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Continuous versus intermittent aerobic exercise in the improvement of quality of life for women with polycystic ovary syndrome: A randomized controlled trial

Victor Barbosa Ribeiro[1,2], Iris Palma Lopes[1], Rosana Maria dos Reis[1], Rafael Costa Silva[1], Maria Célia Mendes[1], Anderson Sanches Melo[1], Hugo Celso Dutra de Souza[3], Rui Alberto Ferriani[1], Gislaine Satyko Kogure[1] and Lúcia Alves da Silva Lara[1]

Abstract

Polycystic ovary syndrome predisposes alterations which contribute to the reduction of quality of life. This randomized controlled clinical trial study was to evaluate the effect of two protocols of aerobic exercise on quality of life in women with polycystic ovary syndrome. Women were allocated to three groups: continuous aerobic training ($n = 28$), intermittent aerobic training ($n = 29$), and control group (no training; $n = 30$). Testosterone levels, body composition indices, and quality of life were assessed at baseline and after 16 weeks of intervention. Both protocols were effective to improve testosterone levels, anthropometric indices, and quality of life in polycystic ovary syndrome women. Thus, these protocols should be included in the clinical environment to improve clinical parameters psychological, biological and social health to this population.

Keywords

aerobic exercise, anthropometric indices, polycystic ovary syndrome, quality of life, testosterone

Introduction

Polycystic ovary syndrome (PCOS) affects 5%–16% of women of reproductive age (Ding et al., 2017) and is characterized by the presence of at least two of the following factors: clinical and biochemical hyperandrogenism, polycystic ovaries, and oligomenorrhea or anovulation (Consensus Amsterdam, 2012; Consensus Rotterdam, 2004). PCOS is marked by hormonal and anthropometric changes, as well as by metabolic disorders, which increase

[1]Ribeirão Preto Medical School, Human Reproduction Sector, Department of Gynecology and Obstetrics, University of São Paulo, Ribeirão Preto, Brazil
[2]Federal Institute of São Paulo, Jacarei Campus, Brazil
[3]Department of Biomechanics, Medicine and Rehabilitation of the Locomotor System, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil.

Corresponding author:
Victor Barbosa Ribeiro, Department of Gynecology and Obstetrics, Ribeirão Preto Medical School, Ribeirão Preto 14049-900, Brazil.
Email: victorbarbosa@ifsp.edu.br

the risk of cardiovascular disease (Alves et al., 2017; Anagnostis et al., 2018; Consensus Rotterdam, 2004; Ribeiro et al., 2016). Furthermore, all of these changes and disorders associated with PCOS culminate in an increased risk of sexual dysfunction, reduced quality of life (QoL), and altered emotional state for those affected by this syndrome (Borghi et al., 2018; Elsenbruch et al., 2003; Lopes et al., 2018; Shafti and Shahbazi, 2016; Stapinska-Syniee et al. 2018).

Previous evaluations of QoL through the use of the 36-Item Short-Form Health Survey (SF-36) in women with PCOS have shown differences in the domains of social functioning, vitality, emotional functioning, and sexual dysfunction (Aliasghari et al., 2017; Elsenbruch et al., 2003; Panico et al., 2017). Possibly, an increase in body mass index (BMI) and hirsutism are factors that interfere with these QoL scores (Aliasghari et al., 2017; Jones et al., 2011; Shishehgar et al., 2016), since these characteristics may cause self-image distortion, leading to a negative self-assessment with implications on the psychological condition of women with and without PCOS (Becker et al., 2017; Campbell and Hausenblas, 2009; Hahn et al., 2005; Kowalczyk et al., 2012). Furthermore, it has been shown that many of the characteristics associated with PCOS contribute to lower self-esteem with negative impact on QoL (Benetti-Pinto et al., 2015; Hahn et al., 2005; Panico et al., 2017; Shishehgar et al., 2016).

Isolated pharmacological treatment has been found to be ineffective in controlling the clinical condition of PCOS, and complementary measures such as lifestyle changes and exercise are recommended (Costa et al., 2018; Kogure et al., 2016; Lara et al., 2015; Lopes et al., 2018; Ribeiro et al., 2016; Thomson et al., 2010). Previous studies conducted by our research group have demonstrated the positive effects of physical strength training on QoL (Ramos et al., 2016), while in another study, the benefits of aerobic exercise in PCOS were demonstrated (Costa et al., 2018). Relatedly, the positive effects of exercise on QoL have been demonstrated in different clinical conditions and different populations (Brown et al., 2018; Hayashino et al., 2018; Vasiliadis and Bélanger, 2018). However, there is a lack of research comparing different protocols of exercise to discriminate which is more effective in improving the QoL of women with specific clinical conditions such as PCOS. This information is relevant as there are indications that intermittent aerobic exercise is associated with greater satisfaction for those performing the exercise, which favors adherence to the exercise program (Thum et al., 2017). Thus, identifying the best exercise protocol is essential for the development of care programs for women with PCOS. Therefore, this study aimed to verify and compare the effects of continuous aerobic exercise and intermittent aerobic exercise protocols on the QoL of women with PCOS.

Methods

Study design and participants

This study was registered in ISRCTN10416750 and approved by the Institutional Review Board of the University Hospital, Ribeirão Preto Medical School, University of São Paulo (protocol no. 9640/2014).

This study was designed as a randomized controlled clinical trial in which women with a diagnosis of PCOS, based on the Rotterdam criteria (Consensus Rotterdam, 2004), were recruited as participants. Advertisements in the city newspaper and on the university website were used to recruit participants for the study.

The women selected as participants were invited to follow up at the Gynecological Endocrinology Outpatient Clinic of the Human Reproduction Sector of the Department of Gynecology and Obstetrics of the Ribeirão Preto Medical School, University of Sao Paulo, the setting for this study. All participants signed an informed consent form prior to being allowed to participate in the study.

Exclusion criteria were age less than 18 years and greater than 39 years, BMI less than 18 and greater than 39.9 kg/m^2, women using drugs that interfered with the hypothalamic-pituitary hormone function (i.e. hormonal contraceptives,

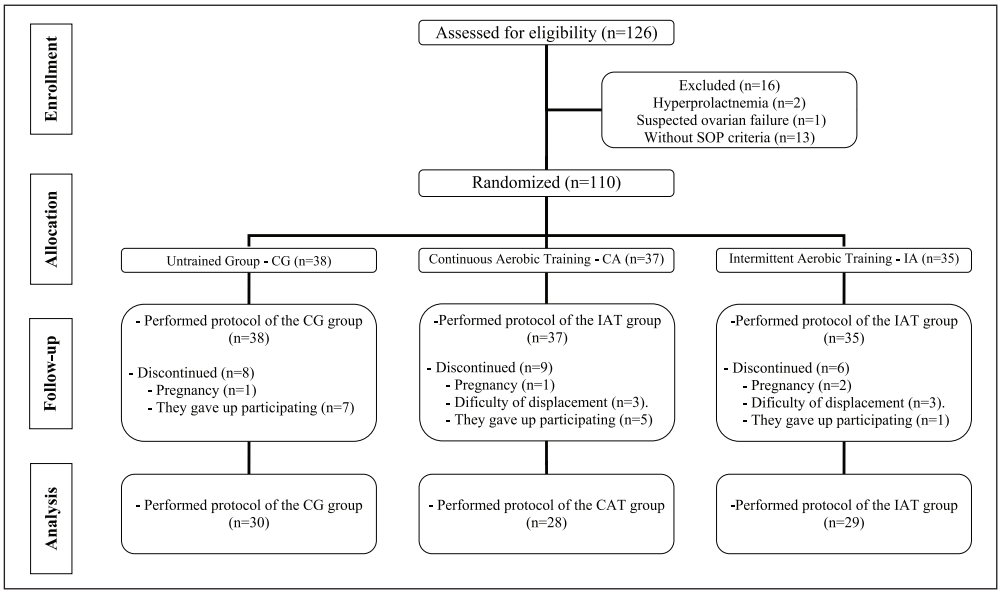

Figure 1. Selection of participants.

estrogen and progestin drugs, hormone therapy, gonadotropin-releasing hormone (GnRH) analogues and antagonists), pregnant women, smokers, and women with diabetes, congenital adrenal hyperplasia, thyroid diseases, hyperprolactinemia, Cushing's syndrome, or musculoskeletal disorders.

In this study, 126 volunteers were recruited. Of these, 16 were excluded during the initial evaluations. Thus, the remaining 110 started the physical training protocols. Of these, 23 were lost in the course of the study and 87 completed the study which were divided into continuous aerobic training (CAT; $n=28$), intermittent aerobic training (IAT; $n=29$), and control group without training (CG; $n=30$). The reasons for exclusions and withdrawals are described in Figure 1.

Randomization

The sample was randomly allocated by placing written assignments in sequentially numbered, sealed, opaque envelopes that were grouped in blocks of 15 participants, with five blocks for each group. The envelopes were consecutively and separately collected, depending on each participant's BMI at the time of inclusion. A list of random numbers was generated by a computer and, after the participant consented to participate, the envelope was opened, and the participant was allocated into one of the three groups, according to the contents of the envelope. The generation of the random sequence was performed by a researcher and the sealing of the envelopes was performed by an assistant, neither of whom participated in the recruitment nor the allocation of the participants. Another researcher recruited and allocated participants to the groups.

Intervention and evaluation

Before and after the intervention, measurements were conducted, with all post-exercise intervention assessments occurring 72 hours after the last exercise training session. The first part of the evaluation included anthropometric measurements. Waist circumference (WC) was measured with the participant in the standing position, with arms at the side of the body, feet together, and with a relaxed abdomen. For WC, a horizontal measurement was obtained on the

Table 1. Protocols of CA and IA physical training.

Week	Duration	CA training	IA training		
		Intensity (% HR maximum)	Series	Recovery intensity (% HR maximum) (3 minutes)	Upper intensity (% HR maximum) (2 minutes)
1	30	65	6	60	70
2	30	65–70	6	60	75
3	30	70	6	60	80
4	35	70	7	60	80
5	35	70–75	7	65	85
6	35	70–75	7	65	85
7	40	70–75	8	65	85
8	40	70–75	8	65	85
9	40	75	8	65–70	85
10	40	75	8	65–70	85
11	45	75	9	65–70	85
12	45	75	9	65–70	85
13	45	75–80	9	65–70	85–90
14	50	75–80	10	65–70	85–90
15	50	75–80	10	65–70	85–90
16	50	75–80	10	65–70	85–90

CA: continuous aerobic; IA: intermittent aerobic; HR: heart rate.
Added 5 minutes of heating and 5 minutes of cool down.

narrower part of the dorsum (above the navel and below the xiphoid process; Ciconelli et al., 1997). Hip circumference (HC) was measured using the same positioning, as the region with the largest circumference of the buttocks (American College of Sports Medicine (ACSM), 2014). Waist-to-hip ratio (WHR) was measured by dividing the WC value by the HC value (ACSM, 2014).

Testosterone was measured before and after the intervention, through the use of the chemiluminescence method (Immulite 1000, Siemens). Prolactin, thyroid stimulating hormone (TSH), and 17-hydroxyprogesterone (17-OHP) were measured before the intervention using the chemiluminescence method (Immulite 2000, Siemens XPI). For these measurements, 20 mL of whole blood was collected until the eighth day of the menstrual cycle (early follicular phase), or any day if the patient was in amenorrhea. Ovary morphology was assessed by ultrasound, using the Voluson E8 Expert (GE HealthCare, Zipf, Austria) equipped with a 5–9 MHz vaginal probe (RIC5-9D).

QoL was assessed by the validated Portuguese version of the self-reported MOS SF-36, which consists of eight subscales: (1) Physical Role Function, (2) Physical Functioning, (3) Bodily Pain, (4) General Health Perception, (5) Vitality, (6) Social Role Functioning, (7) Emotional Role Functioning, and (8) Mental Health. Subscale scores range from 0 to 100, with a lower score indicating lower QoL for that subscale (Ciconelli et al., 1997; Martinez et al., 2004).

Participants were instructed to maintain the same daily diet for the duration of the study. Using Embreex 570-L and Embreex 570-Pro treadmills, the two protocols of aerobic training were performed: Continuous and intermittent aerobic exercise. The duration of the exercise intervention was 16 weeks, with three sessions per week (Table 1). The intensity of the training was monitored by a heart rate monitor (Polar RS810). To ensure equivalent training volume

for both protocols, heart rate percentage was multiplied by the session duration (in minutes; ACSM, 2014). To calculate intensity, a formula of [maximum heart rate (HR_{max}) × % intensity] was used (ACSM, 2014). The training protocol included a 5-minute warm up and a 5-minute cool down between 50% and 60% of the maximum heart rate. The target intensity areas of training followed the recommendations of ACSM (2014). The IAT and CAT protocols were performed in the Cardiovascular Physiology and Physiotherapy Laboratory. Participants' adherence to the training intensity was monitored by a team of personal trainers and physiotherapists.

Sample size

The sample size was calculated using the GPower program, version 3.1.92 (see https://pt.freedownloadmanager.org/Windows-PC/GPower-GRATUITO.html). The sample size was obtained considering a Cohen's *d* effect size of 0.6, a significance level of 5%, and a test power of 80%. According to Cohen's agreement, 24 patients are necessary to achieve a moderate difference between groups (CAT, IAT, and CG). The final sample was increased by to cover the losses (Figure 1; Miot, 2011).

Statistical analyses

Means and standard deviations were calculated for all variables and included a 95% confidence interval (CI), where appropriate. Anthropometric and laboratory measurements, as well as scores on the SF-36 were compared using a planned orthogonal contrast in the mixed effects linear regression model. Repeated measures from the same participant were considered as random effects (i.e. more than one measurement for the same participant). Age, group, time, BMI, WHR, testosterone, and interaction between group and time were examined as covariates for all analyses to evaluate the training effects both within and between groups. All statistical analyses were performed using SAS® Software Version 9.4 (SAS Institute Inc., University of North Carolina, Chapel Hill), with $p < 0.05$ considered to be statistically significant.

Results

Anthropometric and laboratory data

Upon examination of the baseline measurements, no significant differences were found between the three groups with regard to age, height, and levels of prolactin, 17-OHP, and TSH. The groups were also homogeneous with regard to the BMI, WC, and WHR variables. However, the CAT showed significantly higher values of testosterone in relation to the CG ($p = 0.014$) in the baseline measurement (Table 2).

Following the intervention, a significant reduction in WC was found in the CAT ($p = 0.045$) and IAT ($p = 0.049$) groups. Conversely, a significant increase in WC was found in the CG group ($p = 0.014$). HC was significantly reduced in the CAT group ($p = 0.032$). Furthermore, there was a significant reduction of WHR in the IAT group ($p = 0.012$). Finally, testosterone levels in the CAT ($p < 0.001$) and IAT ($p = 0.019$) groups were significantly lowered (Table 2).

QOL—SF-36 scores

At baseline, there was no significant difference between the three groups regarding SF-36 scores. Following the 16-week intervention period, there were no significant differences found in the CG when compared with baseline scores. However, with regard to the CAT group, there was a significant increase in Physical Functioning ($p = 0.022$), Physical Role Functioning ($p < 0.001$), General Health Perception ($p < 0.001$), Vitality ($p < 0.001$), Social Role Functioning ($p < 0.001$), Emotional Role Functioning ($p < 0.001$), and Mental Health ($p = 0.001$). For the IAT group, significant increases were found in Physical Functioning ($p < 0.001$), Physical Role Functioning ($p = 0.027$), General Health Perception ($p < 0.001$), Vitality ($p < 0.001$), Social Role Functioning ($p < 0.001$), Emotional Role Functioning ($p = 0.011$), and Mental Health ($p < 0.001$) (Table 3).

Table 2. Anthropometric and laboratory data of women with PCOS before and after without training (CG) or 16-week physical training.

	CG (N = 30)			CAT (N = 28)			IAT (N = 29)		
	Before	After	Estimation of difference (CI 95%)	Before	After	Estimation of difference (CI 95%)	Before	After	Estimation of difference (CI 95%)
Age (year)	28.5 (5.8)	–	–	29.1 (5.3)	–	–	29.0 (4.3)	–	–
BMI (kg/m²)	29.1 (5.2)	29.3 (5.4)	−0.24 (−0.56 to 0.08)	28.4 (5.6)	28.2 (5.7)	0.25 (−0.07 to 0.58)	28.7 (4.8)	28.5 (4.8)	0.13 (−0.19 to 0.45)
WC (cm)	89.5 (13)	91.0 (13)*	−1.46 (−2.91 to −0.01)	88.1 (14)	86.6 (13.1)*	1.54 (0.04 to 3.05)	90.5 (11.3)	88.7 (12.4)*	1.87 (0.39 to 3.35)
HC (cm)	106.3 (10)	107.2 (9.7)	−0.88 (−2.05 to 0.28)	106 (9.58)	104.5 (10.3)*	1.33 (0.12 to 2.54)	107.3 (9.5)	104.2 (11.0)	0.14 (−1.04 to 1.33)
WHR	0.84 (0.08)	0.85 (0.07)	−0.01 (−0.02 to 0.01)	0.83 (0.08)	0.82 (0.07)	0.01 (−0.01 to 0.02)	0.84 (0.06)	0.83 (0.07)*	0.02 (0.01 to 0.03)
Testosterone (mg/dL)	86 (37)	100 (46)	−13.4 (−29.7 to 2.86)	117 (50)	93 (38)**	24.0 (7.2 to 40.8)	108 (52)	88 (54)*	19.9 (3.30 to 36.4)

PCOS: Polycystic ovary syndrome; CG: control group; CAT: continuous aerobic training; IAT: intermittent aerobic training; CI: confidence interval; BMI: body mass index; WC: waist circumference; HC: hip circumference; WHR: waist-to-hip ratio.
Data are presented as mean and standard deviation and CI.
$*p < 0.05$; $**p < 0.001$.

Discussion

This study aimed to evaluate the effects of continuous and intermittent aerobic exercise protocols on QoL in women with PCOS. Both protocols were found to be effective in improving physical, emotional, and social functioning as well as vitality, mental health, and the perception of general health, as indicated by increased scores on the SF-36, a measure of QoL. In addition, there was a reduction of WC, HC, and testosterone in the CAT group and WC, WHR, and testosterone in the IAT group. Furthermore, there was an increase in WC in the CG group.

Based on a review of related research, it appears that this is the first study to compare the effects of two aerobic exercise protocols on QoL in women with PCOS, making this study particularly relevant to improving care for this population. Although there was no improvement in BMI as previously demonstrated (Frène et al., 2015; Stener-Victorin et al., 2013), this study provided evidence of various benefits from physical exercise. Consistent with the results of this study, a recent study evidenced the effectiveness of a lifestyle and physical exercise program in promoting QoL in women with PCOS, even without improvement in BMI (Frène et al., 2015). Similarly, another study provided evidence of improved depression and QoL in women who were identified as overweight or obese (Thomson et al., 2010).

Different protocols have been used to prove the beneficial effects of exercise on QoL in other populations such as older persons and individuals with cancer and type II diabetes (Brown et al., 2018; Hayashino et al., 2018; Vasiliadis and Bélanger, 2018). In studying women with PCOS, the most recent protocols have involved physical strength training and aerobic exercise (Costa et al., 2018; Ramos et al., 2016). A study by Ramos et al. (2016) included a protocol of progressive intensity with a frequency of three times per week, over a 16-week period. The results of the study showed improvement in the Physical Role Functioning score of the SF-36 and a reduction

Table 3. Comparison of the SF-36 questionnaire scores of women with PCOS before and after the period without training (CG) or 16-week physical training.

	CG (*N* = 30)			CAT (*N* = 28)			IAT (*N* = 29)		
	Before	After	Estimation of difference (CI 95%)	Before	After	Estimation of difference (CI 95%)	Before	After	Estimation of difference (CI 95%)
Physical role functioning	73.8 (21.5)	77.8 (2.1)	−4.63 (−11.60 to 2.32)	81.6 (15.3)	91.3 (13.0)*	−8.53 (−15.85 to −1.26)	76.0 (21.1)	93.5 (7.1)**	−17.04 (−24.21 to −9.87)
Physical functioning	69.2 (38.1)	59.2 (38.0)	10.10 (−3.37 to 23.57)	67.0 (34.7)	90.2 (19.7)**	−23.37 (−37.48 to −9.26)	78.4 (33.2)	93.1 (17.5)*	−15.66 (−29.53 to −1.79)
Bodily pain	53.5 (21.4)	54.6 (23.2)	−0.54 (−8.60 to 7.53)	64.4 (21.2)	68.4 (21.8)	−5.35 (−13.82 to 3.12)	66.9 (21.4)	71.0 (22.8)	−4.92 (−13.26 to 3.41)
General health perception	54.8 (16.3)	54.0 (17.2)	0.28 (−5.17 to 5.74)	53.9 (16.3)	62.5 (17.3)**	−7.97 (−13.7 to −2.23)	53.5 (22.3)	67.3 (16.3)**	−13.26 (−18.91 to −7.62)
Vitality	46.0 (22.1)	51.5 (22.2)	−5.38 (−12.32 to 1.55)	51.4 (17.9)	65.2 (16.7)**	−13.24 (−20.54 to −5.95)	47.8 (21.3)	66.4 (17.4)**	−18.12 (−25.30 to −10.94)
Social role functioning	63.8 (28.3)	70.1 (27.8)	−6.89 (−15.43 to 1.64)	65.7 (25.8)	82.3 (18.1)**	−15.73 (−24.71 to −6.75)	68.9 (24.5)	82.0 (19.9)**	−11.97 (−20.81 to −3.13)
Emotional role functioning	62.2 (42.6)	58.9 (44.4)	1.23 (−14.03 to 16.49)	54.8 (41.8)	82.2 (28.0)**	−23.89 (−39.90 to −7.88)	55.2 (36.0)	79.4 (32.6)*	−20.54 (−36.28 to −4.79)
Mental health	54.3 (21.9)	57.2 (23.1)	−3.54 (−10.17 to 3.08)	55.1 (15.6)	70.1 (16.7)**	−13.96 (−20.93 to −6.98)	60.4 (18.2)	73.0 (15.4)**	−11.68 (−18.54 to −4.81)

PCOS: Polycystic ovary syndrome; CG: control group; CAT: continuous aerobic training; IAT: intermittent aerobic training; CI: confidence interval; CA: continuous aerobic (physical training group); IA: intermittent aerobic (physical training group); SF-36: 36-Item Short-Form Health Survey.
Data are presented as mean and standard deviation and CI.
*$p < 0.05$; **$p < 0.001$.

of WC in this population (Ramos et al., 2016). Similarly, Costa et al. (2018) used a three times per week, 16-week, open-field aerobic exercise protocol which evidenced the improvement of the Physical Role Functioning, General Health Perception, and Mental Health domains of the SF-36 questionnaire. In this study, which included a larger sample size, all of the SF-36 questionnaire scores were increased, with the exception of the Bodily Pain subscale, both in the intermittent and continuous training protocols, thus demonstrating improvement across a broader span of variables related to QoL.

Women with PCOS are frequently dissatisfied with their body image (Micskei et al., 2014). This study found a significant reduction in the anthropometric indices following the exercise protocols, which may have contributed to the improved perception of body image as evidenced by an improvement in QoL scores, mainly with regard to physical and emotional perceptions (Micskei et al., 2014). In addition, there was a significant reduction in the serum concentration of testosterone following both protocols, which may have also contributed to the improvement of QoL scores. Therefore, it is possible that the reduction of testosterone, as observed in this study, may be a predictive factor of improvement in QoL, mainly with regard to emotional functioning and overall general health status. Furthermore, aerobic physical exercise has been found to promote an adjustment in cortisol levels and increase levels of anandamide and serotonin which, together, promote the improvement of mood (Heijnen et al., 2015; Park et al., 2017). Similarly, treadmill exercise has been shown to improve serotonergic function by reducing depressive symptoms (Shin et al., 2017). Previous research has shown that improvements in mood and depressive symptoms may lead to an improved QoL (Böttcher et al., 2018; Wright et al., 2013).

Care was taken in the design of the protocols used in this study to avoid injuries by standardizing the same training volume and duration of the sessions, both for the CAT and IAT interventions. Previous studies have demonstrated that intermittent aerobic exercise allows individuals to perform the same volume as continuous exercise training but with a shorter duration, which seems to favor greater adherence to the exercise program (Thum et al., 2017). In this study, the same training volume intensity and duration of sessions were maintained in order to compare the efficacy of the continuous and intermittent protocols. Furthermore, the intensity of the training was diluted throughout the sessions to avoid injuries, which allowed the training of individuals with a large variation in BMI (18–39.9 kg/m^2), without any cases of orthopedic injury. Although there were cases of participant withdrawal throughout the study for various reasons, there was considerable permanence in the groups trained in both protocols (Figure 1). It is possible that the inclusion of group exercises favored the creation of bonds between the participants, which may have been a stimulus for adherence to the program, as previously demonstrated (Thum et al., 2017).

Strengths and limitations

The main strengths of this study are that this was a randomized clinical trial, and the structure of the two different training protocols was well defined. However, one limitation was the lack of menstrual cycle control and hirsutism observed in some participants after training, which may have directly interfered with the QoL results. In addition, the sample of participants in the training groups did not reach the desired quantitative goal of 30 per group.

Future research

For future research, an objective evaluation of hirsutism through the use of the Ferriman–Gallwey Scale (Ferriman and Gallwey, 1961) after the end of the exercise and control period is suggested in order to control for this variable, which is known to interfere with self-image (Morotti et al., 2013) and may influence the evaluation of QoL of women with PCOS.

Conclusion

Continuous and intermittent aerobic exercise protocols were found to be equally effective in reducing anthropometric indices and hyperandrogenism,

and in the improvement of QoL in women with PCOS. Thus, these protocols should be included in the clinical environment to improve clinical parameters psychological, biological and social health to this population.

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Availability of data and materials

Data sets generated during and/or analyzed during this study are available to the corresponding author upon reasonable request, subject to the privacy of the participants.

Declaration of conflicting interests

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ORCID iDs

Victor Barbosa Ribeiro https://orcid.org/0000-0001-8753-7975
Gislaine Satyko Kogure https://orcid.org/0000-0002-2860-846X
Lúcia Alves da Silva Lara https://orcid.org/0000-0003-1073-238X

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