Prescribing and Regulating Exercise with RPE after Heart Transplant: A Pilot Study

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ABSTRACT

CIOLAC, E. G., R. E. CASTRO, J. M. GREVE, F. BACAL, E. A. BOCCHI, and G. V. GUIMARÃES. Prescribing and Regulating Exercise with RPE after Heart Transplant: A Pilot Study. *Med. Sci. Sports Exerc.*, Vol. 47, No. 7, pp. 1321–1327, 2015. **Purpose**: The objective of this study is to analyze the use of the 6–20 RPE scale for prescribing and self-regulating heated water-based exercise (HEx) and land-based exercise (LEx) in heart transplant recipients. **Methods**: Fifteen (five females) clinically stable heart transplant recipients (time since surgery = 4.0 ± 2.5 yr) age 46.7 ± 11.8 yr underwent a symptom-limited maximal graded exercise test on a treadmill to determine their HR at anaerobic threshold (HR_{AT}), respiratory compensation point (HR_{RCP}), and maximal effort (HR_{max}). After a week, patients were randomized to perform 30 min of both HEx (walking inside the pool) and LEx (treadmill walking) sessions at a pace between 11 and 13 on the 6–20 RPE scale and had their HR measured every 4 min. The interval between sessions was 48–72 h. **Results**: No significant differences between sessions were found in the average HR during HEx and LEx. Patients showed a delay in HR increase during both interventions, with the stabilization beginning after 8 min of exercise. Exercise HR was maintained between the HR_{AT} and HR_{RCP} (in the aerobic exercise training zone) for the most part of both HEx (72% of HR measurements) and LEx (66% of HR measurements). Only a few HR measurements stayed below HR_{AT} (HEx = 9%, LEx = 13%) or above HR_{RCP} (HEx = 19%, LEx = 21%) during both exercise sessions. **Conclusion**: Exercise HR was maintained in the aerobic exercise training zone (between HR_{AT} and HR_{RCP}) for the most part of both sessions, suggesting that the 6–20 RPE scale may be an efficient tool for prescribing and self-regulating HEx and LEx in heart transplant recipients. **Key Words:** AEROBIC EXERCISE, CARDIAC DENERVATION, HEART RATE, HEART TRANSPLANTATION, RATING OF PERCEIVED EXERTION, REHABILITATION

Heart transplantation (HT) is an effective and well-established treatment for patients with heart failure refractory to medical therapy and conventional cardiac surgery (4). Its benefit includes hemodynamic restoration, improvements in survival and quality of life, and social reintegration (3,29). However, exercise capacity still remains subnormal and does not increase over time in HT recipients (6,17). Moreover, a high prevalence of several comorbidities is shown in this population, including arterial hypertension, dyslipidemia, vascular disease, renal failure, and type 2 diabetes (26).

Conventional land-based exercise (LEx) training (i.e., aerobic and resistance training) is a well-established nonpharmacological tool for the rehabilitation and comorbidity management after HT (7,21). Despite this, the optimal exercise type (modality), quantity, and intensity for HT patient improvement are still unknown. For example, heated water-based exercise (HEx) has shown advantages when compared with LEx for cardiovascular improvement of several cardiac populations (12,19,30). Although there was a concern about HEx recommendation for heart disease patients (specially heart failure patients) because of a potentially dangerous cardiovascular response that could be induced by the hydrostatic pressure and water temperature (8), studies with chronic heart failure and resistance hypertensive patients have suggested that it is a safe and efficient exercise modality (12,18,19,30). In addition, the buoyancy effect during HEx reduces loading, facilitating the performance of aerobic and resistance exercise (12). However, little is known about safety and effectiveness of HEx in HT.

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The gold standard method for exercise prescription in HT recipients is based on HR at first and second ventilatory thresholds (anaerobic threshold (AT) and respiratory compensation point (RCP), respectively) during a cardiopulmonary exercise test (7). However, this method requires expensive equipment (respiratory gas analyzer) that may not be available for most cardiology centers (1,7,27). The lack of reliability between HR and $\dot{V}O_2$ observed in HT patients (9), which is caused by the altered HR response to exercise that results from the cardiac denervation after HT (6,31), makes the use of indirect HR methods to prescribe and regulate aerobic exercise in this population inappropriate (7,9,21). In addition, the delayed exercise HR increase commonly found in HT patients could result in early fatigue during the HR-guided exercise session, mainly if the second ventilatory threshold is the target HR (7,21).

RPE (5) is a simple and inexpensive measure that is associated with HR, $\dot{V}O_2$, and ventilatory thresholds in different populations (20,22,25). Furthermore, these associations appear to remain stable regardless of training and health status (25) and are sensitive to training-induced threshold changes (20,22). These advantages make RPE scale an attractive and safe option for exercise prescription and self-regulation in different populations, including heart failure patients performing HEx (8). However, little is known about its usefulness and safety in HT recipients, mainly during HEx. Thus, the purpose of the present study was to analyze the usefulness of RPE scale (5) for prescribing and self-regulating HEx and LEx in HT recipients. We hypothesized that the patient's HR would be maintained between AT and RCP HR (aerobic exercise training zone) during both HEx and LEx, which would support the usefulness of RPE scale for prescribing and self-regulating exercise in this population.

METHODS

Population and study design. We studied heart transplant recipients age 20 to 60 yr that underwent HT for at least 12 months. Inclusion criteria included physical inactivity (involvement in regular physical activity or exercise during the previous 6 months); optimized and unchanged therapy during the previous 3 months; no graft rejection during the previous 6 months; and no musculoskeletal, cardiovascular, and metabolic contraindication to exercise. Patients with psychological disorders, neuromuscular disease, chronic obstructive pulmonary disease, complex ventricular arrhythmia, atrial fibrillation, and alcoholism were also not included in the study. Forty-eight nonconsecutive patients that met all inclusion and exclusion criteria were referred between February 1, 2013, and November 30, 2013, from the HT outpatient clinic at the Heart Institute, School of Medicine, University of São Paulo. After a detailed explanation of the study design and protocol, 15 (five females) clinically stable patients (4 ± 3 yr since HT) agreed to participate in the study and were included (Table 1).

TABLE 1. Subjects characteristics.

Variable	
N (male/female)	15 (10 /5)
Age (yr)	46.7 ± 3.0
Body mass (kg)	74.1 ± 4.4
Height (m)	95.3 ± 4.1
BMI ($kg \cdot m^{-2}$)	27.2 ± 1.6
Time elapsed since HT (yr)	4.0 ± 0.7
Systolic blood pressure (mm Hg)	124.3 ± 3.8
Diastolic blood pressure (mm Hg)	82.9 ± 3.4
Current medication (*N*) (%)	
Immunosuppressives	
Cyclosporine	5 (31.2%)
Prednisone	8 (50%)
Tacrolimus	7 (43.7%)
Azathioprine	5 (31.2%)
Sirolimus	1 (6.2%)
Mycophenolate	6 (37.5%)
Antihypertensives	
Diuretics	2 (12.5%)
ACE inhibitors	1 (6.2%)
Calcium antagonists	12 (75%)
Beta-blocker	1 (6.2%)
Hypolipidemics	
Statins	13 (81.2%)
Ciprofibrate	1 (6.2%)
Hypoglycemics	
Metformin	2 (75%)
Insulin	2 (75%)
Anticoagulants	3 (18.7%)

BMI, body mass index; ACE, angiotensin-converting enzyme.

The present randomized cross-over pilot study was conducted in a single center in Brazil. The patients were allocated to perform both HEx and LEx interventions with 1/1 randomization by drawing lots (envelops in a bag). All patients included in the study underwent a symptom-limited maximal graded exercise test (GXT) on a treadmill, 3 to 5 d before beginning the intervention sessions, for analysis of hemodynamic and ventilatory response to exercise. Patients then were allocated to 30 min of HEx and LEx interventions in random order (2–5 d between sessions). HEx and LEx consisted of aerobic exercise with intensity between 11 and 13 in the 6–20 RPE scale (5). Exercise HR was continuously monitored during both HEx and LEx sessions and recorded for subsequent analysis. All patients were instructed to maintain the same medication treatment during the entire study period. The Ethics Committee of the University of São Paulo approved all procedures. Participants read a detailed description of the protocol and provided written informed consent.

GXT. Patients performed a symptom-limited maximal GXT (between 1:00 and 3:30 p.m.) on a treadmill (TMX425 Stress Treadmill; TrackMaster, Newton, KS) using a modified Naughton protocol at controlled room temperature (20°C–23°C) 3 to 5 d before beginning the intervention sessions as previously described (13). Cardiac rhythm was continuously monitored by 12-lead ECG (CardioSoft 6.5; GE Medical Systems IT, Milwaukee, WI) and recorded for 10 s at the end of rest, at the end of each warm-up and exercise stage, and at the end of each minute of recovery phase. Blood pressure measurements were obtained during rest, exercise, and recovery stages (Tango Stress BP; SunTech Medical, Morrisville, NC). Ventilation ($\dot{V}E$), oxygen uptake ($\dot{V}O_2$), and carbon dioxide output ($\dot{V}CO_2$) were measured breath by breath using a computerized system (Vmax Encore29; SensorMedics, Yorba Linda, CA).

The RER values were recorded as the averaged samples obtained during each stage of the protocol. The highest $\dot{V}O_2$ level was considered the maximal value ($\dot{V}O_{2max}$). AT was determined by the V-slope method, and RCP was determined as the point at which a rapid rise in $\dot{V}E/\dot{V}CO_2$ and a fall in partial pressure of CO_2 were observed (36). AT and RCP were identified by two experienced observers that were blinded to the subjects' characteristics and study protocol. When there was divergence between the two, a third observer was consulted to reach a consensus as previously described (14). All patients were asked to refrain from strenuous physical activities and caffeine and alcoholic beverages for 24 h before GXT and to have a light meal (breakfast) up to 2 h before the start of the test.

Exercise intervention. The exercise (HEx and LEx) interventions took place in the afternoon (1:30 to 2:30 p.m.), 1 wk after GXT (48–72 h between sessions), and were performed in controlled room (20°C–23°C) and swimming pool (30°C–32°C) temperatures. All patients had no experience of walking exercise on a treadmill or in a pool. Both HEx and LEx sessions consisted of 5 min of warm-up, 30 min of walking (0° incline) inside the pool (HEx) or on a motorized treadmill (LEx) at a pace between "relatively easy and slightly tiring" (11 to 13 on the 6–20 RPE scale), and 5 min of cooldown. The pace between 11 and 13 on the 6–20 RPE scale was chosen because it was shown to be adequate to maintain exercise intensity between the ventilatory thresholds (aerobic exercise training zone) in other cardiac populations (8). All patients were immersed in warm water up to the xiphoid process during the HEx session. An investigator that was blinded to the patients' GXT and their HR corresponding to AT (HR_{AT}) and RCP (HR_{RCP}) instructed all patients during both HEx and LEx, and standardized encouragement with phrases such as "If you can walk faster, increase the speed," "If it is tiring, you can reduce the speed," and "If you are feeling good, keep the speed" was provided every 3 min of exercise (8). HEx and LEx exercise intensities (walking speed) were self-regulated by the patients, which were blinded to the treadmill speed (during LEx intervention) and exercise HR (during both HEx and LEx interventions). The patients' HR was continuously monitored (Polar Electro Oy, Kempele, Finland) throughout the HEx and LEx sessions. The blinded investigator checked and recorded patients' HR every 4 min of each exercise session, and mean HR during the 30-min exercise was recorded immediately after each session.

Statistical analyses. Data are reported as mean ± SEM. SigmaStat 3.5 for Windows (Systat Software Inc., Chicago, IL) was used to perform the statistical analysis. The Shapiro–Wilk test was applied to ensure a Gaussian distribution of the data. Paired Student's *t*-test was used to identify differences in absolute and relative average HR between HEx and LEx. Chi-square was used to analyze HR frequencies during interventions (exercise HR < HR_{AT}, exercise HR between HR_{AT} and HR_{RCP}, and exercise HR > HR_{RCP}). Two-way ANOVA with repeated measurements (intervention vs time) was used to indicate inter- and intraintervention differences in exercise HR. The Bonferroni *post hoc* analysis was used to identify significant differences that were indicated by ANOVA. The significance level was set at $P < 0.05$.

RESULTS

Fifteen (five females) clinically stable heart transplant recipients, age 36 to 60 yr, 1 to 9.3 yr elapsed since HT, and with no evidence of tissue rejection (endomyocardial biopsy), participated in the study (Table 1). The GXT was well tolerated (exercise duration from 11 to 21 min), and no significant side effect was reported by all patients. HR, $\dot{V}O_2$, and RER data are displayed in Table 2. As expected, patients showed higher $HR_{resting}$ and lower HR_{max} (55% to 87% of age-predicted HR_{max}) levels than those commonly found in healthy population (35). AT and RCP occurred between 56.5% ± 2.3% and 84.5% ± 2.0% of $\dot{V}O_{2max}$, respectively. All patients showed RER above 1.05 (1.05 to 1.47) at the last stage of GXT, suggesting that they performed maximal efforts (16).

The HEx and LEx interventions were also well tolerated by all patients, and no adverse events occurred during the study. No significant differences between sessions were found in absolute and relative average HR (Table 3). The HR measured every 4 min of the exercise session was maintained between the AT and RCP (in the aerobic exercise training zone) for the most part of both HEx (72% of HR measurements) and LEx (66% of HR measurements). Only a few HR measurements stayed below HR_{AT} (HEx = 9%, LEx = 13%) or above HR_{RCP} (HEx = 19%, LEx = 21%) during both exercise sessions. There were no significant differences in HR frequencies (exercise HR < HR_{AT}, exercise HR between HR_{AT} and HR_{RCP}, and exercise HR > HR_{RCP}) between both HEx and LEx.

No significant interactions between inter- and intraintervention and no significant differences between interventions were found in exercise HR as absolute values, as percentage of HR_{AT}, as percentage of HR_{RCP}, and as percentage of HR_{max}. However, the two-way ANOVA indicated significant intraintervention differences in exercise HR in absolute values ($F_{6,20.96} = 15.122$, $P < 0.001$), as percentage of HR_{AT} ($F_{6,14.67} = 16.440$, $P < 0.001$), as percentage of HR_{RCP} ($F_{6,15.74} = 18.267$, $P < 0.001$), and as percentage of HR_{max} ($F_{6,15.71} = 17.791$, $P < 0.001$). *Post hoc* analysis showed

TABLE 2. GXT parameters.

Variable	
$HR_{resting}$ (bpm)	89.5 ± 4.2
HR_{AT} (bpm)	99.5 ± 4.4
HR_{RCP} (bpm)	117.4 ± 5.6
HR_{max} (bpm)	129.5 ± 5.3
% of age-predicted HR_{max} (%)	74 ± 3.0
$\dot{V}O_{2AT}$ ($mL\cdot kg^{-1}\cdot min^{-1}$)	13.2 ± 1.0
$\dot{V}O_{2RCP}$ ($mL\cdot kg^{-1}\cdot min^{-1}$)	20 ± 1.5
$\dot{V}O_{2max}$ ($mL\cdot kg^{-1}\cdot min^{-1}$)	22.8 ± 1.4
RER	1.17 ± 0.03
Exercise duration (min)	15.8 ± 1.1

TABLE 3. Absolute and relative average HR during HEx and LEx.

Variable	HEx	LEx	*P*
HR (bpm)	114.7 ± 3.8	112.0 ± 4.1	0.613
% of HR_{AT} (%)	112.7 ± 4.0	114.2 ± 4.6	0.969
% of HR_{RCP} (%)	94.0 ± 2.4	96.2 ± 3.8	0.927
% of HR_{max} (%)	84.9 ± 2.5	86.4 ± 3.3	0.927

that HR in the fourth minute of both HEx and LEx was lower than HR from the eighth minute onwards (Fig. 1). HR in the eighth minute of HEx and LEx was lower than HR from the sixteenth minute onwards (Fig. 1). No significant HR differences were found after the eighth minute of both HEx and LEx (Fig. 1). Because the exercise intensity was constant throughout the HEx and LEx (11 to 13 on the 6–20 RPE scale), these results showed a delay in HR increase with the stabilization beginning after the eighth minute of exercise (Fig. 1).

DISCUSSION

The usefulness of RPE for prescribing and regulating LEx in HT recipients has been investigated since the 1990s (22,34). However, to the best of our knowledge, this is the first study to analyze the usefulness of 6 to 20 RPE scale (5) for prescribing and self-regulating HEx in HT recipients. The main finding of the present study was that to prescribe and self-regulate HEx and LEx by RPE between "relatively easy and slightly tiring" (11 and 13 on the 6–20 RPE scale) took the patients' HR between AT and RCP (aerobic exercise training zone) for the most part of both sessions. Although multicenter studies with a larger sample are required to confirm present results, this preliminary finding suggests that RPE scale may be a simple, inexpensive, and useful tool for prescribing and self-regulating HEx and LEx in this population.

Despite the evidence of partial cardiac sympathetic reinnervation (24,37), cardiac denervation after HT makes the patient's exercise HR response to be dependent on the Frank–Starling mechanism and endogenous catecholamines release (7,21), resulting in delayed HR increase during exercise, lower levels of HR at maximal and submaximal efforts, and slow HR decrease after exercise cessation when compared with age-matched healthy subjects (6,9,31), which was confirmed in the present study by the delay in HR increase followed by a stabilization that began after 8 min of both HEx and LEx interventions. This altered HR response turns difficult exercise prescription by traditional indirect methods in this population (7). For example, aerobic

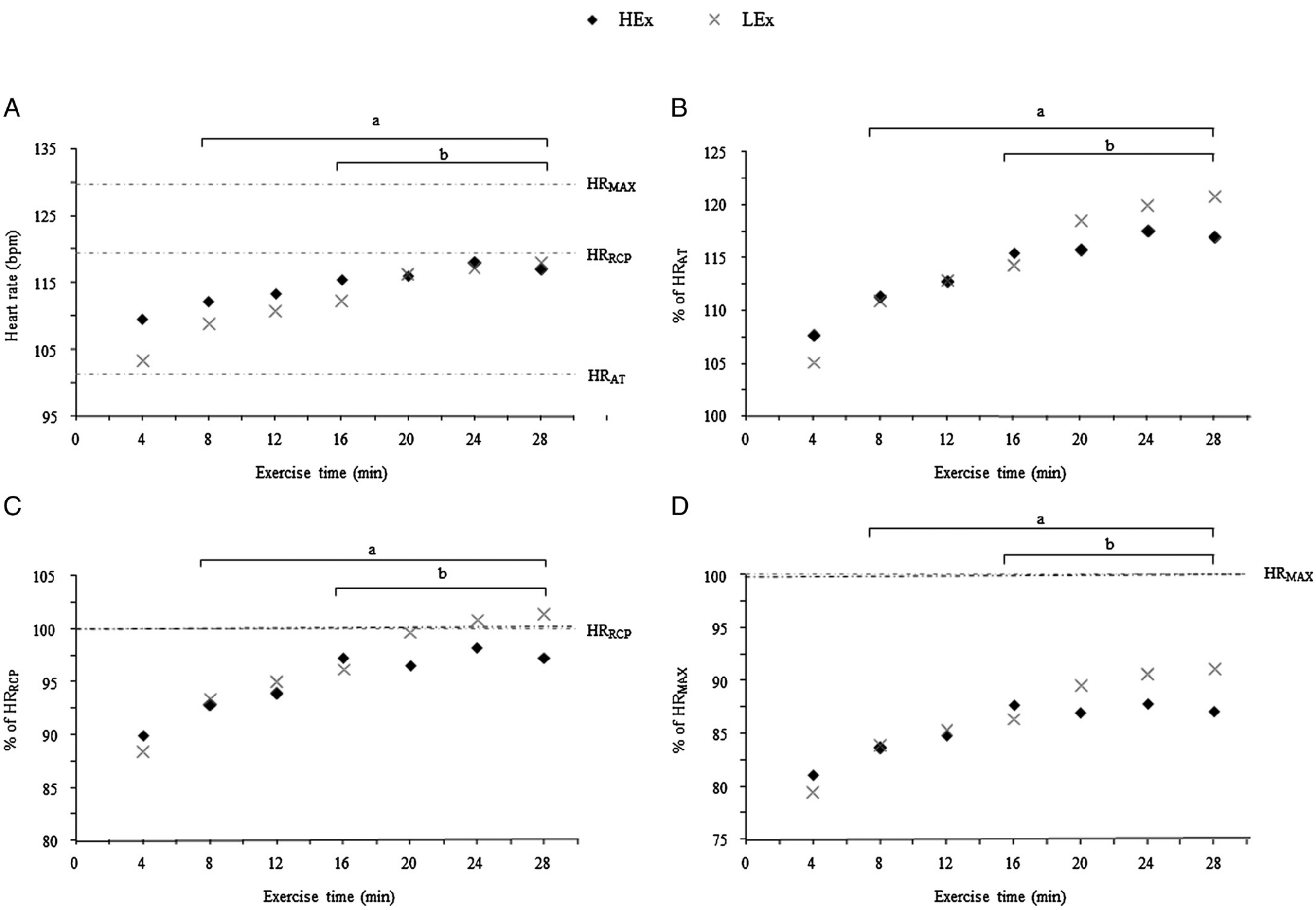

FIGURE 1—HR dynamic during the 30-min HEx and LEx. A, HR dynamic in absolute values. B, HR dynamic as percentage of HR_{AT}. C, HR dynamic as percentage of HR_{RCP}. D, HR dynamic as percentage of HR at maximal effort (HR_{max}). [a]Significantly different from 4 min (*P* < 0.01). [b]Significantly different from 8 min (*P* < 0.01). There were no significant HR changes after the eighth minute of both HEx and LEx.

exercise prescription and regulation by percentage of reserve HR or HR_{max} are useful, effective, and widely applied in healthy and several chronic disease populations because of the close relationship between HR and $\dot{V}O_2$ (7,15). Although a relationship between HR and $\dot{V}O_2$ also occurs in HT, it is not reliable (9), which makes the use of indirect HR methods to prescribe and regulate aerobic exercise in this patients inappropriate (7,9,21).

In this context, the gold standard method for exercise prescription in HT recipients is based on HR at AT and RCP during a cardiopulmonary GXT (7), with the use of percentage $\dot{V}O_{2max}$ also being recommended (7,21). However, this method requires expensive equipment (respiratory gas analyzer) that may not be available for most cardiology centers (1,7,27). In addition, the delayed HR increase during exercise (Fig. 1) could result in early fatigue during the HR-guided exercise session, mainly if the second ventilatory threshold is the target HR (7,21). Thus, the search for simple, inexpensive, and feasible indirect methods (as RPE) for prescribing and self-regulating aerobic exercise after HT is necessary. The usefulness of RPE for prescribing and self-regulating aerobic exercise in both healthy (10,11) and chronic disease populations (8,25) has been shown in previous studies. The use of RPE, mainly in association with ventilatory threshold or percentage of $\dot{V}O_{2max}$, has been suggested to prescribe aerobic exercise in HT recipients (7,21). This recommendation has been based on previous studies with HT recipients analyzing RPE response during maximal GXT (34) or analyzing the mean percentage of maximal and reserve HR maintained during RPE-guided LEx sessions (22). In addition to previous studies, the present study showed for the first time that to prescribe and self-regulate aerobic exercise by the RPE at a level between "relatively easy and slightly tiring" (11,13) maintained HT recipients' HR between the AT and RCP (in the aerobic exercise training zone) for the most part of both HEx (72%) and LEx (65%) sessions, and thus may be an alternative to the gold standard direct methods (7,21).

HEx has recently emerged as an alternative to the traditional LEx (i.e., walking, cycling and running). We and others have shown that HEx promotes important cardiovascular benefits for different cardiac populations (19,28). In addition, the buoyancy effect during HEx reduces loading, facilitating the performance of aerobic and resistance exercise, mainly in subjects with musculoskeletal limitations (12). However, one must argue that the hydrostatic pressure and water temperature during HEx may result in increased cardiovascular response, which may be potentially dangerous for cardiac populations (8). The similar HR response between HEx and LEx observed in the present study does not support this concern. Moreover, the present result also suggests that RPE may be an alternative tool to prescribe and self-regulate HEx in HT patients, which is in accordance with a previous study by our group with chronic heart failure patients (8).

Independent of the method of exercise training, the prescription of adequate intensity is crucial to obtain both an acceptable training stimulus and a reasonable control of the exercise-related risk (15,21). In the case of patients with HT, a well-prescribed aerobic exercise training program was shown to be safe and effective (21). For example, no increase in rejection and infection rate has been shown in HT patients performing low- to moderate-intensity aerobic exercise (23). Benefits of aerobic exercise training after HT include improvements in cardiorespiratory fitness (2,21,23), chronotropic and blood pressure response (2,21), peripheral oxygen extraction and mitochondrial density (21,38), endothelial function (32), ventilatory efficiency during exercise (21,23), and quality of life (21). Moreover, HT recipients show increased prevalence of comorbidities, with systemic arterial hypertension being the most prevalent (nearly 95% of patients are hypertensive 5 yr after HT) (26). HEx was shown to promote important cardiovascular benefits for different cardiac populations (18,19,28), including large blood pressure reduction in subjects with resistant hypertension (18,19), and may be an alternative to the traditional aerobic LEx in HT recipients.

In this context, the results of the present study may have important clinical implications. The effectiveness of RPE scale at a level between 11 and 13 to maintain heart transplant recipients' HR between AT and RCP (in the aerobic exercise training zone) may be a useful tool for prescribing and self-regulating both HEx and LEx. Given the high cost and low access of the direct methods used to prescribe and regulate exercise in these patients (7,21), and the abovementioned health-related benefits of HEx and LEx, the use of the simple and inexpensive tool RPE scale to prescribe and self-regulate exercise may increase access and adherence to these exercise modalities and consequently increase exercise-related benefits after HT. In this context, future multicenter randomized controlled trials that focus on analyzing adherence and health-related benefits of HEx and LEx prescribed and self-regulated by RPE in heart transplant recipients are welcome.

The main limitations of the present study include its design, where the use of a single session of HEx and LEx prescribed and self-regulated by RPE does not allow stating that present results would persist after a long period of training. However, the initial step to evaluate the response to any exercise intervention is to analyze the acute responses that this intervention produces, and training studies may not be justified without demonstrating an efficient acute response first. Moreover, a number of studies have shown that RPE association with exercise intensity remains stable regardless of training and health status (25,33) and is sensitive to training-induced threshold changes (20,22), suggesting that the results of the present study may persist after periods of training. The small sample size and the inclusion of selected patients that underwent HT for at least 1 yr (1 to 9.3 yr) make it difficult to extrapolate the present finding to all HT patients, mainly in more limited patients with less than 4 months that elapsed since surgery. Multicenter longitudinal studies with a larger sample are thus necessary to confirm present results. Finally, the verbal instructions provided every 3 min of exercise may influence patients' exercise intensity during both HEx and LEx sessions, and it is unclear if the same HR response would occur without these instructions. Thus, future studies analyzing the HR response during RPE-guided exercise sessions without verbal instructions are welcome.

In summary, exercise RPE between "relatively easy and slightly tiring" (11 and 13 on the 6–20 RPE scale) was effective in maintaining heart transplant patients' HR between AT and RCP for the most part of both HEx and LEx sessions. Although future studies with larger sample size are required to confirm the present finding, the present study suggests that the 6–20 RPE scale may be an efficient tool for prescribing and self-regulating HEx and LEx programs in this population. In heart transplant rehabilitation, these results may be potentially important for prescribing and managing exercise training programs with no requirement of the GXT with respiratory gas analysis, which may imply lower costs and increased access and compliance.

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There are no conflicts of interest to declare.

The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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