


Figure 1

Association between NYHA functional class III (versus class I/II) and the SF-36 general health domain, adjusted for age and sex by linear regression (β = −7.69; 95% CI −14.13 to −1.26; p = 0.020). CI confidence interval; NYHA New York Heart Association; SF-36 Short Form-36 Health Survey

Supplementary Files

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