The Effect of a Hypocaloric Diet with and without Exercise Training on Body Composition, Cardiometabolic Risk Profile, and Reproductive Function in Overweight and Obese Women with Polycystic Ovary Syndrome

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Context: In overweight women with polycystic ovary syndrome (PCOS), the benefits of the addition of exercise to an energy-restricted diet in further improving cardiometabolic risk factors and reproductive function has not been extensively studied.

Objective: The objective was to evaluate the effects of aerobic and aerobic-resistance exercise when combined with an energy-restricted high protein diet (5000–6000 kJ/d) on metabolic risk factors and reproductive function in women with PCOS.

Design and Setting: A 20-wk outpatient, randomized, parallel study was conducted in a metropolitan research clinic.

Patients and Intervention: Ninety-four overweight and obese women with PCOS (age 29.3 $\pm$ 0.7 yr; body mass index 36.1 $\pm$ 0.5 kg/m^2) were randomized to diet only (DO; n = 30), diet and aerobic exercise (DA; n = 31), or diet and combined aerobic-resistance exercise (DC; n = 33).

Main Outcome Measures: Weight, body composition, cardiometabolic risk factors, hormonal status, menstrual cyclicity, and ovulatory function were assessed.

Results: All interventions reduced weight (DO 8.9 $\pm$ 1.6%, DA 10.6 $\pm$ 1.7%, and DC 8.7 $\pm$ 1.7%; $P < 0.001$) with no difference between treatments ($P = 0.7$, time $\times$ treatment). Fat mass decreased more (3 kg) and fat-free mass decreased less (2 kg) in DA and DC compared with DO ($P \leq 0.03$). Reductions in blood pressure (5.6/2.7 mm Hg), triglycerides (0.4 mmol/liter), total cholesterol (0.5 mmol/liter), low-density lipoprotein cholesterol (0.1 mmol/liter), glucose (0.2 mmol/liter), fasting insulin (4.3 mIU/liter), testosterone (0.4 nmol/liter), and free androgen index (2.8) ($P < 0.001$) and improvements in SHBG (7.0 nmol/liter) and reproductive function occurred in all groups, with no difference between treatments.

Conclusion: In overweight and obese women with PCOS, the addition of aerobic or combined aerobic-resistance exercise to an energy-restricted diet improved body composition but had no additional effect on improvements in cardiometabolic, hormonal, and reproductive outcomes relative to diet alone. **(*J Clin Endocrinol Metab* 93: 3373–3380, 2008)**

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, presenting in approximately 7% of this population (1). PCOS is associated with a number of reproductive disorders and is characterized by the presence of polycystic ovaries, menstrual dysfunction, infertility or reduced fertility, and biochemical or clinical hyperan-

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Abbreviations: AbFM, Abdominal fat mass; BF%, percent body fat; BMI, body mass index; BP, blood pressure; CI, confidence interval; DA, diet and aerobic exercise; DC, diet and combined aerobic-resistance exercise; DO, diet only; FAI, free androgen index; FFM, fat-free mass; FM, fat mass; HR, heart rate; HOMA, homeostatic model assessment of insulin resistance; NR, nonresponder; PCOS, polycystic ovary syndrome; PDG, pregnanediol-3-glucuronide; R, responder; 1RM, one-repetition maximum; WC, waist circumference.

drogenism. PCOS also increases the prevalence and risk of a number of cardiometabolic disturbances including insulin resistance, hypertension, dyslipidemia, and diabetes (2, 3).

Although the pathogenesis of PCOS is complex and not entirely understood, obesity (particularly abdominal obesity) is mediated by the development of insulin resistance (4) and is closely linked to the development of this condition and its clinical features, particularly menstrual irregularities and increased serum androgens (5–7). The central role of insulin resistance in the manifestations of PCOS has led to it becoming a primary target for PCOS management.

Lifestyle modification focusing predominantly on diet and exercise behavior is considered the preferred first-line treatment for PCOS management with the primary goal to normalize serum androgens and restore reproductive function (4). Several studies have shown that weight loss of 5–10% of weight in overweight women with PCOS via energy restriction can reduce circulating insulin levels and hyperandrogenism (8, 9) and improve menstrual cyclicity (10, 11), fertility, and cardiovascular disease risk factors (8). It is considered that the primary determinant underlying many of these reported weight-loss benefits is the accompanying reduction in circulating insulin concentrations (12).

A separate line of evidence has also shown that exercise training independent of weight loss in overweight and obese subjects with cardiometabolic disturbances and a wide range of insulin-resistant states decreases abdominal fat and improves insulin sensitivity and an array of cardiovascular disease risk factors (13). Moreover, recent studies suggest that compared with either aerobic or resistance training alone, combined aerobic-resistance training is more efficacious for improving insulin sensitivity and reducing abdominal fat in a range of obese patient groups (14, 15). However, despite the well established benefits of exercise training and regular exercise being recommended as a cornerstone of PCOS management (12), there is limited research evaluating the effects of exercise training and specific exercise regimes in overweight women with PCOS. Vigorito *et al.* (16) showed that a 3-month aerobic exercise training program improved fasting insulin but did not assess effects on reproductive function. More recently, Palomba *et al.* (17) found that although a 24-wk aerobic exercise program or a hypocaloric high-protein diet improved both menstrual cyclicity and fertility in overweight PCOS patients, the exercising subjects reported significantly higher ovulation rates and menses frequency as well as greater improvements in waist circumference (WC), sex hormones, and insulin levels. However, although this study assessed the relative effects of diet and exercise treatment, it was unable to determine the additive benefit of exercise when it is combined with energy restriction. A small preliminary study (18) showed that although 12-wk lifestyle modification programs consisting of nutritional counseling alone or nutritional counseling plus combined aerobic-resistance exercise both significantly reduced fasting insulin levels, the addition of exercise promoted more favorable changes in the sum of two skinfolds. However, this latter study was limited by a small sample size and the lack of any assessment of reproductive function.

The purpose of the present study was to assess the additive benefit of aerobic or aerobic-resistance exercise training, when it is combined with a moderate hypocaloric weight-loss diet on body composition, cardiometabolic and hormonal profiles, and reproductive function in overweight and obese women with PCOS.

Subjects and Methods

Participants

One hundred four sedentary overweight and obese women with PCOS [age, 18–41 yr; body mass index (BMI): 25–55 kg/m^2] were recruited by public advertisement and from specialist clinics. PCOS was diagnosed according to the Rotterdam criteria (19). Menstrual irregularity was defined as cycle length less than 21 d or greater than 35 d or variation between consecutive cycles of greater than 3 d. Potential participants were excluded if they were using fertility treatments or oral contraceptives; were smokers, pregnant, breastfeeding, or had history of cardiovascular, liver, kidney or respiratory disease, diabetes, uncontrolled hypertension, or malignancy; or were participating in regular physical activity. Subjects were also excluded if they had reproductive disorders unrelated to PCOS, thyroid abnormalities, or nonclassical adrenal hyperplasia. All experimental procedures were approved by the Human Ethics Committees of the Commonwealth Scientific and Industrial Research Organisation and the University of South Australia, and all subjects provided written informed consent.

Study design

In a parallel study design, subjects were randomly assigned by computer generation into three 20-wk lifestyle interventions; diet only (DO), diet and aerobic exercise (DA) and diet and combined aerobic-resistance exercise (DC). At baseline (wk 0), at the midpoint (wk 10), and at the end of the intervention (wk 20), subjects attended the clinic on two occasions. Subjects were advised not to consume alcohol or participate in vigorous physical activity during the 24 h prior to the clinic visits. One of the clinic visits occurred in the morning after an overnight fast, during which height (baseline only), weight, and blood pressure (BP) were measured before the collection of a venous blood sample for the measurement of metabolic and hormonal parameters. On a separate day, after a minimum 3-h fast, body composition was determined, and at baseline and wk 10, an incremental treadmill exercise test to exhaustion was performed and muscle strength assessed by one-repetition maximums (1RM) to set training loads. During the month before study commencement and throughout the intervention, menses calendars were recorded and first morning spot urine samples were collected twice weekly to assess pregnanediol-3-glucuronide (PDG) concentrations as a marker of ovulation. Subjects were requested not to modify their lifestyles during the intervention period other than as necessary to comply with study requirements.

Dietary intervention

All subjects were prescribed the same energy-restricted, high-protein diet (5000–6000 kJ/d) for a planned weight loss of 8–12 kg over the study period. The diet provided 30% of energy as protein, 40% as carbohydrate, and 30% as fat (<8% saturated fat). To facilitate compliance, the diet included specific daily quantities of foods in a checklist that subjects completed daily. Volunteers met with a dietician in small groups or individually fortnightly throughout the study to discuss dietary issues, nutrition guidelines, and the importance of compliance with the diet to promote weight loss.

Exercise intervention

Apart from the energy-restricted diet, subjects randomized to the DA group undertook a walking/jogging program comprising five sessions per week. The training heart rate (HR) was based on a percentage of the maximum HR (HR_{max}) achieved in the treadmill tests conducted at wk

0 and 10. Exercise intensity progressed from 25–30 min at 60–65% HR_{max} during the first week to 45 min at 75–80% HR_{max} by study end. To assist with compliance, HR during exercise was monitored using a personal HR monitor (FS1 Polar Heart Rate Monitor; Polar Electro Oy, Kempele, Finland). Subjects randomized to the DC group performed the same aerobic exercise program as the DA group three times per week, and undertook a progressive resistance training program twice per week on nonconsecutive days. The resistance training program consisted of five resistance exercises: bench press, lat pulldown, leg press, knee extension, and sit-ups. The training load was set using a percentage of 1RM, which was assessed for each exercise. For the first 2 wk, the training load was 50–60% 1RM and increased to 65–75% 1RM for the following weeks. The training load was increased progressively once subjects could successfully perform three sets of 12 repetitions at that load.

Clinical measurements

Height was measured using a stadiometer (SECA, Hamburg, Germany), and weight was measured using electronic digital scales (Mercury, AMZ 14, Tokyo, Japan). BMI was calculated as weight(kg)/height(m)^2. Fat mass (FM), fat-free mass (FFM), and percent body fat (BF%) were determined by dual-energy x-ray absorptiometry (Lunar Prodigy; Lunar Radiation Corp., Madison, WI). Abdominal fat mass (AbFM) was measured as previously described (20). WC was measured 2 cm above the uppermost lateral border of the iliac crest using an anthropometric tape (model W606PM; Lufkin, Cooper Industries Ltd., Houston, TX). Seated BP was measured by automated oscillometry (model T8; Omron Corp., Tokyo, Japan).

Biochemical measurements

Fasting plasma and serum samples were collected and stored at −80 C for analysis after study completion. Serum total cholesterol, high-density lipoprotein cholesterol, triglycerides, and plasma glucose were measured on a Hitachi 902 autoanalyzer (Roche Diagnostics, Indianapolis, IN) using commercial enzymatic kits (Roche Diagnostics, Basel, Switzerland). Low-density lipoprotein cholesterol was calculated using the modified Friedewald equation (21). Plasma insulin concentrations were determined using a commercial ELISA kit (Mercodia ELISA; ALPCO Diagnostics, Uppsala, Sweden). Insulin resistance was estimated using the homeostatic model assessment (HOMA2) online calculator (22). Serum SHBG was measured by coated-tube immunoradiometric assay using commercial kits (Diagnostic Systems Laboratories, Webster, TX). Testosterone was measured by RIA using commercial enzymatic kits (Diagnostic Systems Laboratories). Free androgen index (FAI) was calculated as testosterone/SHBG × 100.

Spot urine samples were stored at −20 C until analysis at completion of the study. Urinary PDG was measured according to the method of Santoro *et al.* (23). Menstrual cyclicity was assessed using completed menses calendars. Improvements in menstrual cyclicity were defined as a change from nonovulatory to ovulatory cycles or from irregular to regular cycles or an improvement in consecutive intercycle variation.

Data analysis

Data were checked for normality. Between-group differences in baseline characteristics were assessed using one-way ANOVA. Effects of the treatments on dependent variables and their interactions over time were analyzed using random-effects mixed modeling, making efficient use of all available measurements (24). Where a statistically significant main effect was found, differences between means were determined by *post hoc* analysis using Bonferroni adjustments for multiple comparisons. Linear regression was used to assess relationships between variables using raw data (*i.e.* non-model-predicted values). χ^2 tests were used to assess changes for categorical variables. An α-level of significance was set at $P < 0.05$. All values reported are model-predicted values ± SD except for age and BMI at baseline, which are the mean of the raw data ± SD. The differences between treatments [with 95% confidence intervals (95% CI)] for changes from baseline to wk 20 are presented for each outcome.

Results

Subjects

Of the 104 subjects recruited, 10 withdrew before commencement, and 94 subjects commenced the study (age 29.3 ± 6.8 yr; BMI 36.1 ± 4.8 kg/m^2). Sixty-three subjects completed to wk 10, and 52 completed to wk 20 (Fig. 1). There were no significant differences in baseline characteristics between treatments (Table 1 and 3) and between subjects who completed or dropped out of the study. The percentages of subjects who completed the study were not different between treatment groups.

Weight and body composition

Overall mean weight loss was 9.4 ± 1.9% of weight ($P < 0.001$) with no difference between treatments ($P = 0.7$; Table 1).

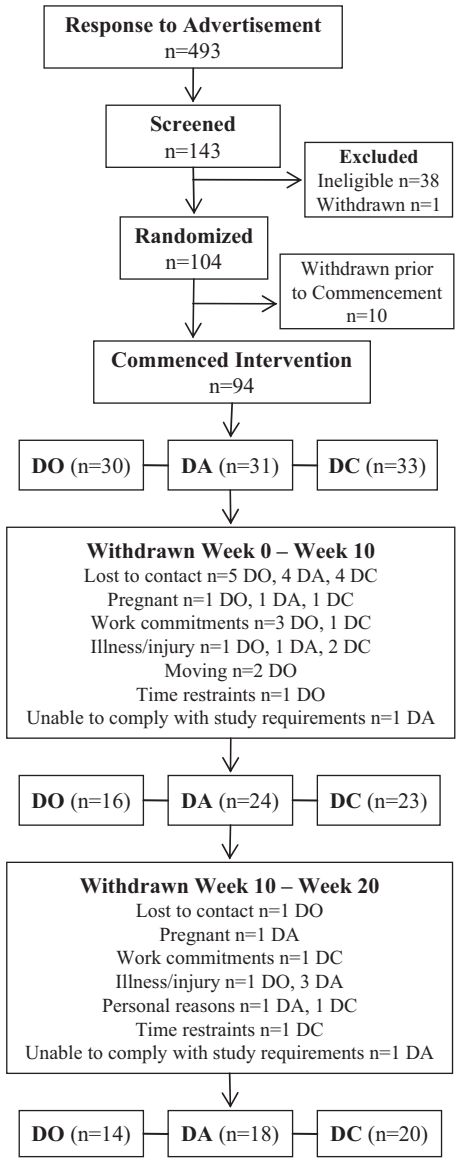

FIG. 1. Study flow diagram.

TABLE 1. Weight and body composition at baseline and after 10 and 20 wk of DO, DA, and DC

	wk 0	wk 10	wk 20	Δwk 20–0	95% CI
Weight (kg)					
DO	100.5 ± 18.1	93.6 ± 18.6[a]	91.9 ± 18.6[a]	−8.6 ± 6.0	−11.4 to −5.9
DA	97.6 ± 18.4	90.7 ± 18.4[a]	87.5 ± 18.4[a,b]	−10.1 ± 5.6	−12.6 to −7.7
DC	102.1 ± 18.4	96.4 ± 18.4[a]	93.5 ± 18.4[a,b]	−8.6 ± 5.2	−10.9 to −6.3
BF%[c] (%)					
DO	46.7 ± 4.4	46.2 ± 4.4	45.8 ± 4.9	−0.9 ± 3.3	−2.4 to −0.6
DA	47.8 ± 3.9	45.8 ± 4.5[a]	43.4 ± 4.5[a,b]	−4.4 ± 2.8[d]	−5.7 to −3.1
DC	47.6 ± 4.0	45.8 ± 4.6[a]	44.5 ± 4.6[a,b]	−3.2 ± 2.9[d]	−4.4 to −1.9
FM[c] (kg)					
DO	46.5 ± 10.4	43.6 ± 11.0[a]	42.5 ± 11.0[a]	−3.9 ± 3.3	−6.0 to −1.9
DA	46.4 ± 10.0	42.0 ± 10.6[a]	38.9 ± 10.6[a,b]	−7.5 ± 3.9[d]	−9.3 to −5.7
DC	48.6 ± 10.3	44.3 ± 10.3[a]	41.9 ± 10.3[a,b]	−6.7 ± 4.0[d]	−8.5 to −5.0
FFM[c] (kg)					
DO	53.1 ± 9.3	49.6 ± 9.3[a]	49.3 ± 9.3[a]	−3.8 ± 3.8	−5.5 to −2.1
DA	50.6 ± 8.9	49.1 ± 8.9[a]	49.4 ± 8.9	−1.2 ± 3.3[d]	−2.7 to −0.2
DC	52.8 ± 9.2	51.4 ± 9.2[a]	51.0 ± 9.2[a]	−1.8 ± 3.4[d]	−3.2 to −0.4
AbFM (kg)					
DO	2.8 ± 8.8	2.6 ± 8.8[a]	2.5 ± 8.8[a]	−0.2 ± 0.3	−0.4 to −0.1
DA	2.6 ± 8.4	2.3 ± 8.4[a]	2.2 ± 8.9[a,b]	−0.4 ± 0.3[d]	−0.6 to −0.3
DC	3.0 ± 8.6	2.8 ± 8.6[a]	2.6 ± 8.6[a,b]	−0.4 ± 0.3[d]	−0.5 to −0.3
WC (cm)					
DO	103.0 ± 12.6	97.1 ± 13.7[a]	92.2 ± 13.7[a,b]	−10.8 ± 7.1	−14.0 to −7.7
DA	100.2 ± 12.2	92.9 ± 12.8[a]	88.5 ± 13.4[a,b]	−11.7 ± 6.1	−14.5 to −9.0
DC	103.8 ± 12.6	98.3 ± 13.2[a]	92.8 ± 13.2[a,b]	−11.0 ± 6.3	−13.6 to −8.3

Values are mean model-predicted values ± SD. Analyses were determined by random-effects mixed-model analysis and pairwise comparisons with Bonferroni adjustment.

[a] Significant change from baseline within group ($P \leq 0.03$).

[b] Significant change from wk 10 within group ($P \leq 0.03$).

[c] Significant treatment × time effect ($P \leq 0.04$).

[d] Significantly different from DO ($P < 0.03$).

Similarly, WC was reduced 11.1% by wk 20 ($P < 0.001$), with no difference between treatments ($P > 0.5$). There was a significant time by treatment interaction for BF%, FM, and FFM ($P \leq 0.04$), such that DA and DC had 45% greater reduction in FM ($P < 0.01$) and 60% lesser reduction in FFM ($P < 0.03$) compared with DO (Tables 1 and 2). There was some evidence for a time by treatment effect for AbFM, although this did not reach statistical significance ($P = 0.08$). Also for the exercising groups (DC and DA), there was greater FFM maintenance from wk 10–20 compared with DO, despite continued significant weight loss during this time. Only the exercising groups experienced continual weight loss and reductions in FM and AbFM and BF% from wk 10–20.

Cardiometabolic and hormonal outcomes

There were significant reductions in BP, fasting glucose and insulin, insulin resistance (HOMA), lipids, testosterone, and FAI and increases in SHBG in all treatment groups at wk 20 ($P < 0.05$), with no difference between treatments ($P > 0.3$; Table 3).

Increases in SHBG were inversely related to weight loss ($r = -0.43$; $P = 0.002$) and reductions in BF% ($r = -0.42$; $P = 0.002$), AbFM ($r = -0.64$; $P < 0.001$), and WC ($r = -0.46$; $P = 0.001$). Reductions in testosterone were positively related to reductions in BF% ($r = 0.30$; $P = 0.03$), AbFM ($r = 0.33$; $P = 0.02$), WC ($r = 0.29$; $P = 0.04$) and weight loss ($r = 0.25$; $P = 0.07$), as was the reduction in FAI (weight loss: $r = 0.30$, $P = 0.04$; BF%: $r = 0.36$, $P = 0.01$; WC: $r = 0.29$, $P = 0.04$; AbFM: $r = 0.27$, $P = 0.06$).

Reproductive function

Data on reproductive function were included only for 59 subjects due to inconclusive results from PDG analysis and menses calendars for the remaining subjects. At baseline, 53 subjects reported menstrual irregularities (28 irregular cycle length, 13 anovulatory, 12 amenorrheic), and six had regular ovulating periods.

Of the 53 subjects with menstrual irregularities, 49.1% reported improvements in ovulation [DO 50% (6 of 12), DA 50.0% (3 of 6), DC 42.9% (3 of 7)] and/or menstrual cyclicity [DO 21.4% (3 of 14), DA 42.9% (9 of 21), DC 44.4% (8 of 18)], with no difference between treatments ($P > 0.1$). There was no difference between groups in the number of menstrual cycles that occurred during the 20-wk study period (DO 2.25 ± 1.35; DA 3.30 ± 1.97; DC 3.00 ± 1.61; $P > 0.3$), but subjects in DA reported a greater number of ovulatory cycles compared with DO (DO 1.33 ± 1.63, DA 3.10 ± 1.97, DC 2.65 ± 1.70; $P = 0.04$). For the subjects that improved in menstrual cycle length, there was an average reduction of 13.8 ± 28.3 d (49.6 ± 25.0 to 32.7 ± 4.3 d), and for those that improved in consecutive intercycle variation, there was an average reduction of 16.0 ± 19.7 d (19.5 ± 20.7 to 3.5 ± 3.5 d). After the intervention, 18 subjects

TABLE 2. Difference between DO, DA, and DC for the change in body composition measures from wk 20 to wk 0

	Mean difference Δwk 20–0	95% CI	*P* value
BF%			
DO *vs.* DA	3.8 ± 4.5	1.9 to −5.1	0.000
DO *vs.* DC	2.3 ± 4.5	0.7 to −3.9	0.005
DA *vs.* DC	−1.2 ± 4.3	−2.7 to −0.3	0.11
FM (kg)			
DO *vs.* DA	3.6 ± 6.2	1.3 to −5.8	0.002
DO *vs.* DC	2.8 ± 6.2	0.6 to −5.0	0.01
DA *vs.* DC	−0.8 ± 6.0	−2.8 to −1.3	0.46
FFM (kg)			
DO *vs.* DA	−2.6 ± 5.0	−4.4 to −0.8	0.006
DO *vs.* DC	−2.0 ± 5.0	−3.8 to −0.2	0.03
DA *vs.* DC	0.6 ± 4.8	−1.0 to −2.3	0.47

Values are mean model-predicted values ± SD. Analyses were determined by random-effects mixed-model analysis and pairwise comparisons with Bonferroni adjustment.

had regular ovulating cycles, five were anovulatory, 27 had irregular cycle lengths, and nine were amenorrheic.

Responders (R) *vs.* nonresponders (NR)

There were no differences in baseline characteristics between subjects who improved reproductive function, determined by improvements in ovulation and menstrual cyclicity (R, n = 26) and those that did not (NR, n = 27) ($P > 0.1$). Women who experienced improvements had greater reductions in weight (R *vs.* NR, 12.2 ± 4.0 *vs.* 6.7 ± 3.8 kg; $P < 0.001$), FM (8.2 ± 3.4 *vs.* 4.7 ± 3.2 kg; $P < 0.01$), AbFM (0.5 ± 0.3 *vs.* 0.3 ± 0.2 kg; $P < 0.02$), and WC (13.4 ± 5.1 *vs.* 10.0 ± 4.8 cm; $P < 0.02$) compared with women who did not. There were no differences in changes in any cardiometabolic or hormonal parameters between R and NR ($P > 0.1$).

Discussion

This study showed that substantial weight loss and improvements in cardiometabolic risk factors, hormonal status, and reproductive function occurred after a structured energy-restricted high-protein diet in overweight and obese women with PCOS. There was no additive benefit from the addition of exercise training in these parameters, but exercise did provide more beneficial changes in body composition with an approximately 45% greater reduction in FM and a 60% better preservation of FFM.

Several studies have shown that weight loss after energy restriction improves body composition by reducing FM, AbFM, and WC in overweight women with PCOS (8, 10), but to date this is the first known study evaluating the added effects of exercise on body composition in these women. The lack of marked additional weight loss after the exercise programs in the present study is not surprising given that numerous short-term studies in other overweight and obese populations have consistently shown exercise alone induces modest weight loss (<5 kg) (25–27), and when combined with dietary restriction, any greater weight loss observed is minimal (13, 27). Nevertheless, the current study showed the addition of exercise to diet provided significantly favorable effects on body composition rather than facilitating weight loss *per se*. Lean tissue loss that often occurs with energy restriction is associated with reductions in resting metabolic rate, acting to preserve fat stores and prevent further weight loss (28). The greater preservation of FFM has important potential implications for long-term weight-loss maintenance (29, 30) because it maintains resting metabolic rate and assists with continued weight (*i.e.* fat) loss and/or weight maintenance (31). The effect of exercise training on resting metabolic rate was not assessed in the current study and warrants further investigation in PCOS. A small preliminary study (18) has also reported greater reductions in the sum of two skinfolds despite an absence of weight loss in women with PCOS when aerobic exercise was added to nutritional counseling. Furthermore, two recent studies in healthy overweight middle-aged women and postmenopausal women with type 2 diabetes reported greater reductions in abdominal fat in subjects who performed combined aerobic-resistance training compared with aerobic exercise only or nonexercise controls (14, 15), suggesting that the incorporation of resistance exercise training may be most beneficial for reducing abdominal fat. In contrast, no differences in effects on body composition were observed between the different exercise treatments in the current study. Previous studies have shown greater preservation of FFM with resistance training compared with aerobic training when combined with energy restriction (32, 33). Resistance training preserves the loss of FFM associated with energy restriction through muscular hypertrophy (33), whereas aerobic exercise is thought to maintain FFM as a result of increased energy expended as fat (34). Possible reasons for the lack of difference between the exercising treatments may be attributed to the earlier studies using more intensive resistance training programs (15, 32–34). Furthermore, the absence of energy restriction in two of the earlier studies may contribute to differing effects on body composition (14, 15).

The lack of difference in the improvements in cardiometabolic or hormonal parameters between treatment groups suggests the improvements were primarily related to energy restriction and weight loss. Previous studies have also shown similar improvements in blood lipid profiles and fasting insulin levels after short-term energy restriction in overweight women with PCOS (6, 8, 10, 35, 36). Reductions in fasting insulin, but not blood lipids, after exercise training alone with minimal weight loss have also been reported in overweight PCOS patients (16, 18). Taken together, these findings suggest exercise training may be effective in women with PCOS for improving insulin resistance even without weight loss, but not for improving blood lipid profile. Previous studies have also reported that combined aerobic-resistance exercise is more effective for improving insulin sensitivity compared with aerobic exercise in overweight women (14, 15). Resistance exercise improves insulin sensitivity by increasing muscle mass and the number of glucose transporter proteins, and aerobic exercise enhances glucose disposal through increases in skeletal muscle capillarization, blood flow, and hexokinase and glycogen synthase activities (37, 38). In the present study, despite greater FFM preservation and FM reductions in

TABLE 3. Cardiometabolic risk factors and sex hormone concentrations at baseline and after 10 and 20 wk of DO, DA, and DC

	wk 0	wk 10	wk 20	Δwk 20–0	95% CI	Time × treatment
SBP (mm Hg)						
DO	119.9 ± 11.0	116.3 ± 14.2	117.8 ± 14.8	−2.1 ± 14.2	−8.4 to −4.3	
DA	117.8 ± 11.1	114.7 ± 12.2	112.2 ± 13.9	−5.6 ± 13.4	−11.4 to −0.2	0.39
DC	119.3 ± 11.5	114.0 ± 12.6[a]	110.6 ± 13.8[b]	−8.7 ± 13.2	−14.2 to −3.2	
DBP (mm Hg)						
DO	66.7 ± 10.4	66.1 ± 12.6	66.6 ± 13.1	−0.1 ± 12.0	−5.3 to −5.0	
DA	66.3 ± 10.0	64.1 ± 11.1	63.9 ± 12.2	−2.4 ± 10.6	−7.1 to −2.3	0.45
DC	65.3 ± 10.3	62.1 ± 11.5	59.9 ± 12.1[a]	−5.4 ± 10.3	−9.9 to −0.9	
Glucose (mmol/liter)						
DO	5.32 ± 0.49	5.15 ± 0.60	4.96 ± 0.60[b]	−0.36 ± 0.55	−0.59 to −0.13	
DA	5.19 ± 0.50	5.04 ± 0.56	4.99 ± 0.61	−0.20 ± 0.50	−0.41 to −0.02	0.35
DC	5.10 ± 0.52	5.00 ± 0.57	5.00 ± 0.57	−0.10 ± 0.46	−0.30 to −0.09	
Insulin (mU/liter)						
DO	17.7 ± 8.2	15.3 ± 3.8	13.5 ± 9.9[b]	−4.2 ± 7.1	−7.3 to −1.1	
DA	14.5 ± 8.4	11.2 ± 8.4[b]	10.9 ± 9.5[b]	−3.7 ± 6.7	−6.5 to −0.8	0.47
DC	16.0 ± 8.0	12.4 ± 8.6[b]	11.1 ± 9.2[b]	−4.9 ± 6.3	−7.5 to −2.3	
HOMA						
DO	2.27 ± 1.04	1.96 ± 1.15	1.71 ± 1.20[b]	−0.56 ± 0.88	−0.95 to −0.17	
DA	1.87 ± 1.00	1.44 ± 1.06[b]	1.40 ± 1.17[b]	−0.47 ± 0.84	−0.83 to −0.11	0.48
DC	2.04 ± 1.03	1.58 ± 1.09[b]	1.41 ± 1.09[b]	−0.63 ± 0.80	−0.96 to −0.31	
TC (mmol/liter)						
DO	5.12 ± 0.99	4.58 ± 1.10[b]	4.79 ± 1.15	−0.32 ± 0.82	−0.70 to −0.05	
DA	5.09 ± 0.95	4.54 ± 1.00[b]	4.57 ± 1.11[b]	−0.52 ± 0.78	−0.86 to −0.17	0.75
DC	5.27 ± 0.98	4.67 ± 1.03[b]	4.68 ± 1.09[b]	−0.58 ± 0.75	−0.90 to −0.27	
HDL (mmol/liter)						
DO	1.15 ± 0.22	1.02 ± 0.27[b]	1.10 ± 0.27	−0.05 ± 0.22	−0.15 to −0.04	
DA	1.21 ± 0.22	1.10 ± 0.28[b]	1.16 ± 0.28	−0.05 ± 0.22	−0.14 to −0.03	0.92
DC	1.19 ± 0.23	1.11 ± 0.29[a]	1.14 ± 0.29	−0.05 ± 0.17	−0.13 to −0.03	
LDL (mmol/liter)						
DO	3.26 ± 0.82	2.89 ± 0.93[b]	3.07 ± 0.99	−0.19 ± 0.66	−0.48 to −0.10	
DA	3.22 ± 0.84	2.84 ± 0.89[b]	2.76 ± 0.95[b]	−0.46 ± 0.61	−0.73 to −0.19	0.41
DC	3.46 ± 0.86	3.04 ± 0.92[b]	3.01 ± 0.92[b]	−0.45 ± 0.57	−0.70 to −0.20	
TG (mmol/liter)						
DO	1.58 ± 0.88	1.49 ± 1.04	1.40 ± 1.04	−0.18 ± 0.88	−0.57 to −0.22	
DA	1.45 ± 0.84	1.33 ± 0.95	1.43 ± 1.00	−0.02 ± 0.84	−0.39 to −0.35	0.79
DC	1.37 ± 0.86	1.16 ± 0.92	1.17 ± 0.98	−0.19 ± 0.80	−0.53 to −0.14	
Testosterone (nmol/liter)						
DO	2.36 ± 0.71	2.09 ± 0.82	2.09 ± 0.98	−0.27 ± 0.71	−0.60 to −0.05	
DA	2.64 ± 0.72	2.21 ± 0.72[b]	2.04 ± 0.88[b]	−0.60 ± 0.67	−0.90 to −0.30	0.41
DC	2.50 ± 0.69	2.13 ± 0.75[b]	2.15 ± 0.84[b]	−0.35 ± 0.63	−0.62 to −0.07	
SHBG (nmol/liter)						
DO	27.4 ± 15.9	31.4 ± 17.5	31.5 ± 17.5	4.2 ± 12.6	−1.4 to −9.8	
DA	36.2 ± 15.6	42.5 ± 16.1[b]	42.9 ± 17.3[b]	6.7 ± 12.2	1.4 to −12.0	0.39
DC	33.8 ± 16.1	39.7 ± 16.7[b]	43.6 ± 17.2[b]	9.8 ± 10.9	5.1 to −14.6	
FAI						
DO	11.2 ± 5.5	9.2 ± 6.6[a]	8.4 ± 6.6[b]	−2.8 ± 4.9	−5.0 to −0.6	
DA	8.5 ± 5.6	6.0 ± 6.1[b]	5.9 ± 6.7[b]	−2.6 ± 5.0	−4.7 to −0.5	0.76
DC	9.1 ± 5.7	6.5 ± 6.3[b]	6.2 ± 6.3[b]	−2.9 ± 4.6	−4.8 to −1.1	

Values are mean model-predicted values ± SD. Analyses were determined by random-effects mixed-model analysis and pairwise comparisons with Bonferroni adjustment. DBP, Diastolic BP; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; SBP, systolic BP; TC, total cholesterol; TG, triglycerides.

[a] Significant change from baseline within group ($P \leq 0.05$).

[b] Significant change from baseline within group ($P < 0.01$).

the exercising groups compared with DO, no difference in insulin resistance was observed. The reason for the lack of any additional insulin-sensitizing effect of exercise is not clear; however, the indirect assessment of insulin resistance (HOMA) used may not have been sensitive enough to detect additional exercise effects, and a more sensitive assessment (hyperinsulinemic-euglycemic clamp) may have been appropriate. Alternatively, the lack of difference between the treatment groups may be due to the insulin-sensitizing effect of energy restriction being larger than those achieved through exercise (27), resulting in a masking of the benefits of exercise.

Previous studies have also shown that lifestyle modifications improve hormonal profile in overweight women with PCOS, through reductions in serum testosterone and FAI and increases in SHBG after weight loss (5, 6, 8, 36, 39, 40). Alternatively, exercise interventions in PCOS show mixed results in their effects

on hormonal profiles, with two studies reporting no changes after 12–24 wk of combined nutritional counseling and aerobic or resistance exercise (16, 18) and another study showing improved testosterone, SHBG, and FAI levels in ovulating patients after a 24-wk energy-restricted diet or aerobic exercise (17). Reductions in abdominal fat have been associated with improved insulin sensitivity and hormonal profile and restored ovarian function (6, 10) as shown by the moderate associations seen between reductions in AbFM and WC and improvements in hormonal profile. Central body fat may contribute to hyperandrogenemia indirectly through adverse effects on insulin sensitivity and consequent effects of hyperinsulinemia on the ovaries (7).

Improvements in reproductive function have also been shown after weight loss in overweight women with PCOS. Previous studies have observed that during 12–24 wk of energy restriction or lifestyle modification, 44–92% of previously anovulatory overweight women resumed spontaneous ovulation (5, 10, 11, 40) or improved menstrual cyclicity (6, 8, 39) after relatively modest weight loss (2–8 kg). Patients with restored ovarian function display improvements in fasting insulin and insulin sensitivity and a redistribution of body fat, particularly central fat, and a more favorable endocrine environment (5, 8, 10, 11, 40), with NR showing no improvements (8, 10, 17). R in the present study experienced significantly greater reductions in weight, FM, AbFM, and WC compared with NR, but both groups experienced similar significant reductions in insulin and hormones. It is difficult to explain why NR also showed improvements in insulin and hormone profile, suggesting that other factors are responsible for changes in reproductive function. Additional research is needed to further explain the improvements in reproductive function in women with PCOS.

In conclusion, weight loss via energy restriction improved reproductive function, cardiometabolic abnormalities, and hormonal parameters in overweight and obese women with PCOS. Addition of regular aerobic or combined aerobic-resistance exercise provided no additional improvement for cardiometabolic, hormonal, or reproductive outcomes but resulted in more favorable changes on body composition. Thus, lifestyle modifications that combine energy restriction for weight loss and regular exercise would appear to be a preferred treatment strategy in overweight women with PCOS. However, these results are limited to overweight and obese women with PCOS, and further research is required to assess the benefits of exercise in lean and normal-weight women with PCOS. Additional studies are also required to evaluate the individual effects of different exercise modalities and the long-term effects of diet and exercise treatment in women with PCOS.

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