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Comparative Analysis of the Health Status of Heart Transplant Patients with Different Levels of Physical Activity

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Abstract: This study's goals were to determine the health status of a group of heart transplant recipients (HTRs) and their level of physical activity and to compare the health status among them and with a group of healthy sedentary individuals. Fifty-four HTRs and eighteen sedentary individuals (S) were assigned to four groups, according to their level of physical activity (determined with the International Physical Activity Questionnaire); patients with a low, moderate, and high level of physical activity (HTRL, HTRM, and HTRH, respectively) and S participants underwent a basic blood analysis and several tests to assess their cardiovascular, neuromuscular, and functional mobility condition and their quality of life. The S and HTRH were very similar in terms of BP, HR, and blood analysis while HTRM and HTRL differed from both S and HTRH in these parameters. Regarding the cardiovascular, neuromuscular, functional mobility, and quality of life variables assessed in this study, HTRH showed the best results across all of them, followed by S, HTRM, and HTRL. It is suggested that the weekly level of physical activity of HTRs should be high, which might help them to enhance their health and quality of life.

Keywords: heart transplant; exercise; cardiovascular function; neuromuscular function; functional mobility condition; quality of life

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1. Introduction

Advanced heart failure is the worsening of the health status of patients suffering from heart failure, mainly due to coronary artery disease and cardiomyopathies. The treatments to which these patients are subjected over time cease to have an effect, which leads to an increase in the frequency of episodes of hospital admission, and for this reason, it is necessary to take additional measures [1]. There are more than fifteen million people affected by heart failure in the world and it causes hundreds of thousands of deaths a year [2].

Heart transplantation is the treatment of choice for patients experiencing advanced heart failure that does not respond to medical, pharmacological, or surgical interventions [3]. After transplantation, patients must begin treatment with immunosuppressive drugs, which they will continue throughout their lives to prevent rejection of the transplanted organ. However, these drugs also have side effects, with atherosclerosis being particularly notable.

Currently, supervised exercise training in cardiac rehabilitation programs is safe and is recommended by professional societies both before and after heart transplantation [4]. Moreover, physical exercise is recognized as an important non-pharmacological therapy for heart transplant recipients (HTRs) to enhance mobility, muscle strength, quality of life, and chronotropic response [5–9]. The scientific literature presents numerous studies that refer to the possible benefits of the practice of physical exercise on heart transplant recipients. Nóbilo et al. (2015) [6] demonstrated how blood pressure values improved in heart transplant patients after twelve weeks of resistance training. Yardley et al. (2017) [7] evaluated the effects of high-intensity interval training in a group of forty-one heart transplant patients for five years and observed that their anxiety levels decreased. Yardley et al. (2018) [8] detected the relationship between good physical capacity after heart transplantation and long-term survival, finding that high-intensity interval training produced superior effects compared to conventional moderate exercise. Schmidt et al. (2020) [9] observed that resistance and strength training can greatly improve muscle function and maximal aerobic performance in heart transplant patients, and it can reduce the side effects of immunosuppressive therapy and control risk factors for cardiac allograft vasculopathy. Nonetheless, the health status of HTRs in relation to their level of physical activity ((PA), low, moderate, or high) remains unknown. This information would be relevant and valuable for researchers and professionals. Among other key utilities, it would provide a deeper understanding of the effect of the exercise on HTRs, guide the design of interventional studies aiming to assess the effect of different training protocols and optimize the supervised exercise that they must perform (e.g., addressing the exercise to higher or lower intensity and volume, in more or fewer sessions per week).

Thus, considering the importance of physical exercise as a non-pharmacological therapy for HTRs and the lack of studies examining the health status of these patients in relation to their PA level, the objectives of this study were to assess the health status of a group of HTRs and their PA level and to compare their health status with that of a group of healthy sedentary individuals (S). It was hypothesized that HTRs with higher levels of PA would exhibit better health statuses than those with moderate or low PA levels, and similar health statuses to the sedentary group.

2. Material and Methods

2.1. Design

The present cross-sectional observational study (clinicaltrials.gov ID: NCT05282342, date of registration 29 December 2021; https://clinicaltrials.gov/ct2/show/NCT05282342) was designed following the recommendations of the declaration of standards for cross-sectional observational studies called Strengthening the Reporting of Observational Studies in Epidemiology (STROBE). The Research Ethics Committee of the University of León, ETICA-ULE-038-2021, approved and authorized the implementation of this study, which was conducted in accordance with the updated version of the Declaration of Helsinki. The study was carried out from January to June of 2022 (the recruitment process was opened during January and February of 2022). The data acquisition sessions were conducted on the Hospital Universitario Puerta de Hierro of Majadahonda (Spain), in the venue of the Fede-ración Española de Trasplantados de Corazón (FETCO) of Valladolid (Spain), and in the Palacio de Congresos of Gijón (Spain).

2.2. Participants

This study's sample size was determined according to Cohen's power analysis for analysis of variance (ANOVA) designs [10] using R software (www.r-project.org, version 3.3.1., 21 June 2016). Four groups of people, an effect size (Cohen's f [10]) of 0.40, a maximum significance level of 0.05 and a minimum power of 0.80 were established. The resulting sample size was 18 participants in each group.

Thus, fifty-four HTR and eighteen S participated in the project. Informed written consent was obtained from all the participants. After the transplant, patients participated in a 4–6-week rehabilitation program consisting of two to three sessions per week on non-consecutive days. These sessions primarily focused on continuous walking or cycling for 20–40 min. The study eligibility criteria were as follows: men and women adult (≥18 years) HTRs who had undergone heart transplantation at least twelve months before the data collection of this study; HTRs classified as having low, moderate, and high levels of PA practice, according to the results of the International Physical Activity Questionnaire—Long

Form (IPAQ-L) [11]; and healthy people classified as sedentary based on the results of the IPAQ-L. People who did not meet the eligibility criteria were excluded from this study. This included individuals with physical disabilities and/or other limiting pathologies that affected their level of PA, as well as those who had undergone cardiac rehabilitation programs within the twelve months prior to this study. According to the IPAQ-L, a high level of PA refers to activities that take hard physical effort and make breathing much harder than normal (only physical activities that last at least 10 min at a time). A moderate level of PA refers to activities that take moderate physical effort and make breathing somewhat harder than normal (only physical activities that last at least 10 min at a time). Finally, a low level of PA refers to time spent walking, which includes at work and at home, walking to travel from place to place, and any other walking performed solely for recreation, sport, exercise, or leisure. Additionally, the low level of PA also refers to the time spent sitting, which includes time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television [11].

Participants were assigned to four groups: patients with a low level of PA (HTRL, $n = 18$), patients with a moderate level of PA (HTRM, $n = 18$), patients with a high level of PA (HTRH, $n = 18$), and sedentary individuals (S, $n = 18$). The HTRs and S were assigned to each group based on the results obtained from the Spanish version of the IPAQ-L [12], which was used as an instrument to determine their level of PA.

2.3. Protocol

All participants underwent an anthropometric assessment. Subsequently, to gain a broad insight into the health status of the patients, they underwent a basic blood analysis and several tests to assess their cardiovascular, neuromuscular, and functional mobility conditions. All tests were brief, simple, and easy to carry out (they do not require complicated protocols or expensive devices) but very useful as clinical outcomes. Finally, participants were also required to evaluate their quality of life. The tests were conducted by the same group of researchers in the aforementioned order, over five days (two days for each patient; the first day for the basic blood analysis and the second one for the rest of tests).

2.4. Outcomes

The primary outcomes of the current study were as follows:

- Cardiovascular condition assessment. It was determined by the measurements of the systolic and diastolic blood pressure [SBP and DBP], the basal heart rate [HR], and the 2 Min Step Test [2MST] [13]. The SBP and DBP were measured after 5 min in the seated position using an automatic blood pressure monitor (Omron HEM-7130, Kyoto, Japan). The basal HR was determined after 5 min in the supine position [14]. The HR was recorded using a HR monitor (Polar S810, OY, Oulu, Finland) with a chest strap. The 2MST assesses the individual's gait in place as fast as possible for 2 min while lifting the knees to a height midway between their patella and iliac crest when standing. Performance on the test is defined as the number of right-side steps of the criterion height completed in 2 min. Two trials are carried out and the best of them is registered [13].
- Neuromuscular condition assessment. It was determined by the measurements of the dominant and non-dominant hand grip strength, the Arm Curl Test (ACT) [13], and the 30-Second Chair Stand Test (30SCST) [15]. The grip strength was measured three times with each hand and the mean value of the three trials was used for analysis. Measurements were taken with a digital and adjustable hand dynamometer (JAMAR smart, Jamar, Lafayette, United States) according to a standard protocol. The overall maximum grip strength was recorded to the nearest 1 kg [16]. The goal of the ACT is to assess the participant's upper body strength within a specified time frame. Performance on the test is defined as the number of curls that participants can express in 30 s. Two trials were conducted, and the result recorded is the best

performance from either trial [13]. The primary objective of the 30SCST is to evaluate the participant's lower body strength and endurance. Performance on the test is defined as the number of times participants successfully rise to a full standing position and sit back down within the 30 s timeframe. Only one trial was performed [15].

The secondary outcomes of the current study were as follows:

- Basic blood analysis: It included the levels of glucose, creatine, uric acid, total cholesterol, high-density lipoproteins (HDL), low-density lipoproteins (LDL), triglycerides, total proteins, albumin, and N-terminal pro-B type Natriuretic peptide pro-hormonal (NT Pro-BNP) (only for HTR since this is a heart damage marker).
- Functional mobility condition assessment: It was evaluated with the Sit and Reach Test (SRT) [17], the Back Scratch Test (BST) [13], the Functional Balance Test [18], the Timed up and Go Test (TUG) [19], and the 10-Meter Walk Test (10MWT) [20]. The SRT assesses the participant's flexibility of the lower back and hamstring muscles. The performance is defined by measuring the distance reached from the fingertips to the edge of the box, with the best distance recorded after three trials. Three trials were carried out and the longest distance reached was recorded [17]. The BST assesses shoulder and upper body flexibility. The performance is defined by measuring the distance between the fingertips, with a zero score if they touch, a negative score if they do not, and a positive score if they overlap. The test was conducted twice on the participant's preferred side, and the best of the two trials was recorded [13]. The FBT evaluates the patient's ability to maintain balance and reach forward. During the test, the patient stands near a wall, positioning the arm closest to the wall at a 90° angle with a fist. The initial position of the third metacarpal head is recorded, and the patient is instructed to reach forward as far as possible without stepping. The final position of the third metacarpal is then recorded, and the test result is determined by the difference between the initial and final positions, representing the patient's reach distance. Three repetitions were conducted, and the average of the last two was noted for assessment [18]. The TUG is carried out when the participant is sitting on a chair and asked to get up from the chair and walk as quickly as possible to a mark three meters away, then walk around the mark and return to the chair to sit down again. Three attempts were made, counting the average of these [19]. The 10MWT demands that the patient walks 10 m as fast as he/she can. The test is carried out three times and the average datum of them is recorded [20].
- Complementary assessment: The patient´s quality of life was assessed with the Short-Form 36 Health Survey (SF-36) [21] in its Spanish version [22].

2.5. Statistical Analysis

All data were analyzed using R software (www.r-project.org, version 3.3.1, 21 June 2016) and were presented as means and standard deviations unless otherwise noted.

Differences in the characteristics among S, HTRH, HTRM, and HTRL were assessed through the Fisher's Exact test and the one-way ANOVA test or the non-parametric Kruskal–Wallis test (if the assumptions of normality and homoscedasticity were not satisfied [Shapiro–Wilk and Bartlett tests, respectively]) for sex and rest of the parameters, respectively ($p > 0.05$).

Given the dependent variables of the study, whether the assumptions were satisfied, the one-way ANOVA was performed to determine whether there were significant differences among them ($p < 0.05$). On the contrary, if the assumptions were not met, the non-parametric Kruskal–Wallis test was performed ($p < 0.05$). As a result, the Tukey HSD *post-hoc* test or the Dunn's test were employed to determine specific differences between the variables for the one-way ANOVA and the Kruskal–Wallis test, respectively.

Effect size was also calculated to establish the magnitude of change when significant differences were detected. Cohen's f ($f = PostM_{EX} - PostM_C/PostSD_C$; small = $f > 0.1$, medium = $f > 0.25$, and large = $f > 0.40$) [8] was used when data normality and homoscedasticity were verified. Rosenthal's r ($r = Z/\sqrt{N}$; the "Z" value was obtained performing the Exact Wilcoxon–Mann–Whitney test; small = r > 0.20, moderate = r > 0.50, and great = r > 0.80) [23]) was used when they were not.

3. Results

The STROBE diagram depicting this study's phases is shown in Figure 1. Significant between-group differences were found in the number of men and women in each group and in age (Table 1). No adverse events were reported during the data acquisition process.

Table 1. Characteristics of the participants.

Characteristics	S (*n* = 18)	HTRH (*n* = 18)	HTRM (*n* = 18)	HTRL (*n* = 18)	*p*-Value
Sex (men/women)	7/11	17/1	13/5	14/4	**0.003** *
Age (years)	56.3 ± 12	54.2 ± 11.5	61.1 ± 14.5	67 ± 9	**0.003** $
Weight (kg)	70 ± 14	74.1 ± 12.4	79 ± 27.5	72 ± 15	0.653 $
Height (cm)	161.1 ± 22	170.4 ± 6.5	161.5 ± 24.2	167 ± 10.5	0.291 $
BMI (kg/m^2)	25.2 ± 5	25.5 ± 3.4	26 ± 4	26 ± 4.5	0.943 &
Reason for transplant	-	4 HM/2 IM/8 DM/4 OR	1 HM/4 IM/6 DM/7 OR	3 HM/7 IM/5 DM/3 OR	-

All values expressed as means and standard deviations unless otherwise noted. Abbreviations: BMI: body mass index; S: healthy sedentary individuals; HTRH: transplanted with a high level of physical activity; HTRM: transplanted with a moderate level of physical activity; HTRL: transplanted with a low level of physical activity; HM: hypertrophic cardiomyopathy; IM: ischemic cardiomyopathy; DM: dilated cardiomyopathy; OR: other reasons. * Fisher´s test; & one-way ANOVA; $ Kruskal–Wallis test. Bold values express significant differences ($p < 0.05$).

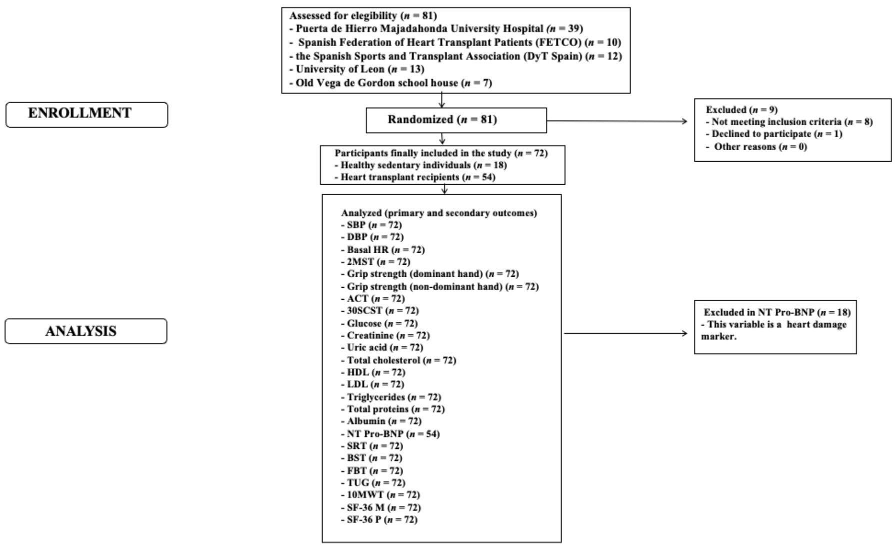

Figure 1. STROBE diagram of the study´s phases. Abbreviations: SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; 2MST: 2 Min Step Test; ACT: Arm Curl Test; 30SCST: 30-Second Chair Stand Test; HDL: high-density lipoproteins; LDL: low-density lipoproteins; NT Pro- BNP: N-terminal pro-B type Natriuretic peptide pro-hormonal; SRT: Sit and Reach Test; BST: Back Scratch Test; FBT: Functional Balance Test; TUG: Time and Up Go Test; 10MWT: 10-Meter Walking Test; SF—36 M: Short-Form 36 Mental Health Survey; SF—36 P: Short-Form 36 Physical Health Survey.

Regarding the primary outcomes of this study, concerning the BP and the basal HR, no differences were detected among groups (Table 2). The 2MST revealed differences between S and HTRM (p = 0.036, small effect), S and HTRL (p = 0.000, moderate effect), HTRH and HTRM (p = 0.029, small effect), HTRH and HTRL (p = 0.000, moderate effect), and HTRM and HTRL (p = 0.008, small effect) (Table 2, Figure 2).

Table 2. Comparison of all outcomes among the four groups of the participants: healthy sedentary individuals, transplanted with a high level of physical activity, transplanted with a moderate level of physical activity, and transplanted with a low level of physical activity.

Outcomes	S (n = 18)	HTRH (n = 18)	HTRM (n = 18)	HTRL (n = 18)	p-Value	Effect Size (f/r)
SBP (mmHg)	133.3 ± 18	133.9 ± 18.1	132.4 ± 18.1	126.11 ± 15.1	0.645	-
DBP (mmHg)	75 ± 10	81.2 ± 10	81.3 ± 9.2	77.2 ± 10.1	0.060	-
Basal HR (bpm)	79 ± 11.7	87 ± 12	86 ± 18.5	87 ± 14	0.553	-
2MST (times)	75.4 ± 15	85 ± 35	65.3 ± 19.3	45 ± 21.2	**0.000**	S vs. HTRM; r = 0.30 S vs. HTRL; r = 0.70 HTRH vs. HTRM; r = 0.30 HTRH vs. HTRL; r = 0.70 HTRM vs. HTRL; r = 0.40
Grip strength (dominant hand) (kg)	29 ± 11.1	34.1 ± 9.1	29 ± 12.1	26.1 ± 9.3	**0.025**	S vs. HTRH; r = 0.30 HTRH vs. HTRM; r = 0.30 HTRH vs. HTRL; r = 0.40
Grip strength (non-dominant hand) (kg)	26 ± 10	31 ± 9	28 ± 12.1	24.3 ± 8.2	**0.051**	S vs. HTRH; r = 0.30 HTRH vs. HTRL; r = 0.30
ACT (times)	9.2 ± 2.5	12 ± 5.1	9.4 ± 3	8.5 ± 2	0.246	HTRH vs. HTRL; r = 0.32
30SCST (times)	13 ± 3	14 ± 6.2	10.1 ± 3.3	9 ± 2.5	**0.000**	S vs. HTRM; r = 0.50 S vs. HTRL; r = 0.60 HTRH vs. HTRM; r = 0.40 HTRH vs. HTRL; r = 0.50
Glucose (mg/dL)	94 ± 14	94 ± 10.3	102 ± 21.5	94 ± 30.2	0.816	-
Creatinine (mg/dL)	0.81 ± 0.1	1.1 ± 0.3	1.1 ± 0.3	1.4 ± 0.5	**0.000**	S vs. HTRH; r = 0.61 S vs. HTRM; r = 0.57 S vs. HTRL; r = 0.65
Uric acid (mg/dL)	4.5 ± 1.2	6.4 ± 1.2	5.9 ± 1.2	6.7 ± 1.5	**0.000**	S vs. HTRH; f = 1.70 S vs. HTRM; f = 0.90 S vs. HTRL; f = 1.30
Total cholesterol (mg/dL)	179 ± 35	161 ± 32.4	165.1 ± 28	173 ± 46	0.331	-
HDL (mg/dL)	60.4 ± 15	56 ± 16.4	67.3 ± 19.4	58 ± 25.1	0.388	-
LDL (mg/dL)	105± 24.5	86.3 ± 24.5	74 ± 22	81 ± 33	**0.026**	S vs. HTRH; r = 0.41 S vs. HTRM; r = 0.56 S vs. HTRL; r = 0.35
Triglycerides (mg/dL)	100 ± 29	110 ± 54.1	120.4 ± 55	136.2 ± 80.4	0.490	-
Total proteins (g/dL)	7.2 ± 0.4	7 ± 1	7 ± 0.5	7 ± 0.5	**0.042**	S vs. HTRH; r = 0.33 S vs. HTRM; r = 0.42 S vs. HTRL; r = 0.45
Albumin (g/dL)	5 ± 1	4.3 ± 0.5	4.5 ± 0.4	5 ± 2	0.740	-

Table 2. *Cont.*

Outcomes	S (n = 18)	HTRH (n = 18)	HTRM (n = 18)	HTRL (n = 18)	p-Value	Effect Size (f/r)
NT Pro-BNP * (pg/mL)	-	1434 ± 3125.3	765.3 ± 782	948.3 ± 1650	0.944	-
SRT (cm)	12.5 ± 8.1	13.3 ± 7.3	9.3 ± 7	11 ± 7	0.491	-
BST (cm)	5.1 ± 7.1	0.14 ± 10	−9 ± 17	−10 ± 21	**0.004**	S vs. HTRM; r = 0.50 S vs. HTRL; r = 0.40 HTRH vs. HTRM; r = 0.40 HTRH vs. HTRL; r = 0.27
FBT (cm)	34 ± 8.2	41 ± 8	33.2 ± 6.4	30 ± 12	**0.004**	HTRH vs. HTRL; f = 0.9
TUG (sec)	7 ± 1.3	6.4 ± 2	9 ± 2.2	11 ± 2.5	**0.000**	S vs. HTRM; r = 0.66 S vs. HTRL; r = 1.32 HTRH vs. HTRM; r = 0.40 HTRH vs. HTRL; r = 0.22
10MWT (sec)	3 ± 0.5	3.2 ± 0.5	4 ± 1	4.3 ± 2	**0.000**	S vs. HTRM; f = 1.26 S vs. HTRL; f = 0.80 HTRH vs. HTRL; f = 2.26
SF—36 M (points)	51 ± 9.1	53 ± 7.9	50 ± 10	52.4 ± 11.5	0.778	-
SF—36 P (points)	54 ± 4	53.4 ± 5.2	50 ± 7.1	44.5 ± 10.2	**0.007**	S vs. HTRL; r = 0.50 HTRH vs. HTRL; r = 0.50

All values expressed as means and standard deviations unless otherwise noted. Abbreviations: S: healthy sedentary individuals; HTRH: transplanted with a high level of physical activity; HTRM: transplanted with a moderate level of physical activity; HTRL: transplanted with a low level of physical activity; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; 2MST: 2 Min Step Test; ACT: Arm Curl Test; 30SCST: 30-Second Chair Stand Test; HDL: high-density lipoproteins; LDL: low-density lipoproteins; NT Pro-BNP: N-terminal pro-B type Natriuretic peptide pro-hormonal; SRT: Sit and Reach Test; BST: Back Scratch Test; FBT: Functional Balance Test; TUG: Time and Up Go Test; 10MWT: 10-Meter Walking Test; SF—36 M: Short-Form 36 Mental Health Survey; SF—36 P: Short-Form-36 Physical Health Survey; f: Cohen's f; Rosenthal's r. * Only in transplanted individuals since NT Pro-NP is a heart damage marker. Bold values express significant differences ($p < 0.05$).

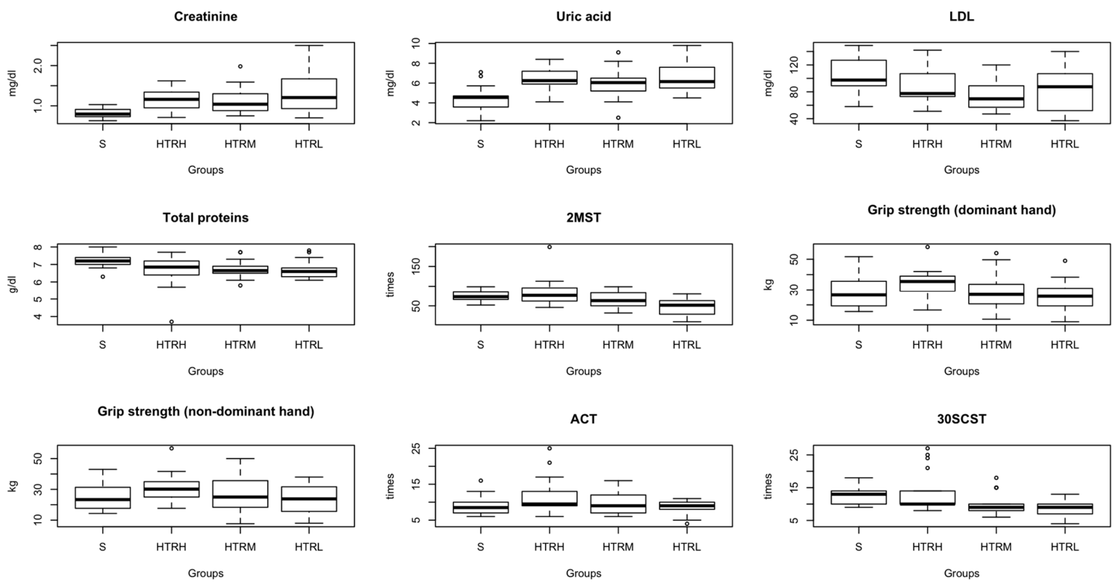

Figure 2. The primary outcomes that expressed significant differences among groups. Abbreviations: S: healthy sedentary individuals; HTRH: transplanted with a high level of physical activity; HTRM: transplanted with a moderate level of physical activity; HTRL: transplanted with a low level of physical activity; 2MST: 2 Min Step Test; ACT: Arm Curl Test; 30SCST: 30-Second Chair Stand Test.

With respect to grip strength, considering the dominant hand, significant differences were detected between S and HTRH (p = 0.003, small effect), HTRH and HTRM (p = 0.029, small effect), and HTRH and HTRL (p = 0.006, small effect). Regarding the non-dominant hand differences, these were expressed between S and HTRH showed significant differences (p = 0.004, small effect) and HTRH and HTRL (p = 0.021, small effect) (Table 2, Figure 2).

Regarding the ACT, significant differences were detected between HTRH and HTRL (p = 0.034, small effect) (Table 2, Figure 2).

Regarding the 30SCST, differences were observed between S and HTRM (p = 0.001, small effect) and S and HTRL (p = 0.000, moderate effect). (Table 2, Figure 2).

Concerning the secondary outcomes of this study, concerning the basic blood analysis, creatinine showed significant differences between S and all HTR groups (all comparisons with a p-value of 0.000 and a moderate effect) (Table 2, Figure 2). For uric acid, significant differences were observed between S and HTRH (p = 0.000, large effect), between S and HTRM (p = 0.024, large effect), and between S and HTRL (p = 0.000, large effect) (Table 2, Figure 2). About LDL, significant differences were identified between S and HTRH (p = 0.035, small effect), between S and HTRM (p = 0.001, moderate effect), and between S and HTRL (p = 0.035, small effect) (Table 2, Figure 2). As for total proteins, significant differences were found between S and HTRH (p = 0.019, small effect), between S and HTRM (p = 0.008, small effect), and between S and HTRL (p = 0.004, small effect) (Table 2, Figure 2). No significant differences were found among the patient groups in NT Pro-BNP (Table 2, Figure 2).

Given the SRT, no differences were detected among groups. Concerning the BST, differences were found between S and HTRM (p = 0.001, small effect), S and HTRL (p = 0.003, small effect), HTRH and HTRM (p = 0.040, small effect), and HTSRTRH and HTRL (p = 0.046, small effect) (Table 2, Figure 3).

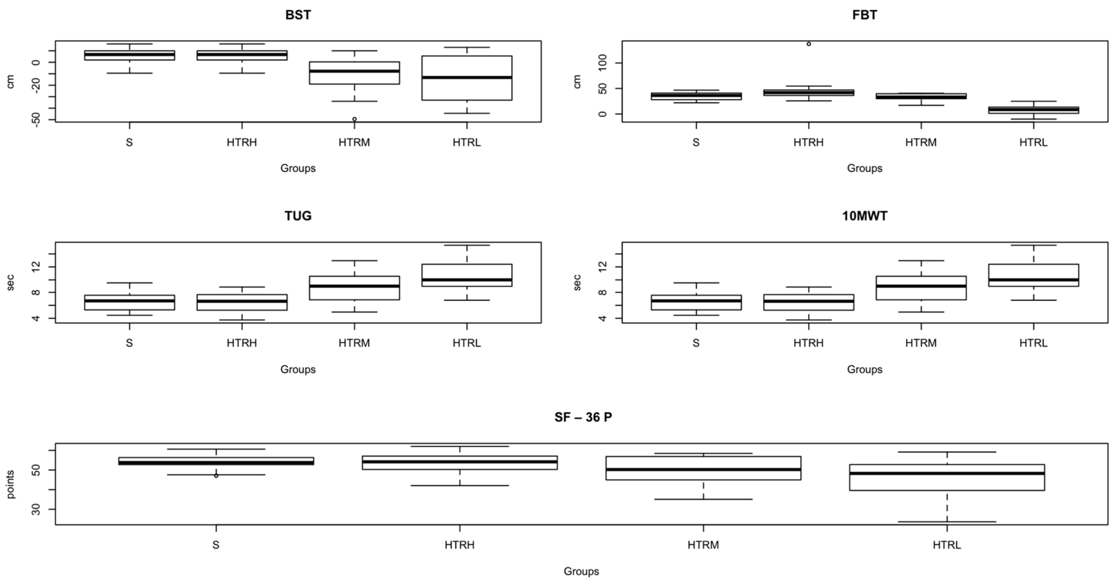

Figure 3. The secondary outcomes that expressed significant differences among groups. Abbreviations: S: healthy sedentary individuals; HTRH: transplanted with a high level of physical activity; HTRM: transplanted with a moderate level of physical activity; HTRL: transplanted with a low level of physical activity; LDL: low-density lipoproteins; BST: Back Scratch Test; FBT: Functional Balance Test; TUG: Time and Up Go Test; 10MWT: 10-Meter Walking Test; SF—36 P: Short-Form 36 Physical Health Survey.

Considering the FBT, differences were detected between HTRH and HTRL (p = 0.002, great effect) (Table 2, Figure 3). Results of the TUG showed differences between S and HTRM (p = 0.003, small effect), S and HTRL (p = 0.000, moderate effect), HTRH and HTRM (p = 0.001, small effect), HTRH and HTRL (p = 0.000, moderate effect), and HTRM and

HTRL (p = 0.046, small effect) (Table 2, Figure 3). Given data of the 10MWT, differences were revealed between S and HTRM (p = 0.010, great effect), S and HTRL (p = 0.000, moderate effect), and HTRH and HTRL (p = 0.000, great effect) (Table 2, Figure 3).

Finally, regarding the SF-36 (complementary assessment), within mental health, no differences were observed among any of the groups (Table 2). Concerning the section of the physical health, differences were found between S and HTRL (p = 0.002, small effect) and TPH and TPL (p = 0.001, small effect) (Table 2, Figure 3).

4. Discussion

The goals of this study were to determine the health status of a group of HTRs and their level of PA and to compare their health status with that of a group of S. This study's hypothesis was partially confirmed, as HTRH did not exhibit better data than the other groups of patients across all variables, nor did they demonstrate similar health status to S across all assessed variables. Overall, S and HTRH were very similar in terms of BP, HR, and blood analysis while HTRM and HTRL differed from both S and HTRH in these parameters. Regarding the cardiovascular, neuromuscular, functional mobility, and quality of life variables assessed in this study, HTRH showed the best results across all of them, followed by S, HTRM, and HTRL.

Considering the cardiovascular function assessment, notably, all groups exhibited healthy BP values. Thus, it is suggested that the patients of the current study expressed healthy BP levels due to PA, since HTRs can improve their BP levels through PA [24]. The fact that the basal HR of both S and HTRs in the current study did not show any significant differences is a positive finding, since HTRs often experience elevated resting HR [25]. Thus, PA could serve as an effective tool in maintaining healthy basal HR levels for HTRs. Concerning the 2MST, results suggest that the aerobic condition of S and HTRH are similar and that HTRH is better than the rest of patients. Consequently, the outcomes of this study underscore the potential of PA in aiding patients to attain and sustain aerobic fitness levels akin to those observed in S.

Given the neuromuscular assessment, in terms of handgrip strength, HTRH and HTRM expressed the highest performance in the dominant and in the non-dominant hand. Observations in healthy individuals revealed a positive correlation between the PA levels and the handgrip strength levels [26]. The present study's findings align with this trend; a higher level of PA among patients corresponds to a higher level of handgrip strength. In the ACT, no disparities emerged between S and HTRs. This observation might stem from the fact that HTRs often experience reduced muscle mass and strength owing to their immunosuppressive treatment [27]. These findings deserve attention as they reflect a positive outcome; the patients' performance closely approximates that of healthy sedentary individuals. In the 30SCST, HTRH achieved the highest scores. Therefore, it is suggested that PA holds the potential to contribute to the attainment and maintenance of robust lower extremity extension muscle strength and endurance in HTRs.

In respect to the blood analysis, no differences among groups were expressed in the values of glucose, total cholesterol, HDL, triglycerides, or albumin. Given that all groups in this study exhibited healthy values for these variables, it can be hypothesized that exercise has a positive effect on these variables in HTRs. Although is needed to note that a healthy diet can also have a positive impact in these parameters, and the patient's diet was not considered in the current study's results. Additionally, it is important to note that one of the side effects of immunosuppressive medication in HTR is an increase in blood glucose levels, increasing the risk of developing diabetes [28], and the patients' groups of this study presented healthy levels in this variable. Regarding the rest of the blood variables (creatinine, uric acid, LDL, and total protein levels), all groups in this study also expressed healthy values of them, but significative differences between S and HTRs were observed. S showed healthier values than HTRs, which might be attributed to immunosuppressives' toxic effects (HTRs may exhibit elevated creatinine levels due to the immunosuppressive´s toxic effects) [29]. Thus, it is suggested that PA could help to HTRs to maintain these markers in healthy levels. No differences were found among the patient´s groups in the NT Pro-BNP levels. In studies with patients with heart failure, the NT Pro-BNP levels can be lowered with supervised exercise training [30]. Thus, considering the present study's results, a moderate level of PA could be the most beneficial for this variable in HTRs, since HTRM expressed the lowest NT pro-BNP values.

Considering the functional assessment, a common trend was identified for the SRT, BST, FBT, TUG, and 10MWT; engaging in PA graded as high-level enables HTRs to express performance levels in these outcomes comparable to those seen in S. The 10MWT's results merge special consideration since the gait speed has been shown to be an indicator of disability [31], health care utilization [32], and survival [33] in older adults. Thus, it is suggested a high level of PA is recommended for this aspect of the health of HTRs.

Finally, regarding the SF-36 questionnaire (complementary assessment), no differences among groups in terms of mental health were observed. However, differences were detected in physical health between S and HTRL, as well as between HTRH and HTRL. These findings suggest that engaging in graded high-intensity physical activities may foster a self-perceived state of physical health among HTRs, akin to that of S.

Analyzing results of the primary outcomes within this study globally, it becomes evident that HTRs engaging in high levels of PA exhibit a healthier status compared to those practicing moderate or low levels of activity. Remarkably, in some variables, patients with high PA levels even outperform to healthy sedentary individuals. Echoing this trend, the secondary variables follow a similar pattern, where heightened degrees of PA seem to be linked to better evaluation outcomes.

The results of this study can be applied to the rehabilitation process of HTRs. Firstly, the weekly level of PA for HTRs should be high (according to the IPAQ´s criteria). This level of PA should be achieved by practicing at least three days per week, although more days could be used (also according to the IPAQ's criteria). The recommendations of Schmidt et al. (2021) [9] for the planning and execution of exercise training after heart transplantation should be considered when making this decision, including the current clinical condition, the individual comorbidities, and possible transplant-related complications of the patients. Secondly, the topics of the supervised exercise for HTRs could be all those that can improve cardiovascular condition, neuromuscular condition, basic blood parameters, functional mobility condition, and quality of life of the patients. Finally, the tests used in this study to assess the health status of the patients might be also used to evaluate the effects of the exercise on HTRs and as clinical outcomes for them. Additionally, the test results of the present study on HTRs with a high level of PA might serve as benchmarks.

This study has limitations: Firstly, there are significant differences in the number of men and women of the groups as well as in the mean age of the members of the groups. However, given this study's sample size, the results can be considered a valid reference for both sexes. Secondly, the PA levels of participants were assessed through self-reported measures as the IPAQ-L. However, the IPAQ has been widely used in numerous epidemiological studies globally and has undergone extensive validation in various populations, and its widespread use allows for comparability with the existing literature, promoting a more comprehensive understanding of PA patterns across different cohorts. And finally, while this study includes a variety of outcome measures, there may be other relevant factors affecting the health status of heart transplant recipients that were not considered (e.g., dietary habits, psychological factors, and social support could influence outcomes but are not explicitly addressed).

5. Conclusions

In summary, the results of this study reveal that heart transplant recipients who engage in high levels of physical activity exhibit better overall health compared to those who express moderate or low levels. Moreover, these highly physically active patients achieve better results in certain health variables than healthy sedentary individuals. Thus, it is suggested that the weekly level of physical activity of heart transplant recipients should be high, which might help them to enhance their health and quality of life.

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