Aerobic Training Improves Quality of Life in Women with Polycystic Ovary Syndrome

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ABSTRACT

COSTA, E. C., J. C. F de SÁ, N. K. STEPTO, I. B. B. COSTA, L. F. FARIAS-JUNIOR, S. da N. T. MOREIRA, E. M. M. SOARES, T. M. A. M. LEMOS, R. A. V. BROWNE, and G. D. AZEVEDO. Aerobic Training Improves Quality of Life in Women with Polycystic Ovary Syndrome. *Med. Sci. Sports Exerc.*, Vol. 50, No. 7, pp. 1357–1366, 2018. **Purpose**: To investigate the effects of a supervised aerobic exercise training intervention on health-related quality of life (HRQL), cardiorespiratory fitness, cardiometabolic profile, and affective response in overweight/obese women with polycystic ovary syndrome (PCOS). **Methods**: Twenty-seven overweight/obese inactive women with PCOS (body mass index, ≥ 25 kg·m^{-2}; age 18 to 34 yr) were allocated into an exercise group (n = 14) and a control group (n = 13). Progressive aerobic exercise training was performed three times per week (~150 min·wk^{-1}) over 16 wk. Cardiorespiratory fitness, HRQL, and cardiometabolic profile were evaluated before and after the intervention. Affective response (i.e., feeling of pleasure/displeasure) was evaluated during the exercise sessions. **Results**: The exercise group improved 21% ± 12% of cardiorespiratory fitness (P < 0.001) and HRQL in the following domains: physical functioning, general health, and mental health (P < 0.05). Moreover, the exercise group decreased body mass index, waist circumference, systolic and diastolic blood pressure, and total cholesterol level (P < 0.05). The affective response varied from "good" to "fairly good" (i.e., positive affective response) in an exercise intensity-dependent manner during the exercise training sessions. **Conclusions**: Progressive aerobic exercise training improved HRQL, cardiorespiratory fitness, and cardiometabolic profile of overweight/obese women with PCOS. Moreover, the participants reported the exercise training sessions as pleasant over the intervention. These results reinforce the importance of supervised exercise training as a therapeutic approach for overweight/obese women with PCOS.
Key Words: PCOS, EXERCISE, HEALTH-RELATED QUALITY OF LIFE, OBESITY, AFFECT

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in reproductive age women. The main clinical features of PCOS include menstrual dysfunction (i.e., oligomenorrhea or amenorrhea), obesity, hirsutism, and infertility (1). Polycystic ovary syndrome is also associated with several cardiometabolic risk factors, such as central obesity (2), insulin resistance (3), metabolic syndrome (4), hypertension (5), low-grade chronic inflammation (6), and poor cardiorespiratory fitness (7). Consensus among international experts (1) and the first evidence-based guideline (8) recommend that an adequate assessment and intervention on cardiometabolic health should be part of clinical management for women with PCOS, especially those with overweight and obesity.

Moreover, women with PCOS present poor health-related quality of life (HRQL) (9,10). It seems that the wide spectrum of health issues involving PCOS affects mental health, well-being, and HRQL of these women (11). Thus, mental health and HRQL should be considered in women with PCOS, and therapeutic approaches need to be implemented

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to improve their health in a more comprehensive perspective (12). Recently, Conte et al. (13) highlighted a limited number of studies that have investigated HRQL of outcomes after physical exercise interventions in women with PCOS. To date, only Stener-Victorin et al. (14) have investigated the independent effects of physical exercise on HRQL in women with PCOS. The authors did not find significant improvements on HRQL after an aerobic exercise intervention; however, the exercise intervention was not formally supervised. Although other studies have explored the role of exercise in improving HRQL, most interventions have included additional approaches (e.g., diet intervention) (15) or did not establish a control group (13). However, epidemiological evidence suggests that being physically active is associated with better HRQL specifically with reduced anxiety and depression (16). Therefore, further research investigating the effects of exercise training interventions, especially supervised ones, on HRQL outcomes in women with PCOS are urgently needed. These studies are likely to provide valuable information to improve clinical management for these women.

Lifestyle modification is the first-line therapy for overweight/obese women with PCOS (8), and physical exercise is a cornerstone of lifestyle intervention because it promotes several benefits on the health status of women with PCOS (17,18). Internationally, consensus statements (1) and evidence-based guidelines (8) recommend that further research on aspects related to participation and compliance in lifestyle programs is needed to optimize clinical approaches to treat and manage PCOS. Given the importance of physical exercise in lifestyle modification programs, it seems important to investigate aspects that could help to increase adherence and decrease dropout of women with PCOS during this intervention. Basic affective response (i.e., feeling of pleasure/displeasure) during exercise has been considered an important factor for participation and adherence to exercise training (19). Thus, exercise interventions should improve health-related outcomes and individuals should perceive it as pleasant and enjoyable, which may help to increase the long-term adherence rate. This is particularly important for those with excess body weight, who present high dropout rates during exercise training programs (20). In a previous study (21), we instructed overweight/obese women with PCOS to self-select an exercise intensity that feels pleasant [i.e., feeling "good" and "very good" on the Feeling Scale (FS) (22)] while exercising for 40 min. Interestingly, they spent 81% of this exercise training session at the moderate intensity level [i.e., 64%–76% of HR_{max}, which is recommended by the American College of Sports Medicine (23) to improve fitness- and health-related outcomes. However, to the best of our knowledge, no previous study has assessed the basic affective response to exercise during a prolonged training intervention in overweight/obese women with PCOS.

Therefore, the primary aim of this study was to investigate the effects of a supervised aerobic exercise training intervention on HRQL, cardiorespiratory fitness and cardiometabolic profile in overweight/obese women with PCOS. The secondary aim was to assess the basic affective response reported by the participants during the exercise training sessions over the intervention.

METHODS

Subjects. Overweight and obese (body mass index [BMI], between 25 and 39.9 $kg \cdot m^{-2}$) women with PCOS age from 18 to 34 yr were recruited from the University Hospital, Federal University of Rio Grande do Norte, Natal/RN, Brazil. Only physically inactive women were considered for the study; that is, no participation in exercise training program in the last 3 months and do not perform 150 $min \cdot wk^{-1}$ or more of moderate to vigorous physical activity. The diagnosis of PCOS was made according to Rotterdam criteria (24) by at least two clinicians. For PCOS diagnosis two of the following (i) oligovulation or anovulation, (ii) clinical (hirsutism and acne) and/or biochemical hyperandrogenism, and (iii) polycystic ovaries on ultrasound (24) must be present with the exclusion of other disorders known to cause hyperandrogenism, such as nonclassical congenital adrenal hyperplasia, thyroid dysfunction, and hyperprolactinemia. Additional exclusion criteria for this study were renal or hepatic dysfunction, or use of medications (including over the counter preparations) known to impact anxiety, depression, reproductive, cardiovascular or metabolic function within 90 d of study entry. This study was approved by the Institutional Ethics Committee (protocol 222/08). All volunteers gave written informed consent before participation.

Study design. Participants were randomized into a two-group, parallel, controlled clinical trial to assess the efficacy of a supervised aerobic exercise training intervention on cardiorespiratory fitness, HRQL, cardiometabolic profile, and affective response in women with PCOS. The CONSORT guideline was followed (25). The study was carried out from February 2010 to December 2011 at the university campus. At baseline and after 16 wk, cardiorespiratory fitness, HRQL, and cardiometabolic risk factors were assessed in both groups. During each exercise training session over the intervention, the participants from the exercise group reported the basic affective response. Participants from both groups were counselled to maintain their habitual diet. The postexercise intervention assessments occurred 72 h after the last exercise training session.

Sample size and randomization. A statistical power analysis *a priori* was conducted considering an absolute change in $\dot{V}O_{2peak}$ of 5.0 $mL \cdot kg^{-1} \cdot min^{-1}$ (SD of 4.0) based on previous studies (17,26), a statistical power $1 - \beta$ of 90%, and an alpha of 5%. The sample size required for the study was 13 participants per group. Considering a dropout rate of 15% to 20%, we recruited 15 participants per group. A total of 30 volunteers were recruited for this clinical trial (Fig. 1). The participants were randomly allocated, where possible, to the supervised exercise group or the control group. Allocation to exercise group was based on ability to attend the 16 wk of training, which was limited for some participants (n = 5) due to their remote geographical location. The randomization sequence was computer generated (randomization.com).

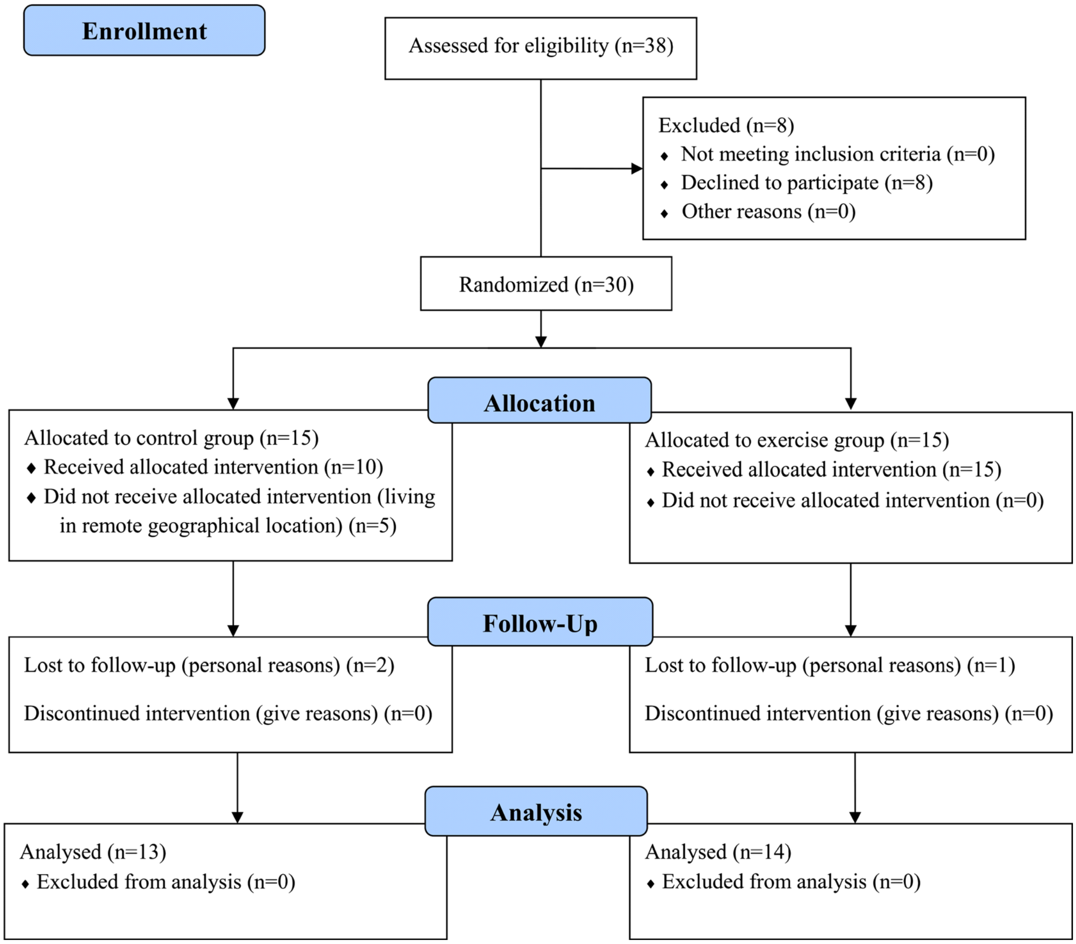

FIGURE 1—Flow diagram of the study.

Health-related quality of life. The Brazilian-Portuguese version of the 36-Item Short Form Health Survey (SF-36) was used to assess HRQL of participants before and after the 16-wk intervention. This psychometric tool included eight domains, involving both physical and emotional aspects: physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health. The validated Brazilian–Portuguese version of the SF-36 was used in this study (27).

Cardiorespiratory fitness. Participants undertook a graded exercise test on a treadmill (Inbrasport®, Porto Alegre, Brazil) to assess cardiorespiratory fitness at baseline and after the 16-wk intervention. The treadmill exercise protocol was an incremental test. After a 1-min warm-up, the test started at a speed of 2 $km \cdot h^{-1}$ without gradient and progressed with increasing speed (0.5 $km \cdot h^{-1}$) and gradient (1% grade) every minute until volitional exhaustion. This protocol was based on previous studies that have assessed cardiorespiratory fitness of overweight/obese women with PCOS using treadmill (26,28). A 12-lead electrocardiogram was continuously monitored during the test. Oxygen consumption ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), and minute ventilation ($\dot{V}_E$) were assessed from expired air using VO2000 $\dot{V}O_2$ testing system (MedGraphics®, St. Paul, MN) every 20 s while participants were exercising. Peak oxygen uptake ($\dot{V}O_{2peak}$) was determined by the presence of at least one of the following criteria: (i) presence of respiratory exchange ratio ($\dot{V}CO_2/\dot{V}O_2$) > 1.1, (ii) occurrence of plateau in oxygen uptake, (iii) volitional physical exhaustion. The ventilatory threshold (VT) was determined when $\dot{V}_E/\dot{V}O_2$ and $PETO_2$ increased, whereas $\dot{V}_E/\dot{V}CO_2$ and $PETCO_2$ remained stable. The respiratory compensation point was determined at a moment where $\dot{V}_E$ started to change out of proportion of $\dot{V}CO_2$ (i.e., systematic increase in $\dot{V}_E/\dot{V}CO_2$) with a consequent decline on $PETCO_2$ (29).

Cardiometabolic profile. All patients underwent a clinical examination, where body weight (kg), height (m), waist circumference (cm), and blood pressure (BP) were measured. Body mass index was calculated as weight (kg) divided by the square of height in meters ($kg \cdot m^{-2}$). Waist circumference was obtained at the midpoint between the lateral iliac crest and the lowest rib margin at the end of normal expiration. Blood pressure was measured in a seated position according to VI Brazilian Guidelines on Hypertension (30) using automated oscillometric device (Omron® HEM-780-E, Kyoto, Japan) and reported as the mean of the second and the third measurements.

A blood sample was collected after a 12-h overnight fast. The metabolic profile included fasting glucose, a 75-g oral glucose tolerance test (OGTT), total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and fasting insulin. The OGTT assay was performed by oral administration of 75 g anhydrous glucose ingested in a maximum time of 5 min. Plasma glucose was determined after 30, 60, 90, and 120 min. All biochemical assays were determined using commercial kits (Diagnostic Labtest-SA®, São Paulo, Brazil) by the colorimetric method/enzyme in equipment Bioplus, 2000 model (Barueri, Brazil). Luteinizing hormone, follicle-stimulating hormone, estradiol, progesterone, total testosterone, prolactin, dehydroepiandrosterone sulfate, and insulin were also analyzed. Tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP) were assessed as proinflammatory markers. These measurements were performed by chemiluminescence (Immulite 1000®; Diagnostic Products Corporation, Los Angeles, CA), except CRP which was measured by immunoturbidimetric assay based on immunoprecipitation reaction (Labmax 240; Labtest Diagnostic-SA®, São Paulo, Brazil). Low-density lipoprotein cholesterol was determined using the Friedewald formula: (total cholesterol − [HDL + triglycerides/5]). The homeostatic model assessment of insulin resistance (HOMA-IR) was used to determine insulin resistance by formula: (fasting glucose in mg·dL^{-1} × 0.05551) × fasting insulin in U·mL^{-1}]/22.5.

Supervised aerobic exercise training. The supervised aerobic exercise training was performed three times per week for 16 wk. Participants performed 40 min of aerobic exercise during each training session, which was preceded by 5 min of warm-up and followed by 5 min of cool-down. The aerobic exercise training program is detailed in the supplementary data (see Table, Supplemental Digital Content 1, Progressive aerobic exercise training program, http://links.lww.com/MSS/B211). It was structured according to the practical exercise intensity scheme classification, based on HR_{max}, of the American College of Sports Medicine (23). The HR_{max} obtained at the initial cardiopulmonary exercise test was used to determine the specific exercise training zones used in each exercise session during the training intervention (see Table, Supplemental Digital Content 1, Progressive aerobic exercise training program, http://links.lww.com/MSS/B211). The exercise sessions were performed under the supervision of an exercise physiologist in the afternoon (between 4:00 PM and 6:00 PM) on a standard outdoor 400-m track. Each participant was fitted with a HR monitor (Polar® FT1 C, Kempele, Finland), and they were instructed to regulate their exercise pacing (i.e., walking and/or jogging) according to their specific HR exercise training zones. The participants exercised in small groups (i.e., 2–4 participants per group), according to their fitness level. After the initial stretching and warming up routine, the groups completed 40 min in the specific HR training zones according to the exercise training program (see supplementary data).

Affective response during exercise. The FS (22) is an 11-point bipolar scale ranging from +5 to −5, commonly used to measure basic affective response (i.e., pleasure/displeasure) during exercise. This scale presents the following verbal anchors: −5, very bad; −3, bad; −1, fairly bad; 0, neutral; +1, fairly good; +3, good; and +5, very good. The American College of Sports Medicine recommends this scale to measure basic affective response during exercise (23). The participants received standard instructions regarding the FS in the first exercise training session as described by Hardy and Rejeski (22). During the training sessions, the FS scores were recorded every 10 min by an exercise physiologist, and the mean FS score for each exercise training session was obtained. Then, the mean FS score for each different training periods (i.e., 60%–70%, 70%–75%, 75%–80%, and 80%–85% of HR_{max}; see Table 1) of the aerobic exercise training intervention was calculated.

Statistical analysis. Data are presented as mean ± SD. Shapiro–Wilk test confirmed the normal distribution of the data. The baseline differences between groups were assessed using independent samples *t* test for continuous data and Fisher exact test for categorical data. A generalized estimating equation followed by Bonferroni *post hoc* test was used to assess the efficacy of aerobic exercise training on cardiorespiratory fitness, HRQL scores, and cardiometabolic risk factors. The generalized estimating equation model for each outcome was based on the goodness of fit. The normality of the residuals was verified by normal Q–Q plot. Some cardiometabolic variables were transformed due to the high variability among individuals, using (i) square root transformation for triglycerides, (ii) logarithmic transformation for insulin and CRP, and (iii) inverse transformation for IL-6 and TNF-α. To compare the basic affective response among the different phases of the aerobic exercise training intervention the repeated-measures ANOVA followed by Bonferroni *post hoc* test was used. For all analyses, a two-tailed $P < 0.05$ was considered statistically significant. Data analysis was performed using SPSS® version 22.0 for Windows (SPSS®, Chicago, IL).

All between-group differences with a $P < 0.09$ for group–time interaction were further explored using magnitude-based inference (MBI) statistics using standardized effect sizes (ES) and clinical inferences (harm or benefit) (31). Data were entered in custom excel spreadsheets for controlled trial (32), which calculated the ES, and the 95% confidence limits (95% CL) based the smallest worthwhile change of 0.2× between

TABLE 1. Baseline characteristics of the exercise and control groups.

	Control Group	Exercise Group	*P*
Age (yr)	24.4 ± 5.0	27.6 ± 4.5	0.087
Ferriman–Gallwey score	5.92 ± 4.37	7.43 ± 2.06	0.274
Total testosterone (nmol·L^{-1})	3.24 ± 1.08	4.26 ± 2.11	0.130
DHEA-S (nmol·L^{-1})	5.00 ± 4.03	4.82 ± 3.25	0.896
LH (IU·L^{-1})	5.48 ± 5.37	5.02 ± 3.27	0.794
FSH (IU·L^{-1})	3.36 ± 1.58	3.02 ± 1.54	0.589
$\dot{V}O_{2peak}$ (mL·kg^{-1}·min^{-1})	26.8 ± 6.2	27.9 ± 3.3	0.579
HR_{max} (bpm)	183.7 ± 15.3	187.6 ± 6.1	0.413
% HR_{max} at VT	79 ± 4	77 ± 5	0.321
% HR_{max} at RCP	92 ± 3	90 ± 4	0.298

Data are presented as mean ± SD.
FSH, follicle-stimulating hormone; LH, luteinizing hormone; DHEA-S, dehydroepiandrosterone sulfate; RCP, respiratory compensation point.

group SD. The criteria to interpret the magnitude of the ES were as follows: <0.2 is trivial, 0.2 to 0.5 is small, 0.6 to 1.1 is moderate, 1.2 to 1.9 is large, and 2.0 to 4.0 is very large. The chance that the true (unknown) values for exercise group was beneficial, unclear, or harmful for change was calculated. The chances of beneficial or harmful effect were assessed qualitatively as follows: <1%, almost certainly not; 1%–5%, very unlikely; 5%–25%, unlikely; 25%–75%, possibly; 75%–95%, likely; 95%–99%, very likely; >99%, almost certainly. If the chance of having beneficial or harmful changes was both >5%, the true difference was assessed as unclear.

RESULTS

Table 1 shows the baseline characteristics of the participants. There were no differences between the exercise and the control group ($P > 0.05$). The prevalence of prediabetes was 25% and 14.3% in the control group and exercise group, respectively. The prevalence of prehypertension was 15.4% and 21.4% in the control group and exercise group, respectively. No differences in the prevalence of prediabetes ($P = 0.635$) and prehypertension ($P = 1.0$) were observed between the groups.

Table 2 shows the results of HRQL of the exercise and the control groups. There was a significant group–time interaction for physical functioning (ES, 1.2; 95% CL, 0.5–1.9; $P = 0.004$), general health (ES 0.9 [95% CL 0.2, 1.7]; $P = 0.012$), and mental health (ES, 1.0; 95% CL, 0.0–2.0; $P = 0.042$) scores. There were trends for group–time interaction for physical role (ES, 1.0; 95% CL, 0.1–1.8; $P = 0.062$) and emotional role (ES, 0.8; 95% CL, 0.0–1.6; $P = 0.072$), but no significant interactions for bodily pain, vitality, and social functioning.

Table 3 shows the results of cardiorespiratory fitness and cardiometabolic risk profile of the exercise and the control groups. Regarding the cardiorespiratory fitness, there was a significant time–group interaction for relative $\dot{V}O_{2peak}$ (ES 1.2 [95% CL 0.6, 1.8]; $P < 0.001$). The exercise group increased the $\dot{V}O_{2peak}$ in 21% ± 12% (5.9 $mL \cdot kg^{-1} \cdot min^{-1}$; 95% confidence interval [CI], 4.0–7.8]; $P < 0.001$) after 16 wk, whereas the control group did not present significant change (0.2 $mL \cdot kg^{-1} \cdot min^{-1}$; 95% CI, −1.8 to 2.1]; $P = 1.00$). There was a significant time–group interaction for absolute $\dot{V}O_{2peak}$ (ES, 0.9; 95% CL, 0.4–1.5; $P < 0.001$), BMI (ES, −0.3; 95% CL, −0.4 to −0.1]; $P < 0.001$), waist circumference (ES, −0.7; 95% CL, −1.1 to −0.3; $P < 0.001$), systolic BP (ES, −0.9; 95% CL, −1.6 to −0.2; $P = 0.011$), diastolic BP (ES, −1.0; 95% CL, −1.7 to −0.2; $P = 0.004$), mean BP (ES, −1.0; 95% CL, −1.7 to −0.3; $P = 0.002$), total cholesterol (ES, −1.1; 95%, CL, −2.3 to 0.1; $P = 0.043$), LDL cholesterol (ES, −1.0; 95% CL, −1.9 to 0.0; $P = 0.037$), TNF-α (ES, −1.2; 95% CL, −2.1 to −0.2; $P = 0.019$), and CRP levels (ES, −0.7; 95% CL, −1.4 to 0.0; $P = 0.037$). The exercise group decreased the BMI and waist circumference, whereas the control group increased the BMI after 16 wk. The exercise group decreased the total cholesterol level and systolic, diastolic, and mean BP, whereas the control group did not present significant change. The control group increased the TNF-α level, whereas the exercise group did not present significant change. There was no significant time–group interaction for HDL cholesterol, triglycerides, fasting glucose, 2-h postprandial glucose, area under the curve of OGTT, insulin, HOMA-IR, and IL-6 levels.

Table 4 shows the clinical significance of the exercise-related changes on the HRQL and cardiometabolic risk profile using the MBI proposed by Hopkins et al. (31). With regard to the HRQL, the physical functioning domain presented a large improvement, and the physical role, general health, emotional role, and mental health domains presented a moderate improvement. $\dot{V}O_{2peak}$ and TNF-α had a large improvement and the BP, total cholesterol, LDL cholesterol, and CRP had a moderate improvement after 16 wk of aerobic exercise training.

As planned, the mean HR in the four different phases of the supervised exercise training program increased significantly ($P < 0.01$): weeks 1 to 4 (60%–70% HR_{max}): 127 ± 4 bpm (~67% of HR_{max}); weeks 5 to 8 (70%–75% HR_{max}): 138 ± 3 bpm (~73% of HR_{max}); weeks 9 to 12 (75%–80% HR_{max}): 147 ± 3 bpm (~78% of HR_{max}); weeks 13 to 16 (80%–85% HR_{max}): 156 ± 3 bpm (~83% of HR_{max}). Figure 2 shows the basic affective response during the aerobic exercise training intervention. The overall basic affective responses varied from +3.4 ± 0.9 ("good") to +1.3 ± 1.6 ("fairly good") in weeks 1 to 4 and weeks 13 to 16, respectively ($F(2, 23) = 20.58$, $P < 0.001$, partial $\eta^2 = 0.613$). The basic affective response was lower in the weeks 9 to 12 (+2.3 ± 1.3) and weeks 13 to 16 (+1.3 ± 1.6) compared with weeks 1 to 4 (+3.4 ± 0.9) and weeks 5 to 8 (+3.3 ± 1) ($P < 0.01$). Moreover, the basic affective response was lower in weeks 13 to 16 compared with

TABLE 2. HRQL of overweight/obese women with PCOS at baseline and after 16 wk: exercise versus control group.

	Control Group			Exercise Group				
Variables	Baseline	16 wk	Δ (95% CI)	Baseline	16 wk	Δ (95% CI)	β (95% CI) Group–Time	P
Physical functioning	60.8 ± 23.6	56.2 ± 20.9	−4.6 (−15.8 to 6.6)	67.9 ± 19.5	88.9 ± 10.8*,**	21.1 (10.3 to 31.9)	0.35 (0.11 to 0.58)	0.004
Physical role	51.9 ± 37.4	53.8 ± 32.0	1.9 (−21.0 to 24.8)	50.0 ± 39.2	89.3 ± 16.2	39.3 (17.2 to 61.4)	0.54 (−0.03 to 1.12)	0.062
Bodily pain	53.1 ± 25.2	63.7 ± 26.9	10.6 (−5.2 to 26.4)	57.9 ± 23.3	69.9 ± 22.5	12.0 (−3.2 to 27.2)	0.01 (−0.33 to 0.34)	0.971
General health	54.2 ± 19.2	54.2 ± 17.6	0.0 (−10.9 to 10.9)	48.9 ± 19.4	67.1 ± 23.9*	18.1 (7.7 to 28.6)	0.32 (0.07 to 0.56)	0.012
Vitality	41.9 ± 15.1	54.6 ± 22.4	12.7 (1.2 to 24.2)	52.5 ± 17.3	70.7 ± 16.9	18.2 (7.2 to 29.3)	0.03 (−0.25 to 0.31)	0.816
Social functioning	62.5 ± 27.0	70.2 ± 26.8	7.7 (−6.5 to 21.9)	61.6 ± 24.3	81.3 ± 23.9	19.6 (6.0 to 33.3)	0.16 (−0.11 to 0.44)	0.253
Emotional role	51.3 ± 40.0	61.6 ± 35.7	10.4 (−11.6 to 32.3)	38.1 ± 36.7	78.6 ± 31.0	40.6 (19.4 to 61.7)	0.54 (−0.05 to 1.13)	0.072
Mental health	60.9 ± 19.3	58.5 ± 20.9	−2.5 (−15.3 to 10.4)	55.7 ± 16.8	71.1 ± 20.7*	15.4 (3.0 to 27.8)	0.29 (0.01 to 0.56)	0.042

Values are presented as mean ± SD.
*$P < 0.05$ compared with baseline.
**$P < 0.05$ compared with same moment of the control group.

TABLE 3. Cardiometabolic profile of overweight/obese women with PCOS at baseline and after 16 wk: exercise versus control group.

	Control Group			Exercise Group				
Variables	**Baseline**	**16 wk**	**Δ (95% CI)**	**Baseline**	**16 wk**	**Δ (95% CI)**	**β (95% CI) Group–Time**	***P***
BMI ($kg \cdot m^{-2}$)	33.6 ± 5.1	34.3 ± 4.9[a]	0.7 (0.1 to 1.2)	32 ± 4.2	31.3 ± 4.5[a]	−0.6 (−1.1 to −0.1)	−0.04 (−0.06 to −0.02)	<0.001
WC (cm)	94.1 ± 11.6	97.9 ± 11.3	3.8 (1.1 to 6.6)	92.8 ± 10.3	89.1 ± 10.2[a]	−3.7 (−6.4 to −1.0)	−0.08 (−0.12 to −0.04)	<0.001
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	26.8 ± 6.2	26.9 ± 5.0	0.2 (−1.8 to 2.1)	27.9 ± 3.3	33.8 ± 5.0[a,b]	5.9 (4.0 to 7.8)	0.19 (0.10 to 0.27)	<0.001
$\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	2.22 ± 0.45	2.26 ± 0.34	0.04 (−0.10 to 0.19)	2.15 ± 0.27	2.53 ± 0.45[a]	0.38 (0.24 to 0.53)	0.14 (0.07 to 0.22)	<0.001
SBP (mm Hg)	113.8 ± 8.8	112.7 ± 11.5	−1.2 (−5.7 to 3.4)	118.8 ± 8.2	109.9 ± 10.8[a]	−8.9 (−13.2 to −4.5)	−0.07 (−0.12 to −0.02)	0.011
DBP (mm Hg)	73.1 ± 8.5	75.4 ± 8.4	2.3 (−2.0 to 6.6)	78.6 ± 7.7	72.8 ± 7.4[a]	−5.8 (−10.0 to −1.6)	−0.11 (−0.18 to −0.03)	0.004
MBP (mm Hg)	86.7 ± 8.0	87.8 ± 9.2	1.2 (−2.8 to 5.1)	92.0 ± 7.5	85.2 ± 8.1[a]	−6.8 (−10.6 to −3.0)	−0.09 (−0.15 to −0.03)	0.002
TC ($mmol \cdot L^{-1}$)	3.80 ± 0.71	4.18 ± 0.66	0.38 (−0.13 to 0.89)	3.87 ± 0.50	3.58 ± 0.54[b]	−0.29 (−0.78 to 0.20)	−0.17 (−0.34 to −0.01)	0.043
HDL ($mmol \cdot L^{-1}$)	0.85 ± 0.19	0.87 ± 0.19	0.02 (−0.09 to 0.13)	0.91 ± 0.20	0.95 ± 0.21	0.04 (−0.06 to 0.14)	0.02 (−0.12 to 0.17)	0.751
LDL ($mmol \cdot L^{-1}$)	2.09 ± 0.75	2.49 ± 0.64	0.39 (−0.07 to 0.86)	2.44 ± 0.57	2.18 ± 0.58	−0.26 (−0.71 to 0.19)	−0.28 (−0.55 to −0.02)	0.037
TG ($mmol \cdot L^{-1}$)	1.68 ± 0.70	1.80 ± 1.36	0.12 (−0.34 to 12.0)	1.13 ± 0.51	0.97 ± 0.38	−0.16 (−0.60 to 0.27)	—	—
Log TG ($mmol \cdot L^{-1}$)[a]	1.27 ± 0.27	1.28 ± 0.41	0.01 (−0.13 to 0.15)	1.04 ± 0.23	0.97 ± 0.20	−0.08 (−0.21 to 0.06)	−0.08 (−0.24 to 0.07)	0.281
FG ($mmol \cdot L^{-1}$)	4.09 ± 0.82	4.02 ± 0.95	−0.07 (−0.50 to 0.35)	3.66 ± 0.76	3.89 ± 0.53	0.22 (−0.19 to 0.63)	0.08 (−0.06 to 0.22)	0.283
2 h-PG ($mmol \cdot L^{-1}$)	6.96 ± 2.25	5.40 ± 1.64	−1.56 (−3.79 to 0.67)	6.17 ± 1.85	5.46 ± 1.17	−0.72 (−1.48 to 0.04)	0.05 (−0.21 to 0.32)	0.688
AUC-OGTT ($mmol \cdot L^{-1}$)	771.7 ± 198.8	713.7 ± 226.2	−58.0 (−184.4 to 68.4)	754.0 ± 211.6	683.1 ± 146.7	−70.9 (−187.9 to 46.2)	−0.02 (−0.24 to 0.20)	0.856
Insulin ($pmol \cdot L^{-1}$)	106.6 ± 81.0	78.5 ± 42.0	−28.1 (−66.6 to 10.4)	54.4 ± 28.9	37.0 ± 24.1	−17.4 (−54.5 to 19.7)	—	—
Log insulin ($pmol \cdot L^{-1}$)[b]	1.90 ± 0.37	1.82 ± 0.29	−0.08 (−0.27 to 0.11)	1.67 ± 0.25	1.47 ± 0.31	−0.20 (−0.39 to −0.02)	−0.08 (−0.23 to 0.06)	0.252
HOMA-IR	13.9 ± 5.4	13.6 ± 6.4	−0.3 (−3.0 to 2.4)	11.2 ± 4.7	12.3 ± 3.5	1.1 (−1.5 to 3.7)	0.12 (−0.15 to 0.39)	0.395
IL-6 ($pg \cdot mL^{-1}$)	8.5 ± 6.0	15.3 ± 19.6	6.8 (−0.8 to 14.4)	6.6 ± 2.2	7.2 ± 3.3	0.6 (−6.8 to 8.0)	—	—
Log IL-6 ($pg \cdot mL^{-1}$)[c]	0.147 ± 0.054	0.121 ± 0.059	−0.026 (−0.070 to 0.019)	0.168 ± 0.061	0.172 ± 0.097	0.003 (−0.039 to 0.046)	0.214 (−0.132 to 0.561)	0.225
TNF-α ($pg \cdot mL^{-1}$)	5.5 ± 2.4	21.3 ± 51.3	15.9 (−4.5 to 36.2)	7.3 ± 2.6	7.6 ± 3.9	0.3 (−19.3 to 19.9)	—	—
Log TNF-α ($pg \cdot mL^{-1}$)[c]	0.206 ± 0.062	0.147 ± 0.072[a]	−0.059 (−0.102 to −0.016)	0.152 ± 0.050	0.164 ± 0.073	0.012 (−0.030 to 0.054)	0.412 (0.069 to 0.756)	0.019
CRP ($pg \cdot mL^{-1}$)	317.0 ± 223.0	373.4 ± 223.3	56.4 (−25.6 to 138.5)	257.9 ± 147.2	206.9 ± 127.3	−50.9 (−130.0 to 28.1)	—	—
Log CRP ($pg \cdot mL^{-1}$)[b]	2.41 ± 0.29	2.48 ± 0.31	0.07 (−0.06 to 0.21)	2.34 ± 0.25	2.24 ± 0.28	−0.11 (−0.23 to 0.02)	−0.08 (−0.15 to 0.00)	0.037

Values are presented as mean ± SD.
[a]Square root transformation.
[b]Logarithmic transformation.
[c]Inverse transformation, (a) $P < 0.05$ compared to baseline, and (b) $P < 0.05$ compared to same moment of the control group.
AUC-OGTT, area under the curve OGTT; CRP, C-reactive protein; DBP, diastolic BP; FG, fasting glucose; MBP, mean BP; SBP, systolic BP; TC, total cholesterol; TG, triglycerides; WC, waist circumference; 2 h-PG, 2-h postprandial glucose.

TABLE 4. Clinical significance of the changes in the HRQL and cardiometabolic profile of overweight/obese women with PCOS after 16 wk of aerobic exercise training.

	ES (95% CL)	Quantitative Chance			Qualitative Chance	Magnitude
		Harmful	Trivial	Beneficial		
HRQL						
Physical functioning	1.2 (0.5 to 1.9)	0%	0%	99%	Almost certainly	Large
Physical role	1.0 (0.1 to 1.8)	0%	3%	97%	Very likely	Moderate
General health	0.9 (0.2 to 1.7)	0%	3%	97%	Very likely	Moderate
Emotional role	0.8 (0.0 to 1.6)	1%	6%	93%	Likely	Moderate
Mental health	1.0 (0.0 to 2.0)	1%	5%	94%	Likely	Moderate
Cardiometabolic profile						
BMI ($kg \cdot m^{-2}$)	−0.3 (−0.4 to −0.1)	0%	15%	85%	Likely	Small
WC (cm)	−0.7 (−1.1 to −0.3)	0%	1%	99%	Almost certainly	Moderate
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	1.2 (0.6 to 1.8)	0%	0%	100%	Almost certainly	Large
$\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	0.9 (0.4 to 1.5)	0%	1%	99%	Almost certainly	Moderate
SBP (mm Hg)	−0.9 (−1.6 to −0.2)	0%	3%	97%	Very likely	Moderate
DBP (mm Hg)	−1.0 (−1.7 to −0.2)	0%	2%	98%	Very likely	Moderate
MBP (mm Hg)	−1.0 (−1.7 to −0.3)	0%	1%	99%	Very likely	Moderate
TC ($mmol \cdot L^{-1}$)	−1.1 (−2.3 to 0.1)	2%	5%	93%	Likely	Moderate
LDL ($mmol \cdot L^{-1}$)	−1.0 (−1.9 to 0.0)	1%	5%	94%	Likely	Moderate
Log TNF-α ($pg \cdot mL^{-1}$)	−1.2 (−2.1 to −0.2)	0%	2%	97%	Very likely	Large
Log CRP ($pg \cdot mL^{-1}$)	−0.7 (−1.4 to 0.0)	1%	8%	91%	Likely	Moderate

ES are Cohen *d* (standardized mean difference between exercise group and control group) and 95% CL.

weeks 9 to 12 ($P < 0.02$). The attendance to the exercise training session was high (81% ± 5%; 37–43 of the 48 training sessions).

DISCUSSION

The main findings of this study were: (i) the supervised aerobic exercise training intervention improved HRQL and cardiorespiratory fitness in overweight/obese women with PCOS; (ii) the participants from the exercise group improved cardiometabolic profile, reducing BMI, waist circumference, resting systolic, diastolic and mean BP, and total cholesterol level; (iii) the participants reported an overall positive basic affective response (i.e., feeling of pleasure) during the exercise training sessions over the whole intervention. To the best of our knowledge, this is the first study to report the benefits of a supervised and progressive aerobic exercise training intervention on HRQL in overweight/obese women with PCOS.

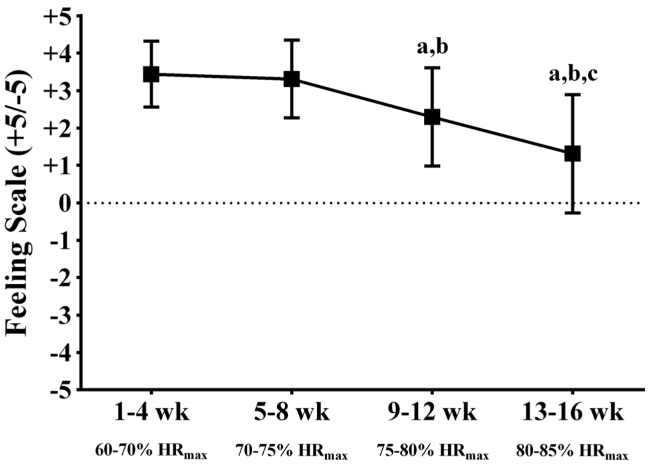

FIGURE 2—Basic affective response of overweight/obese women with PCOS during 16 wk of aerobic exercise training. [a]$P < 0.05$ compared with 1 to 4 wk, [b]$P < 0.05$ compared with 5 to 8 wk, and [c]$P < 0.05$ compared with 9 to 12 wk.

We observed that after the supervised aerobic exercise training intervention, the participants improved the physical functioning, general health, and mental health domains of the SF-36 compared with the control group. Moreover, clinical inferences based on MBI analysis (31) demonstrated that the participants in the 16-wk exercise intervention have a very likely moderate improvement in the physical role domain, and a likely moderate improvement in the emotional role domain compared with controls. Therefore, it seems clear that the supervised exercise training intervention improved the physical and mental health aspects of the HRQL in overweight/obese women with PCOS. In a recent review, Conte et al. (13) identified a single study (14) investigating the specific role of physical exercise on HRQL in women with PCOS. This study (14) failed to show any meaningful changes in HRQL after a 16-wk aerobic exercise intervention in women with PCOS. The lack of detectable effects in this intervention may be due to the nature of the exercise intervention, which lacked direct supervision and monitoring (i.e., HR, perceived exertion, etc.) of the exercise sessions. Participants performed brisk walking, cycling, or any other aerobic exercise at a self-selected pace described as "faster than normal walking," sustained for at least 30 min, three times per week. They received initial instructions on how to exercise and self-monitor the exercise intensity to ensure an HR ≥ 120 bpm. In contrast, our study included exercise training session supervision by a fitness professional (i.e., an exercise physiologist) and had quarterly (4 weekly) progressive overload where exercise intensity levels were increased to optimize cardiorespiratory fitness improvements (23). In addition, the group-training format during the exercise training sessions allowed participants to socialize and share experiences to each other. These differences in the interventions between our work and Stener-Victorin et al.'s (14) may explain the contrasting findings in the physical and mental health aspects of HRQL that we observed in the supervised exercise group compared with the control group.

Cardiorespiratory fitness improved ~1.7 METs, which was 21% higher than the baseline values (9.7 ± 1.4 vs 8.0 ± 0.9 METs) in the supervised exercise group. In general, women with PCOS have a "well below average" cardiorespiratory fitness for their age, irrespective of whether they are considered to have lower (7) or similar (26,28) cardiorespiratory fitness as matched control women. Poor cardiorespiratory fitness is an independent predictor of cardiovascular events and all-cause mortality in women (33). In the Cooper Center Longitudinal Study (11,335 women, mean follow-up of 12.3 ± 8.2 yr), Farrel et al. (33) showed that all-cause mortality was lower in women with high (i.e., >10.3 METs; age group 20–39 yr) and moderate (i.e., 8.2–10.3 METs) cardiorespiratory fitness compared to those with low (i.e., <8.2 METs) cardiorespiratory fitness. Interestingly, the authors observed that the all-cause mortality rate of fit-overweight/obese women (i.e., BMI ≥ 25 $kg \cdot m^{-2}$ and/or waist circumference ≥ 88 cm) was not different from mortality rate of their fit-normal-weight counterparts. Our results showed improvements in cardiorespiratory fitness after the supervised exercise training intervention confirming the findings of previous studies, where supervised moderate-vigorous intensity aerobic exercise were performed three times per week for at least 3 months improved cardiorespiratory fitness of overweight/obese women with PCOS (17,28). Considering obesity and PCOS are synergistic in worsening cardiometabolic health trajectories (34), exercise-induced improvements in $\dot{V}O_{2peak}$ may provide a cardioprotective effect for women with PCOS.

The exercise group reduced BMI (net effect [change of exercise group − change of control group]: 1.3 $kg \cdot m^{-2}$) and waist circumference (net effect, 7.5 cm), even with the counseling to maintain the dietary behavior. The magnitude of these changes is similar to previous studies that have investigated the effects of supervised aerobic exercise training without associated hypocaloric diet in overweight/obese women with PCOS (17,35). Moreover, we observed a reduction of ~9 and ~6 mm Hg in the systolic BP and the diastolic BP after 16 wk only in the exercise group. This result may be explained partially by the improvements in the cardiac autonomic modulation after the exercise training intervention. Previously, we demonstrated that aerobic exercise training increases vagal modulation and decreases sympathetic modulation in overweight/obese women with PCOS (36). Although the *post hoc* tests did not reveal differences in total cholesterol and LDL cholesterol in the exercise group, there was a significant group–time interaction in these lipid outcomes. The exercise group had an average decrease of 6.5% and 7.9% in total cholesterol and LDL cholesterol levels, respectively. These results further reinforces the evidence for clinical improvement induced by the supervised exercise reflected in the reduced cardiovascular disease risk factors including blood biomarkers, body weight, abdominal obesity, and BP. No modifications were observed for fasting glucose and insulin, OGTT, and HOMA-IR in either the control or exercise groups. The lack of changes in these variables may be partially explained by measures used (i.e., not an insulin clamp) (29), and most participants had no clinically diagnosed glycemic dysfunction.

Another important finding of our study was that the participants reported positive basic affective response (i.e., feeling of pleasure) over the whole intervention. This may partially explain the high attendance rate to the exercise training sessions and the absence of dropout. We reinforce the original study on affective response (22) and the most recent American College of Sports Medicine guidelines (23) that state that "exercise that is pleasant and enjoyable can improve adaption and adherence to prescribed exercise programs." Thus, it seems important to consider the use of feasible tools to assess perceived pleasure during exercise training sessions, such as the FS, considering that positive affective response predicts adherence and long-term exercise engagement (37) and consequently health- and fitness-related benefits. Continued long-term engagement in regular exercise is important as any adaptive responses are readily lost. Orio et al. (17) demonstrated that all health benefits gained from exercise were completely lost after exercise training was ceased for 12 wk after their exercise intervention. This highlights the importance of sustainability of exercise beyond the initial intervention, and that positive affective responses to the exercise may be the key for its successful use in long-term therapy in overweight women with PCOS and more broadly in obesity.

According to the "dual mode" model, the basic affective response is mainly influenced by the exercise intensity (38). This model states that exercise performed below the VT generates homogeneous responses of pleasure with low-moderate influence of cognitive factors (e.g., personality, physical self-efficacy, etc.). On the other hand, responses of displeasure are expected when exercise is performed above the VT, with strong influence of interoceptive factors (e.g., mechanoreceptors, baroreceptors, thermoreceptors, etc.). In general, our data aligned with this dual-model theoretical framework with the affect response scores dropping significantly in training zones prescribed for weeks 9 to 12 (i.e., 75%–80% of HR_{max}) and weeks 13 to 16 (i.e., 80%–85% of HR_{max}), which were at or above the VT (79% ± 4% of the HR_{max}). Additionally, when exercise was performed close to the VT a higher variability of basic affective response occurred, that is, some individuals reported pleasure while others report displeasure (38). Therefore, the lower values and the higher variability in the basic affective responses found between weeks 9 and 16 (i.e., 75%–85% of HR_{max}) compared with weeks 1 to 8 (i.e., 60%–75% of HR_{max}) are likely due to the perception of higher physiological demand during exercise when performed at intensities close to or above the participant's VT. These results reinforce previous findings from our group where a single exercise session using the "affect-regulated exercise" approach associated positive basic affective response in overweight/obese women with PCOS with sustained exercise intensities needed for health benefits, namely, moderate-intensity exercise (21). Here, we instructed the participants to self-select an exercise intensity that felt pleasant (i.e., feeling "good" and "very good" on the FS) during the 40-min exercise session. The mean exercise intensity was 73% (69%–78%) of HR_{max}, and the participants spent 81% of the exercise training session at the moderate-intensity level (i.e., 64%–76% of HR_{max}) (21). Therefore, from a practical perspective, exercise prescribed at an intensity ≤75% of HR_{max} seems to be more pleasant for inactive overweight/obese women with PCOS and should be considered as the starting point for exercise interventions in this population of women.

It should be noted that the exercise training sessions were performed on a standard outdoor 400 m track, providing a pleasant environment to exercise surrounded by trees and vegetation, and associated bird life. Previously, we have shown the influence of environmental settings (outdoor vs. indoor) on physiological and psychological responses to exercise in women with obesity (39). Specifically, we observed that 30 min of self-paced walking at the same exercise intensity (i.e., oxygen uptake and HR) performed outdoors presented psychological advantages compared to walking indoors on a treadmill, including higher affective response and enjoyment, attentional focus more externally focused, and lower perceived exertion (39). Also, the participants reported higher intentions to walk in the future after the outdoor trial compared with the indoor trial, which correlated strongly ($r = 0.90$; $P < 0.01$) with attentional focus in the outdoor trial. Therefore, we believe that the outdoor exercise intervention setting may have contributed to the positive affective responses observed in our study.

Our studies' limitations should be also considered. Firstly, given that absence of a validated Brazilian–Portuguese version of HRQL questionnaire for PCOS patients, we used the SF-36, which is a generic questionnaire to assess HRQL. Thus, specific PCOS HRQL domains (i.e., emotions, hair growth, body weight, infertility and menstrual problems) (40) could not be assessed in the present study. Second, we could not randomize all participant allocation to exercise or control groups. As such, our control group contained 5 participants that are considered a sample of convenience. This was due to some participants living in areas too remote for easy access to the training venue and was factored into our study protocol. This latter limitation may bias our adherence and dropout data in the exercise group. Finally, our sample size was *a priori* powered for changes in $\dot{V}O_{2peak}$, one of the primary outcomes. However, we were able to show statistically significant preexercise to postexercise changes in a number of other variables. To overcome this sample size issue, we explored strong statistical trends in our between group data using MBI statistics to understand the practical and clinical significance of these other outcomes variables. Furthermore, our design could not disconnect the impact of the patient–therapist relationship established in supervised exercise group on our primary outcomes. Despite these limitations, this study provides meaningful and novel insights into the impact of a 16-wk outdoor supervised aerobic exercise training intervention on HRQL, cardiorespiratory fitness, cardiometabolic health, and basic affective responses to exercise in overweight/obese women with PCOS. Further large-scale randomized control trials are needed and should include PCOS-specific HRQL questionnaires to validate our initial findings.

CONCLUSIONS

In summary, our supervised aerobic exercise training intervention improved HRQL, cardiorespiratory fitness, and cardiometabolic health of overweight/obese women with PCOS. Moreover, the participants reported the exercise training sessions as pleasant over the whole intervention. These results reinforce the importance of supervised exercise training as a therapeutic approach for overweight/obese women with PCOS, and that exercise therapy can be achieved outside the traditional exercise facilities (gyms, fitness centers, and exercise clinics).

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