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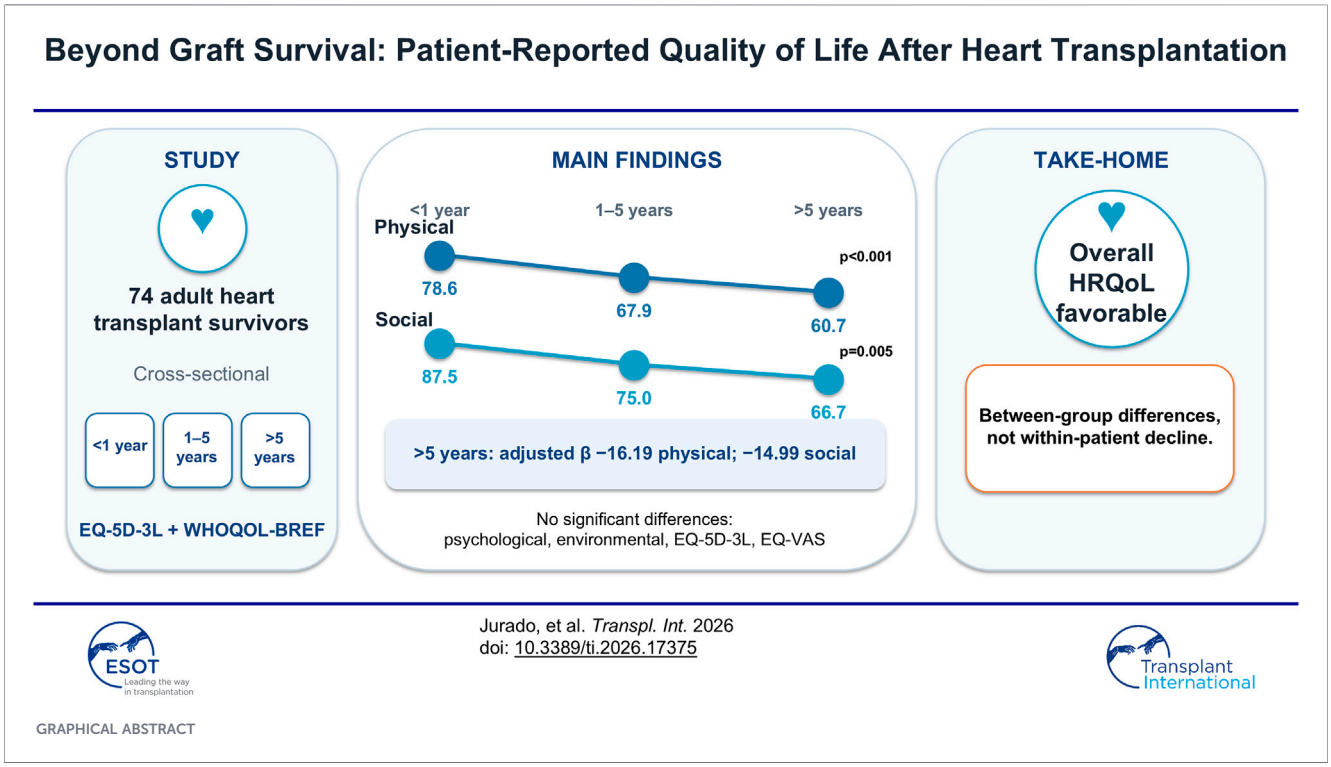
Beyond graft survival: patient-reported quality of life after heart transplantation

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Heart transplantation improves survival in advanced heart failure; however, long-term success also includes patient-reported outcomes such as health-related quality of life (HRQoL). To assess HRQoL among heart transplant recipients and examine associations with sociodemographic and clinical characteristics, we conducted an analytical cross-sectional study nested within a historical cohort. Seventy-four surviving heart transplant recipients completed a structured interview. HRQoL was assessed using the EQ-5D-3L and WHOQOL-BREF instruments. WHOQOL-BREF scores were compared across post-transplant time groups (<1 year, 1–5 years, and >5 years) using the Kruskal–Wallis test. Multivariable linear regression examined adjusted associations with WHOQOL-BREF domains. Overall HRQoL was favorable, with most participants reporting no limitations across EQ-5D-3L dimensions. Physical and social scores differed across post-transplant time groups ($p < 0.001$ and $p = 0.005$, respectively) and were lower with longer time since transplantation. More than 5 years since transplantation was associated with lower physical ($\beta = -16.19$; 95% CI, −25.70 to −6.68; $p = 0.001$) and social scores ($\beta = -14.99$; 95% CI, −27.13 to −2.86; $p = 0.016$). Older age was associated with lower social scores ($\beta = -0.46$; $p = 0.002$), whereas higher socioeconomic status was associated with higher environmental scores ($\beta = 32.03$; $p = 0.010$). HRQoL was generally favorable among surviving recipients. In sensitivity analyses additionally accounting for frailty and GAD-2, the association with the physical domain remained, whereas the association with the social domain was attenuated. Longer time since transplantation was associated with lower physical and social scores, whereas psychological and environmental scores did not differ significantly. These cross-sectional findings do not demonstrate within-patient decline over time.

KEYWORDS
activities of daily living, health status, heart transplantation, psychosocial factors, quality of life



Introduction

Heart failure remains a major cause of morbidity, mortality, and healthcare utilization worldwide. In Latin America, its burden is further intensified by persistent inequalities in access to specialized care and advanced heart failure therapies [1, 2]. For carefully selected patients with advanced heart failure who remain symptomatic despite optimal medical and device-based treatment, heart transplantation represents the definitive therapeutic option, offering substantial benefits in survival, functional capacity, and quality of life [3–5].

Advances in surgical techniques, perioperative management, immunosuppressive therapy, and post-transplant care have markedly improved survival after heart and solid organ transplantation. Nevertheless, long-term outcomes remain influenced by complications such as rejection, cardiac allograft vasculopathy, infection, malignancy, renal dysfunction, and the cumulative effects of chronic immunosuppression [6, 7]. Consequently, the success of heart transplantation cannot be evaluated solely in terms of patient or graft survival, graft function, or rejection rates. Increasing emphasis is therefore being placed on patient-centered outcomes that more comprehensively reflect the long-term experience of transplant recipients, including health-related quality of life (HRQoL), functional recovery, social participation, and the ability to resume meaningful daily activities. Recent perspectives in transplantation have accordingly highlighted the need to move beyond traditional survival-based outcomes toward the broader goal of enabling recipients not only to live longer, but also to live well after transplantation [8].

Patient-reported outcomes have therefore gained increasing importance as measures of outcomes that are directly meaningful to transplant recipients [9]. Health-related quality of life (HRQoL) is particularly relevant because the goals of transplantation extend beyond prolonging life to include improvements in functional capacity, psychological wellbeing, social participation, and daily functioning. Cross-sectional studies, prospective cohorts, and systematic reviews have shown that HRQoL generally improves after heart transplantation, particularly during the first post-transplant year, and is often better than that reported by patients with advanced heart failure [10–13]. Nevertheless, these benefits are not uniform. Some recipients continue to experience physical limitations, symptom burden, psychological distress, or difficulties in social functioning despite satisfactory graft function and survival [14, 15]. HRQoL may also be shaped by age, comorbidity burden, exercise capacity, depression, treatment-related symptoms, socioeconomic conditions, and social support [16, 17].

The EQ-5D-3L assesses mobility, self-care, usual activities, pain or discomfort, anxiety or depression, and overall self-rated health [18]. In contrast, the WHOQOL-BREF evaluates broader physical, psychological, social, and environmental dimensions of quality of life [19]. Used together, these instruments provide complementary information on perceived health status and multidimensional wellbeing. Despite the extensive international literature, evidence from Latin American and middle-income settings remains limited. Regional studies have predominantly focused on transplant activity, survival, and clinical outcomes, with less attention to multidimensional patient-reported outcomes among adult survivors [6, 7]. Therefore, this study aimed to assess HRQoL among heart transplant recipients and examine its associations with sociodemographic and clinical characteristics.

Materials and methods

Study design and population

A cross-sectional analysis of survivors from a historical cohort of heart transplant recipients was conducted at a national cardiovascular referral center in a middle-income country. Quality-of-life assessment was performed at a single time point among surviving recipients listed in the institutional transplant database who could be contacted by telephone and agreed to participate. The source cohort comprised all patients who underwent heart transplantation at the institution between June 6, 2006, and January 22, 2026. Therefore, the analytical sample represented surviving, contactable recipients who completed the interview rather than the entire historical transplant cohort, which should be considered when interpreting the representativeness of the findings.

For the present analysis, adult heart transplant recipients who were alive at the time of contact and were able to complete the structured interview were considered eligible. Patients who had died before the interview, those without updated contact information, and those who could not be contacted or did not complete the interview were excluded. A total of 74 surviving heart transplant recipients completed the interview and were included in the final analysis (Figure 1).

Data collection

Data were collected through a structured telephone interview conducted by trained personnel using electronic forms developed in REDCap. Information obtained during the interview was complemented by clinical data previously recorded in the institutional heart transplant database [20, 21].Prior to analysis, data-quality checks were performed to assess internal consistency, missingness, and coherence across variables. Validated Spanish-language versions of the EQ-5D-3L and WHOQOL-BREF were administered to assess HRQoL.

During the interview, standardized instruments were administered to evaluate health-related quality of life. The EQ-5D-3L and WHOQOL-BREF questionnaires were used; both are widely validated generic patient-reported outcome measures [18, 19].

The EQ-5D-3L evaluates five dimensions of health status: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It also includes a visual analogue scale (EQ-VAS), on which participants rate their overall health from 0 to 100. The WHOQOL-BREF assesses quality of life across four domains: physical health, psychological wellbeing, social relationships, and environment. The combined use of these instruments provided complementary information on perceived health status and broader dimensions of wellbeing.

Study variables

The dependent variables were the domain scores of the WHOQOL-BREF. Independent variables included sociodemographic characteristics such as age at transplantation and at the time of the interview, sex, educational level, marital status, type of health insurance, area of residence, and socioeconomic status. Clinical variables included transplant period, time since transplantation, waiting-list time, etiology of heart failure, recipient status at listing, New York Heart Association (NYHA) functional class, left ventricular ejection fraction classification, transplant type, blood group, *Trypanosoma cruzi* serology, and prior comorbidities. Anxiety symptoms were screened using the 2-item Generalized Anxiety Disorder scale (GAD-2), an ultra-brief instrument derived from the GAD-7, with scores ranging from 0 to 6 [22]. Frailty was assessed using the 5-item FRAIL Scale, which evaluates fatigue, resistance, ambulation, illnesses, and weight loss; participants were classified as robust (0 points), prefrail (1–2 points), or frail (3–5 points) [23].

Statistical analysis

A descriptive analysis of the study population was performed. Continuous variables were summarized as mean ± standard deviation (SD) for normally distributed data, or as median and interquartile range (IQR) otherwise. Normality of continuous variables was assessed using graphical methods and the Shapiro–Wilk test. Categorical variables were reported as absolute and relative frequencies. For the EQ-5D-3L, each dimension (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) was described according to the proportion of participants reporting no problems, some problems, or extreme problems. EQ-VAS and WHOQOL-BREF domain scores were treated as continuous variables. WHOQOL-BREF domain scores were calculated according to the instrument manual and transformed to a 0–100 scale, with higher scores indicating better quality of life [24].

WHOQOL-BREF domain scores were also compared across post-transplant time groups (<1 year, 1–5 years, and >5 years) using the Kruskal–Wallis test. Bivariate associations between WHOQOL-BREF domains and sociodemographic, clinical, and transplant-related variables were assessed using linear regression models, with categorical variables encoded as dummy variables. Variables with clinical relevance or a p-value <0.20 in bivariate analysis were considered for inclusion in multivariable models. Multivariable linear regression models were fitted to examine adjusted associations with WHOQOL-BREF domain scores, and regression coefficients (β) with 95% confidence intervals (CI) were reported.

Model assumptions, including linearity, normality of residuals, homoscedasticity, and absence of multicollinearity (assessed using variance inflation factors, VIF), were evaluated. Normality of residuals was assessed using graphical methods (Q–Q plots) and the Shapiro–Wilk test. Model fit was assessed using the coefficient of determination (R^2) and residual diagnostics. Parsimonious models were prioritized to minimize overfitting given the sample size. Analyses were conducted using available data for each variable, and no imputation was performed for missing data.

To further address potential clinical and psychological confounding, we performed extended multivariable analyses incorporating concurrent frailty status and anxiety symptoms. Frailty was dichotomized as non-frail versus pre-frail/frail because of the small number of participants classified as frail, and anxiety symptoms were modeled using the continuous GAD-2 score. The extended models were considered sensitivity analyses because frailty and anxiety were assessed contemporaneously with HRQoL and could represent intermediate clinical characteristics rather than baseline confounders. All statistical tests were two-sided,

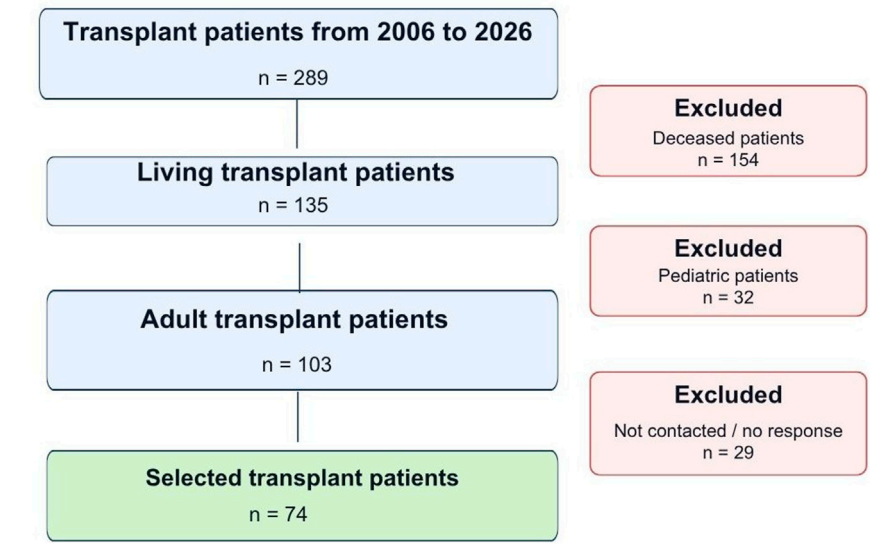


FIGURE 1
Flowchart of heart transplant recipients included in the study.

with statistical significance set at $p < 0.05$. Analyses were performed using Stata version 16.0 (StataCorp, College Station, TX, USA).

Ethical considerations

The study was conducted in accordance with ethical principles for research involving human subjects and institutional regulations. Data was stored in a secure REDCap database with restricted access to authorized investigators. Interviews were conducted ensuring participants' privacy and confidentiality. The study protocol was approved by the institutional ethics committee (Approval No. CEI 2026-11023), in accordance with national regulations for observational studies in human subjects.

Results

A total of 74 heart transplant recipients were included in the study. Most participants were male (79.73%). The median age at the time of transplantation was 51 years (IQR: 44–56), and at the time of the interview was 59 years (IQR: 53–64). Regarding marital status, 71.62% were living with a partner. Most participants were affiliated with the contributory health insurance regime (52.70%), followed by the subsidized regime (36.49%). The majority resided in urban areas (93.24%), and most belonged to a low socioeconomic stratum (66.22%). In terms of transplant characteristics, most procedures were orthotopic (97.30%), and more than half were performed between 2020 and 2026 (58.11%). Regarding time since transplantation, 45.95% of patients had 1–5 years of follow-up and 45.95% had more than 5 years (Figure 2).

The clinical characteristics of the study indicate advanced heart failure and severe systolic dysfunction. Among the 45 patients with available data, the median waiting-list time was 21 days (IQR: 6–56). Chagasic cardiomyopathy was the most frequent etiology (33.78%), followed by dilated (29.73%) and ischemic cardiomyopathy (17.57%). At the time of listing, half of the patients were classified as urgent (0A) (50.00%), and 27.27% as intermediate (0B), indicating a cohort with substantial clinical severity. This is consistent with functional status, as most patients were in New York Heart Association (NYHA) functional class III (46.15%) or IV (51.92%). Blood group distribution was predominantly O+ (48.65%). Regarding comorbidities, arterial hypertension (18.92%) and diabetes mellitus (12.16%) were the most frequent and previous cardiovascular surgery was documented in 18.18% of patients with available data (Table 1).

In the overall sample, most participants reported no limitations across EQ-5D-3L dimensions. The highest proportions of "no problems" were observed in self-care (93.2%) and anxiety/depression (91.9%), followed by usual activities (85.1%) and mobility (77.0%). Pain/discomfort showed the greatest residual burden, with 31.1% of participants reporting some level of impairment. When stratified by time since transplantation, no statistically significant differences were observed across groups in any EQ-5D-3L dimension (Figure 3).

In the mobility domain, the proportion of patients reporting any problem was 0.0% in the <1 year group, 17.6% in the 1–5 years group, and 32.4% in the >5 years group ($p = 0.134$). In self-care, these proportions were 0.0%, 8.8%, and 5.9%, respectively ($p = 0.702$). For usual activities, the frequency of problems was similar across groups (16.7%, 14.7%, and 14.7%; $p = 0.992$). In pain/discomfort, the proportion reporting impairment was 33.3% in the <1 year group, 38.2% in the 1–5 years group, and 23.5% in the >5 years group ($p = 0.421$). Finally, in anxiety/depression, the proportions were 0.0%, 2.9%, and 14.7%, respectively ($p = 0.155$).

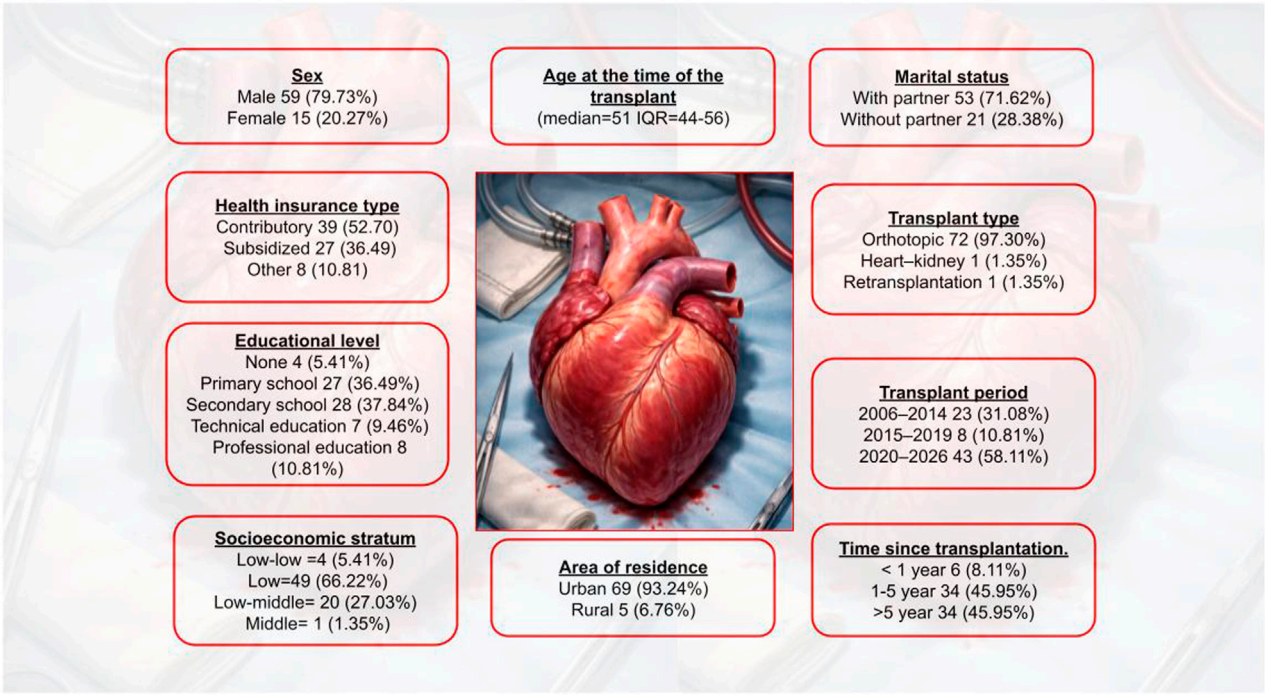


FIGURE 2
Sociodemographic and transplant-related characteristics of heart transplant recipients.

Overall health perception assessed by the EQ-5D visual analogue scale did not differ significantly according to time since transplantation. Median scores were 88 (IQR: 80–98) in patients with <1 year, 85 (IQR: 80–90) in those with 1–5 years, and 80 (IQR: 80–90) in those with >5 years (p = 0.500) (Figure 3).

For the two global WHOQOL-BREF items, participants generally reported a favorable perception of quality of life. Overall, 78.4% rated their quality of life as "quite good", and 9.5% as "very good", whereas 12.2% placed it in an intermediate category. Similarly, 71.6% reported being quite satisfied with their health, 13.5% were very satisfied, 13.5% expressed an intermediate perception, and 1.4% reported dissatisfaction. When these responses were examined according to time since transplantation, the <1 year group concentrated a greater proportion of favorable responses, whereas the >5 years group showed a relatively broader distribution toward intermediate or less favorable categories (Figure 4).

The physical and social relationships domains of the WHOQOL-BREF showed statistically significant differences across time-since-transplant groups. In the physical domain, the median score was 78.6 (IQR: 64.3–85.7) in patients with <1 year since transplantation, 67.9 (IQR: 64.3–75.0) in those with 1–5 years, and 60.7 (IQR: 50.0–67.9) in the >5 years group (p = 0.0005). A similar pattern was observed in the social relationships domain. Median scores were 87.5 (IQR: 75.0–100.0) in the <1 year group, 75.0 (IQR: 66.7–83.3) in the 1–5 years group, and 66.7 (IQR: 58.3–75.0) in the >5 years group, with a statistically significant difference (p = 0.005) (Figure 4).

In contrast, no significant differences were identified in the psychological or environment domains. In the psychological domain, median scores were 85.4 (IQR: 83.3–95.8) in the <1 year group, 79.2 (IQR: 66.7–87.5) in the 1–5 years group, and 77.1 (IQR: 70.8–83.3) in the >5 years group (p = 0.272). For the environment domain, median scores were 76.6 (IQR: 65.6–90.6), 75.0 (IQR: 71.4–84.4), and 71.9 (IQR: 67.9–75.0), respectively (p = 0.148) (Figure 4).

In the multivariable linear regression analyses of WHOQOL-BREF domains, time since transplantation was significantly associated with the physical domain. Patients with more than 5 years post-transplant had lower physical domain scores compared with the reference group (β = −16.19, 95% CI −25.70 to −6.68, p = 0.001), whereas patients 1–5 years post-transplant did not differ significantly (β = −7.06, 95% CI −16.57 to 2.46, p = 0.144). In the social domain, older age at the interview remained associated with lower social domain scores after multivariable adjustment (β = −0.46, 95% CI −0.75 to −0.17, p = 0.002). Compared with patients transplanted less than 1 year previously, those 1–5 years post-transplant had lower social scores, although the association was not statistically significant (β = −10.62, 95% CI −22.58 to 1.35, p = 0.081), whereas patients more than 5 years post-transplant had significantly lower social scores (β = −14.99, 95% CI −27.13 to −2.86, p = 0.016). These estimates represent cross-sectional differences between groups defined by time since transplantation and should not be interpreted as within-patient change over time (Table 2).

All models were statistically significant. The physical domain model explained 20.8% of the variability in scores (F = 9.33, p = 0.0003), followed by the social domain (R^2 = 0.203; F = 7.20, p = 0.0003) and the environmental domain (R^2 = 0.123; F = 3.28, p = 0.0258). No relevant multicollinearity was detected across models (mean VIF range: 2.80–3.60).

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TABLE 1 Clinical characteristics of heart transplant recipients included in the study.

Variable	n (%)
Waiting-list time, days - median (IQR), n = 45	21.00 (6.00–56.00)*
Heart failure etiology	
Chagasic	25 (33.78)
Dilated	22 (29.73)
Ischemic	13 (17.57)
Idiopathic	5 (6.76)
Congenital	2 (2.70)
Hypertensive	2 (2.70)
Valvular	2 (2.70)
Other	1 (1.35)
Chemotoxicity-related	1 (1.35)
Restrictive	1 (1.35)
Recipient status at listing	
Unclassified	5 (6.76)
Urgent 0A	22 (29.73)
Intermediate 0B	12 (16.22)
Elective	5 (6.76)
Missing	30 (40.54)
AHA stage	
Stage C	12 (16.22)
Stage D	9 (12.16)
Missing	53 (71.62)
NYHA functional class	
II	1 (1.35)
III	24 (32.43)
IV	27 (36.49)
Missing	22 (29.73)
LVEF classification	
Reduced	60 (81.08)
Missing	14 (18.92)
Blood group	
O+	36 (48.65)
A+	21 (28.38)
B+	11 (14.86)
A−	2 (2.70)
AB+	2 (2.70)
O−	2 (2.70)
***Trypanosoma cruzi* serology**	
Negative	28 (37.84)
Positive	13 (17.57)
Not performed	1 (1.35)
Missing	32 (43.24)
Comorbidities	
Arterial hypertension	14 (18.92)
Diabetes mellitus	9 (12.16)
Dyslipidemia	3 (4.05)
Coronary artery disease	8 (10.81)
Smoking	6 (8.11)
Alcohol use	0 (0.00)
Previous cardiovascular surgery	4 (5.41)
Frailty status, n = 72	
Non-frail	39 (54.17)
Pre-frail	28 (38.89)
Frail	5 (6.94)
GAD-2 score, n = 73	0 (0–2)*
GAD-2 screening, n = 72	
No probable anxiety	70 (97.22)
Probable anxiety	2 (2.78)

AHA, American Heart Association; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction. Data are presented as n (%) or median (interquartile range, IQR). Percentages were calculated using available data for each variable. Denominators vary due to missing data as follows: recipient status at listing (n = 44), NYHA functional class (n = 52), LVEF classification (n = 60), *Trypanosoma cruzi* serology (n = 43), and previous cardiovascular surgery (n = 22). *Values are presented as median (interquartile range, IQR).

In extended multivariable analyses additionally (Table 3) accounting for frailty status and GAD-2 score, the association between being assessed more than 5 years after transplantation and lower physical HRQoL remained significant (β = −17.69; 95% CI, −26.96 to −8.43; $p < 0.001$). Higher GAD-2 scores were also independently associated with lower physical-domain scores (β = −3.00 per point; 95% CI, −5.71 to −0.29; $p = 0.031$), whereas pre-frail/frail status was not independently associated with the physical domain (β = −3.93; 95% CI, −9.06 to 1.21; $p = 0.132$).

For the social domain, recipients assessed more than 5 years after transplantation continued to have lower scores after additional adjustment for frailty and GAD-2 (β = −13.40; 95% CI, −26.10 to −0.69; $p = 0.039$). Older age also remained independently associated with lower social-domain scores (β = −0.52 per year; 95% CI, −0.83 to −0.21; $p = 0.001$), whereas neither GAD-2 score nor frailty status was independently associated with the social domain.

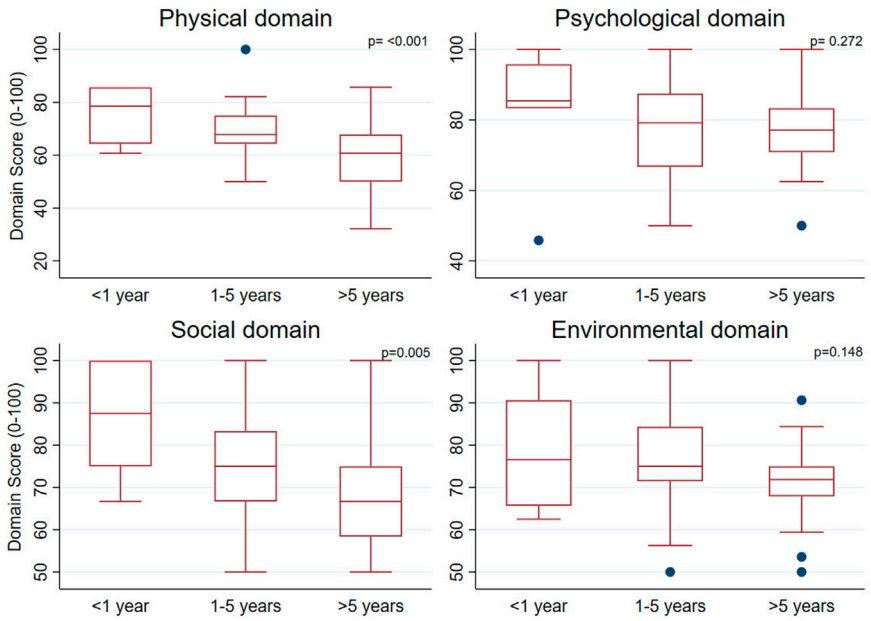


FIGURE 3
EQ-5D-3L dimensions and overall health perception according to time since heart transplantation.

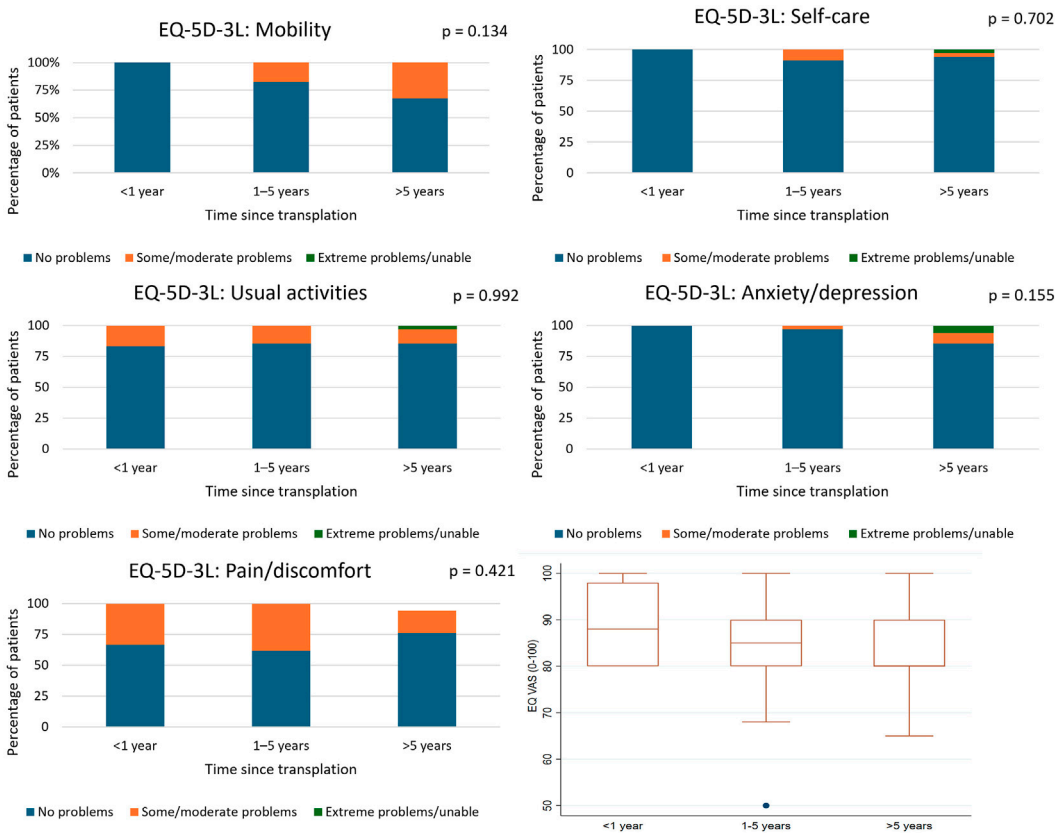


FIGURE 4
WHOQOL-BREF domain scores according to time since heart transplantation.

TABLE 2 **Multivariable linear regression results by WHOQOL-BREF domain.**

Domain	Variable	β (coefficient)	95% CI	p-value
Physical	1–5 years post-transplant	−7.06	−16.57 to 2.46	0.144
	>5 years post-transplant	−16.19	−25.70 to −6.68	0.001
Social	Age at the interview (Years)	−0.46	−0.75 to −0.17	0.002
	1–5 years post-transplant	−10.62	−22.58 to 1.35	0.081
	>5 years post-transplant	−14.99	−27.13 to −2.86	0.016
Environmental	Socioeconomic stratum low	5.25	−6.01 to 16.52	0.356
	Socioeconomic stratum low- middle	10.15	−1.71 to 22.02	0.092
	Socioeconomic stratum middle	32.03	7.80 to 56.26	0.010

Post-transplant time was categorized as <1 year, 1–5 years, and >5 years, using <1 year as the reference category. For the environmental domain, socioeconomic strata were compared using the low–low stratum as the reference group.

TABLE 3 **Extended multivariable sensitivity analyses of WHOQOL-BREF physical and social domains.**

Domain	Variable	β coefficient	95% CI	p-value
Physical	1–5 years post-transplant	−7.74	−17.12 to 1.65	0.105
	>5 years post-transplant	−17.69	−26.96 to −8.43	<0.001
	GAD-2 score, per point	−3.00	−5.71 to −0.29	0.031
	Pre-frail/frail	−3.93	−9.06 to 1.21	0.132
Social	Age at interview, per year	−0.52	−0.83 to −0.21	0.001
	1–5 years post-transplant	−8.69	−21.31 to 3.93	0.174
	>5 years post-transplant	−13.40	−26.10 to −0.69	0.039
	GAD-2 score, per point	−1.15	−4.86 to 2.56	0.540
	Pre-frail/frail	2.72	−4.33 to 9.78	0.444

Extended models additionally included concurrent frailty status and GAD-2 score. Frailty was dichotomized as non-frail versus pre-frail/frail because of the small number of participants classified as frail. GAD-2 was modeled as a continuous score. Post-transplant time was categorized as <1 year, 1–5 years, and >5 years, using <1 year as the reference category. The physical-domain model included post-transplant time, GAD-2 score, and frailty status. The social-domain model additionally included age at interview. Analyses were performed using complete available observations (n = 72).

Discussion

In this cross-sectional study of 74 surviving heart transplant recipients, participants evaluated more than 5 years after transplantation had lower physical and social WHOQOL-BREF domain scores than those assessed within the first post-transplant year. Recipients evaluated 1–5 years after transplantation also had lower social scores, although this difference did not reach statistical significance. Older age was associated with lower social domain scores, whereas psychological and environmental scores did not differ significantly across time-since-transplant groups. These findings represent between-group differences observed at a single point in time and should not be interpreted as evidence of within-patient decline, stability, or longitudinal HRQoL trajectories.

A growing body of evidence indicates that, although heart transplantation substantially improves survival and early HRQoL, long-term outcomes remain heterogeneous and are associated with a range of clinical and non-clinical factors [7]. Contemporary data show that survival beyond the first post-transplant year exceeds 90%, reflecting major advances in surgical techniques, perioperative management, and immunosuppressive therapy. Nevertheless, long-term outcomes continue to be affected by cardiac allograft vasculopathy, malignancy, infection, renal dysfunction, and the cumulative toxicity of chronic immunosuppression [25]. In addition to increasing morbidity and mortality, these complications may be associated with functional impairment and reduced physical capacity among long-term survivors. Studies evaluating recipients more than two decades after transplantation have similarly shown that, despite preserved cardiac function and relatively favorable psychological wellbeing, some patients continue to report lower physical quality of life and persistent somatic symptoms compared with the general population [26, 27].

Qualitative and systematic evidence further emphasizes the multidimensional nature of HRQoL after heart transplantation, highlighting the relation between social support, psychological adaptation, and environmental conditions on long-term wellbeing

[28]. These observations reinforce the need to view heart transplantation not only as a life-saving intervention but also as a chronic health condition requiring sustained multidisciplinary care focused on physical functioning, psychosocial adaptation, social participation, and patient-reported outcomes.

The lower physical domain scores observed among recipients evaluated more than 5 years after transplantation are consistent with previous reports describing persistent functional limitations in some long-term heart transplant survivors [16, 17, 28, 29]. Longitudinal evidence suggests that the greatest gains in HRQoL generally occur during the first post-transplant year, followed by variable patterns over subsequent years [28]. However, the differences identified in the present study cannot be attributed to post-transplant duration alone. Patients with longer time since transplantation were also older and may have had greater cumulative exposure to chronic immunosuppression, comorbidities, cardiac allograft vasculopathy, renal dysfunction, frailty, reduced exercise capacity, and other late complications that were not measured. Accordingly, the lower physical scores may reflect aging, accumulated disease burden, unmeasured post-transplant complications, or survivor characteristics rather than an independent effect of transplant duration.

Importantly, the association between assessment more than 5 years after transplantation and lower physical HRQoL remained robust in the extended analysis after accounting for concurrent frailty status and anxiety symptoms. Higher GAD-2 scores were independently associated with lower physical-domain scores, supporting the relevance of psychological symptoms to perceived health and functional wellbeing after heart transplantation. For the social domain, the association with more than 5 years since transplantation also persisted after additional adjustment, although its magnitude was modestly attenuated, while older age remained independently associated with lower social HRQoL. Neither concurrent frailty status nor GAD-2 score was independently associated with the social domain. These findings further support the multifactorial nature of HRQoL and suggest that the observed differences according to post-transplant time cannot be explained solely by concurrent frailty or anxiety symptoms.

The association between older age and lower social domain scores should also be interpreted cautiously. Previous studies have shown that long-term HRQoL after heart transplantation is shaped by multiple biopsychosocial factors, including social support, functional status, stress, employment, and sociodemographic characteristics [14]. Thus, the lower social scores observed among older recipients may reflect age-related differences in social participation, support networks, functional capacity, or unmeasured psychosocial circumstances rather than age itself. Systematic reviews indicate that, although overall HRQoL generally improves after transplantation, social and emotional outcomes vary considerably according to employment, marital status, social integration, and perceived support [11]. Satisfaction with social support has also been identified as an important correlate of HRQoL among recipients 5–10 years after transplantation [16]. Importantly, social reintegration may also involve resumption of meaningful occupational roles. In a nationwide Danish study, Mols et al. reported that only 30% of surviving working-age heart transplant recipients participated in the labor market 5 years after transplantation, with lower participation among recipients with multimorbidity and socioeconomic disadvantage [30]. Although employment was not directly assessed in our study, these findings support the broader relevance of vocational and social participation when evaluating long-term outcomes after heart transplantation.

In contrast to the physical and social domains, psychological and environmental scores did not differ significantly across time-since-transplant groups. This finding is consistent with studies suggesting that psychological wellbeing may remain relatively preserved after heart transplantation, even when physical limitations persist, particularly among patients who develop effective coping strategies and maintain supportive social networks [17]. Similarly, studies using the WHOQOL-BREF in heart transplant populations have reported generally favorable psychological domain scores despite ongoing physical symptoms and treatment-related challenges [31]. Nevertheless, the absence of statistically significant differences should not be interpreted as evidence that these domains remain unchanged over time, particularly given the cross-sectional design and limited sample size.

Importantly, the association between assessment more than 5 years after transplantation and lower physical HRQoL remained in the extended analysis after accounting for concurrent frailty status and anxiety symptoms. Higher GAD-2 scores were independently associated with lower physical-domain scores, supporting the relevance of psychological symptoms to perceived health and functional wellbeing after heart transplantation. Previous studies in heart transplant recipients have similarly reported associations between greater anxiety or depressive symptom burden and poorer HRQoL [17, 32]. In contrast, the association between more than 5 years since transplantation and the social domain was attenuated after additional adjustment for frailty and GAD-2, whereas older age remained independently associated with lower social HRQoL. These findings reinforce the multifactorial nature of HRQoL and suggest that the observed differences according to post-transplant time should be interpreted in the context of concurrent psychological, functional, and sociodemographic characteristics rather than as an isolated effect of transplant duration.

The generally favorable HRQoL observed in this sample should be interpreted in light of potential survivor and selection bias. Only recipients who were alive, contactable, and willing to complete the interview were included. Patients with severe complications, greater functional impairment, institutionalization, or poorer overall health may therefore have been underrepresented, potentially leading to an overestimation of HRQoL relative to the full historical transplant cohort. This limitation is particularly relevant when interpreting comparisons across time since transplantation, because long-term survivors constitute a selected group that may differ systematically from recipients who died or were unavailable for assessment.

The association between socioeconomic status and the environmental domain underscores the potential relevance of social determinants on quality of life after transplantation. The WHOQOL-BREF environmental domain encompasses financial resources, access to healthcare, transportation, housing, safety, and opportunities for recreation and participation. Therefore, higher scores among participants from more favorable socioeconomic backgrounds may reflect broader differences in living conditions and access to supportive resources rather than transplant-related factors alone. This interpretation is consistent with evidence linking socioeconomic conditions to environmental and overall quality-of-life outcomes measured using the WHOQOL-BREF [33].

Several limitations should be considered when interpreting these findings. First, the cross-sectional design precludes causal inference and does not allow characterization of within-patient changes in HRQoL over time. HRQoL was assessed at a single time point in different individuals representing distinct post-transplant periods rather than repeatedly within the same recipients. Therefore, the lower physical and social scores observed among participants evaluated more than 5 years after transplantation reflect between-group differences and should not be interpreted as evidence of longitudinal deterioration. In addition, chronological age and time since transplantation are closely related, and adjustment for age in the multivariable models may not have fully disentangled the effects of aging from those associated with longer post-transplant duration. Residual confounding by unmeasured factors, including exercise capacity, comorbidity burden, cardiac allograft vasculopathy, renal dysfunction, medication-related adverse effects, and other late post-transplant complications, may also have contributed to the observed associations with HRQoL.

Second, selection and survivor biases should be considered. The study included only heart transplant recipients who were alive at the time of assessment, could be contacted by telephone, agreed to participate, and were able to complete the questionnaires. Recipients who had died, experienced severe complications or substantial functional impairment, were institutionalized, or could not be reached may therefore have been underrepresented. This selective inclusion of surviving and assessable recipients may have resulted in an overestimation of HRQoL relative to the broader population of heart transplant recipients treated at our institution. Additionally, we were unable to systematically compare participants with eligible recipients who did not participate; therefore, the magnitude and direction of potential selection bias could not be quantified.

Furthermore, this was a single-center study conducted at a national cardiovascular referral center, and the sample was predominantly male and urban, with a substantial proportion of participants from lower socioeconomic strata. These characteristics may limit the generalizability of the findings to other transplant programs, women, rural populations, and healthcare settings with different demographic and socioeconomic profiles. Additionally, we were unable to systematically compare participants with eligible recipients who did not participate; therefore, the magnitude and direction of potential selection bias could not be quantified.

Third, the relatively small sample size, particularly in the <1-year post-transplant group, limited statistical power, subgroup analyses, and the number of covariates that could be included in multivariable models without increasing the risk of overfitting. The wide range of post-transplant durations and missing data for several clinical variables may have further reduced the precision of the estimates.

Finally, HRQoL was assessed using self-reported questionnaires administered by telephone. Although patient-reported measures are essential for capturing quality of life from the recipient's perspective, responses may have been influenced by recall bias, social desirability, and interview-related factors. Telephone administration may also have contributed to selection bias by excluding recipients who were unable to participate because of severe clinical, cognitive, communication, or functional limitations. In addition, although the EQ-5D-3L and WHOQOL-BREF are validated instruments that provide complementary assessments of health status and quality of life, both are generic measures and may not fully capture transplant-specific concerns, including adverse effects of immunosuppressive therapy, fear of rejection, infection-related concerns, graft-related symptoms, treatment burden, and challenges associated with long-term medication adherence. Future studies incorporating transplant-specific patient-reported outcome measures alongside generic HRQoL instruments could provide a more comprehensive assessment of the long-term experience of heart transplant recipients.

Conclusion

Heart transplant recipients in this study generally reported favorable HRQoL. Nevertheless, recipients assessed more than 5 years after transplantation had lower physical and social HRQoL scores than those assessed earlier after transplantation. These cross-sectional findings highlight the importance of incorporating patient-reported outcomes, physical function, pain, rehabilitation, social participation, and support networks into long-term post-transplant care. Longitudinal studies incorporating comprehensive clinical variables and repeated HRQoL assessments are needed to characterize individual trajectories and identify potentially modifiable determinants of quality of life after heart transplantation.

Data availability statement

The datasets generated and analyzed during the current study are not publicly available due to patient confidentiality and institutional data protection policies. However, de-identified data may be made available from the corresponding author upon reasonable request, subject to institutional approval and applicable ethical regulations.

Ethics statement

The studies involving humans were approved by Comité de Ética en Investigación de la Fundación Cardiovascular de Colombia (CEI-FCV). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent was waived by the institutional ethics committee because data collection was conducted remotely via structured telephone interviews. Instead, verbal informed consent was obtained from all participants prior to the start of the interview, and the study was classified and approved as minimal risk observational research.

Author contributions

AJ: Data collection, database construction, manuscript drafting, and critical revision. ML-A: Conceptualization, methodology, formal analysis, manuscript writing, and final revision. EM-H: Conceptualization, methodology, Supervision, formal analysis, Data curation, Writing – original draft, Writing – review and editing. JV:

Data collection, database construction, conceptualization, manuscript writing, and final revision. KC: Manuscript writing and critical revision. AB: Manuscript writing and critical revision. AH-O: Conceptualization, methodology, formal analysis, manuscript writing, and final revision. LE: Manuscript writing and critical revision.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declared that generative AI was used in the creation of this manuscript. During the preparation of this manuscript, the authors used ChatGPT (OpenAI) to assist with the graphic design and visual organization of Figure 2. The tool was used solely to support the presentation of author-provided study information and was not used to generate, modify, analyze, or interpret study data or results. The authors carefully reviewed and edited the AI-assisted material, verified its accuracy and consistency with the underlying study data, and take full responsibility for the final content of the manuscript and figure.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

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