Thieme

Oral Contraceptive Use does not Negatively Affect Body Composition and Strength Adaptations in Trained Women

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ABSTRACT

The purpose was to analyze the influence of oral contraceptive use on body composition and strength levels in trained women. Twenty-three resistance-trained women participated in this study (age = 27.4 ± 3.4 years; fat mass = 28.0 ± 5.0 %; BMI = 22.9 ± 2.7 kg·m-2). Subjects performed an 8-week non-linear resistance-training program. Participants were assigned to either a group that consumed oral contraceptives (n = 12, OC) or to a group that did not consume (n = 11, NOC). Changes in body composition were measured by dual energy X-ray absorptiometry. Strength performance was assessed via the one maximum repetition (1RM) test in the squat and bench press, and muscular power was evaluated using the countermovement jump (CMJ) test. Fat free mass increased significantly in OC but no changes were seen in NOC. There were no changes in fat mass for either OC or NOC. Significant changes were found in bench press 1RM for both OC and NOC; similarly, increases in squat 1RM were reported in OC and NOC. Alternatively, no significant changes were found in CMJ in both OC and NOC. No significant between-group differences were detected in any of the studied variables. The use of oral contraceptives during resistance training did not negatively affect body composition or strength levels in trained women.

Introduction

In recent years, the use of oral contraceptives (OCs) has gained popularity among female athletes, and it is now the preferred birth control strategy in this population [1]. However, the impact of OCs on body composition and sports performance is not yet fully known due to the diverse formulations of these products and individual factors such as menstrual cycle, age and differences between sport requirements.

The first combined oral contraceptive, marketed in the 1960s, was a formulation containing a progestogen (norethynodrel) and an estrogen derivative (mestranol). The latter component is me-

tabolized in the liver into a compound called ethinylestradiol (EE), which is used in most OCs today. Over the years, the dose of EE has been reduced by up to ten fold thanks to the discovery of new progestogens that decrease cardiovascular risk and thus the need for estrogens [2, 3]. These progestogens can be classified into either progesterone, testosterone or spironolactone derivatives.

The effects of the progestogen depend not only on its nature, but also its interaction with and affinity for the progesterone, androgen, estrogen, mineralocorticoid or glucocorticoid receptors found in different tissues. Thus, the dose and the selectivity index for these receptors can affect body mass, carbohydrate and fat metabolism and even body temperature [4, 6], which in turn can affect performance in various sports. In sports requiring high levels of strength, there are other important factors to consider, such as the possible impact of OCs on androgen production, since the latter affects sports performance [7, 8]. Indeed, a 2–5 % competitive advantage has been estimated in women with higher androgen levels [8].

Testosterone levels in women are regulated by the peripheral conversion of prohormones such as dehydroepiandrosterone (DHEA) and androstenedione (A). The latter plays a critical role in this process since approximately 50 % of testosterone is produced from the conversion of androstenedione [9]. In women using OCs, various formulations have been found to lower DHEA and A levels [9]; this is one of the possible mechanisms by which OC use is associated with lower testosterone levels [10].

Another important factor is the impact of OCs on the production of sex hormone binding globulin (SHBG), which binds to testosterone, facilitating its transport; in fact, 65–70 % of testosterone is bound to this protein. Zimmerman et al. [11] found that OC use increased SHBG levels, causing a decrease in free testosterone levels of up to 60 %, regardless of the estrogen dose or type of progestogen used. Additionally, they found that the use of lower doses of EE and second-generation progestogens (e. g., levonorgestrel) resulted in a lower impact on SHBG levels, raising the prospect that new recommendations are warranted for OC use in strength athletes.

Despite the changes in androgen production caused by OC use, few studies have reported changes in strength. Research to date has centered on elucidating the effects of OC on exercise-related outcomes in young, sedentary or recreationally active women [12, 14] and women athletes without strength-training experience [15]. To our knowledge, only one study endeavored to investigate the effects of OC on exercise-related changes in body composition and muscular adaptations in strength-trained women [16], and its focus was specific to the frequency of lower-limb training. Considering the paucity of research on the topic in strength-trained women, our study aimed to analyze the effect of OC on body composition and strength levels after an 8-week undulating torso/leg training program in women with previous strength-training experience. We hypothesized that OC would not negatively impact body composition or strength levels during supervised RT while following a controlled dietary regimen.

Methods

Subjects

Twenty-three women (age = 27.4 ± 3.4 years; height = 162.7 ± 6.1 cm; body mass = 60.5 ± 7.8 kg; fat mass = 28.0 ± 5.0 %; BMI = 22.8 ± 2.7 kg · m^{-2}) with over 2 years of continuous experience in strength training volunteered to participate in this study (▶ **Table 1**). All participants committed to following the prescribed RT and diet protocols, and to be monitored during the 8 weeks of study. The subjects were informed of the possible risks of the experiment and signed an informed consent form. The study was developed in accordance with the ethical guidelines of the World Medical Association Declaration of Helsinki and approved by the ethics committee at University of Málaga (code: 38-2019-H). The study meets the guidelines set forth by the International Journal of Sports Medicine for publication in this journal [17].

Subjects who self-reported the use of doping agents (e. g., anabolic-androgenic steroids) during the previous 2 years or admitted to taking any dietary supplement during the program were excluded from participation. Women with oligomenorrhea or polycystic ovarian syndrome, were excluded as well. Participants were instructed to avoid performing any structured exercise during the study period other than that prescribed for the intervention. ▶ **Fig. 1** presents a diagram of subject enrollment, randomization, and attrition as recommended by the Consolidated Standards of Reporting Trials (CONSORT).

Experimental design

The sample was comprised of strength-trained women who fulfilled all inclusion requirements to participate in this overload protocol including; i) no risk factors or any reported disease that could affect the intervention, ii) follow training guidelines, iii) no other training regime during our study. The participants did not smoke, had no existing co-morbidities, and the only reported medication taken were OCs. All participants abstained from performing any activities other than the 4 days of strength training throughout the 15-week intervention.

Participants were allocated to either an OC group (n = 12) or a non-OC (n = 11) based on their current use or abstention from OC. There were no significant between-group differences in baseline measurements (height, body mass, BMI), body composition (FM, FFM) or strength (BP, squat, CMJ) (▶ **Table 1**).

The OC group was comprised of: i) 4 subjects who took monophasic pills in doses of 0.15/0.03 mg of levonorgestrel and ethinyl

▶ **Table 1** Baseline characteristics of participants.

	NOC (n = 11)	OC (n = 12)	p-value
Age (y)	28.3 ± 4.1	26.6 ± 3.7	0.308
Height (cm)	162.6 ± 6.2	162.7 ± 6.3	0.978
BM (kg)	61.9 ± 5.8	59.1 ± 9.3	0.410
BMI (kg · m^{-2})	23.4 ± 2.2	22.3 ± 3.0	0.320
FM (kg)	18.3 ± 4.3	16.1 ± 5.3	0.288
FM (%)	29.4 ± 4.5	26.8 ± 5.4	0.227
FFM (kg)	43.5 ± 2.8	43.0 ± 5.1	0.754
PB (kg)	39.8 ± 7.1	37.8 ± 7.6	0.518
Squat (kg)	64.5 ± 11.3	68.2 ± 8.5	0.399
CMJ (cm)	24.0 ± 5.0	25.2 ± 4.4	0.522

Data are means ± SD; BM = body mass; BMI = body mass index; FM = fat mass; FFM = fat-free mass; PB = press bench; CMJ = counter-movement jump.

estradiol, respectively. And ii) 8 subjects who consumed triphasic pills with 0.03 mg ethinyl estradiol and 0.05 mg gestodene.

All women in the NOC group reported to have regular menstrual cycles (i. e., occurring on a 28- to 30-day cycle) and had not taken any form of synthetic estrogen or progesterone for at least six months prior to the study. Both groups began the programmed intervention and controlled diet after a 3-week familiarization phase. Training loads were recorded daily throughout the study.

Exercise protocol

The subjects in both groups initially completed a 3-week familiarization period to establish training loads for each exercise, followed by an 8-week intervention period. Cadence of repetitions was controlled by a metronome (Metronome M1, JSplash Apps). All subjects performed the same exercises encompassing the major muscles of the body throughout the duration of the program. The upper limb exercises were the bench press, barbell row, military press, lat pulldown, incline chest press, biceps curl and triceps pushdown. Lower limb exercises included the squat, lunge, leg press, hip thrust, leg extension, lying leg curl and standing calf raise.

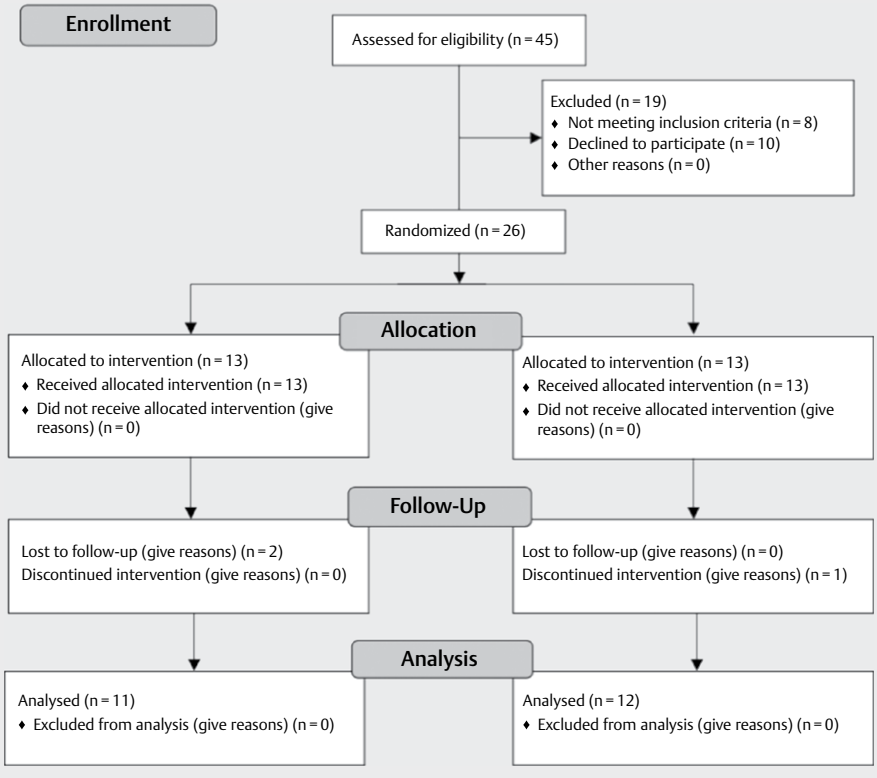
After familiarization, subjects completed four training sessions per week (divided into two four-week cycles) for 8 weeks. An upper/lower body split routine was used, with a 72-h recovery period between sessions for the same muscle complex. Both groups used a nonlinear periodized workout scheme, with the variables manipulated based on the objective of each phase as follows: strength, hypertrophy and muscular endurance. This sequence was followed by a deload whereby the training volume was reduced (series × repetition × load) in the last week of each cycle (recovery phase). In total, two four-week cycles were completed. ▶ **Table 2** provides the specific manipulation of variables for each phase of the training cycle.

Training sessions were monitored by RT specialists, adjusting the loads whenever necessary. The lifted loads and perceived exertion in each exercise were monitored by the physical conditioning and strength specialist using a paper tracking form throughout the experiment.

Dietary intervention

To avoid low energy availability and consequent changes in the menstrual cycle, the subjects' dietary needs were set at 45 kcal·kg^{-1} fat-free mass (FFM), which is higher than that used in some previous studies (30 kcal·kg^{-1} FFM) [18, 19]. Participants were prescribed to consume 2 g·kg^{-1}·d^{-1} of protein, which is higher than the recommendation of 1.7 g·kg^{-1}·d^{-1} as a function of the menstrual cycle in the luteal phase [20]. Fat intake was set at 1 g·kg^{-1}·d^{-1}, and the remainder of caloric intake was obtained from carbohydrates.

To monitor dietary intake, participants recorded their daily macronutrient intake via a smartphone app (MyFitnessPal, LLC, CA, USA), which has been validated as viable tool for energy and macronutrient assessment [21]. A sports nutritionist with experience in RT instructed participants on the proper use of the app and managed dietary consumption over the course of the study.



▶ **Fig. 1** CONSORT diagram.

Measurements

Body composition

Body composition was measured seven days after menstruation in both the NOC and OC pre- and postintervention to avoid the potential for body mass increases due to water retention mediated by hormonal fluctuations [22, 23]. Further, CMJ and RM measurements were made on the same day and at the same time in the pre- and post-body composition analysis, 7 days after menstruation. This would coincide with the follicular phase of the menstrual cycle, which has been shown to be most correlated with strength increases following regimented resistance training [24]. All subjects in the OC group reported that they took the pill in the active phase at the time the evaluations were made.

Total body and regional body composition were estimated using dual-energy X-ray absorptiometry (DXA). Each subject was scanned by a certified technician, and the distinguished bone and soft tissue, edge detection, and regional demarcations were analyzed by computer algorithms (software version APEX 3.0, Hologic QDR 4500, Bedford, MA). For each scan, subjects wore sport clothes and removed all materials that could attenuate the X-ray beam including jewelry items and underwear containing wire. Calibration of the densitometer was checked daily against a standard calibration block supplied by the manufacturer. The coefficient of variation values was less than 1.5 % for all whole body and segmental body composition measurements including bone mineral density (g/cm^2), mineral content (g), FM (%), FM (g), lean mass (g) and total body mass (g).

Countermovement jump (CMJ) test

For measurement of variables related to muscular strength and power, subjects were instructed to avoid vigorous exercise for 72 h before the tests in both the pre- and posttest periods. Participants performed general warm-up exercises consisting of stretching and stationary cycling for 10–12 min.

The CMJ test was performed on a jump mat (Smart Jump; Fusion Sport, Coopers Plains, Australia) after instructing participants on proper jump execution. Subjects were instructed to initiate the move by reaching 90° of knee flexion while keeping their hands at the waist and their trunk erect. Instructions emphasized that the movement should be performed without interruption from the beginning to the end of the jump. A total of 3–5 attempts were performed for familiarization before measurements were taken. After familiarization, two jumps were recorded with a rest interval of 1 min between each, and the highest value was computed.

Repetition maximum (RM) test

RM was evaluated in the squat (SQ) and bench press (BP) performed on a Smith machine (Gervasport, Madrid, Spain) both at the beginning and at the end of the study. Subjects reported to the laboratory having refrained from any exercise other than activities of daily living for at least 48 h before baseline testing and at least 48 h before testing at the conclusion of the study. In brief, subjects performed a general warm-up before testing that consisted of light cardiovascular exercise lasting approximately 7–10 min. A specific warm-up set of the given exercise was performed for 12–15 repetitions at ~40 % of subjects' perceived 1RM followed by two to three sets of two to three repetitions at a load corresponding to approximately 60–80 % 1RM. Subjects then performed sets of one repetition of increasing weight for 1RM determination. A three- to 5-min rest interval was provided between each successive attempt. Subjects were required to reach parallel in the 1RM SQ; confirmation of squat depth was obtained by a research assistant positioned laterally to the subject to ensure accuracy. Successful 1RM BP was achieved if the subject displayed a five-point body contact position (head, upper back, and buttocks firmly on the bench with both feet flat on the floor) and executed full-elbow extension. 1RM SQ testing was conducted before 1RM BP with a 7-min rest period separating tests. Participants then performed as many attempts as necessary until repetition failure, using the protocol described by McGuigan [25]. Bench placement was set by marking the floor with adhesive tape, to maintain the same placement for both measurements. All testing sessions were supervised by the research team to achieve a consensus for success on each trial.

Statistical analysis

The results are expressed as the mean and standard deviation. A repeated-measures general linear model (GLM) was used to evaluate study outcomes, considering the effect of Time (within-subject factor with two levels: pre-test and post-test), Group (inter-subject factor: OC vs. NOC) and the Time × Group interaction. Interpreta-

▶ **Table 2** Exercise protocol characteristics.

			Week 1	Week 2	Week 3	Week 4
Phases (Training goal)			Strength	Hypertrophy	Muscular endurance	Recovery
Goal repetitions			3–5 RM *	8–10 RM (failure)	20–25 RM (failure)	12–15 RM * *
Rest			3 min	1.5 min	45 sec	2–3 min
Tempo			1–0-X (1–0–1)	2–0–1	2–0–1	1–0–1
Sets			3	3	3	3
Work organization						
Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Leg	Torso		Leg	Torso		

1–0–1 = a second eccentric phase, zero isometric and 1 s in the concentric. All exercises were performed at a cadence of 1–0-X, except squats and deadlifts which were performed at 1–0–1 to control the risk of injury. RM = repetition maximum; * 1 or 2 reps before the failure; * * before the failure. Training phases (strength, hypertrophy and muscular endurance) and goal repetitions according to established criteria by National Strength and Conditioning Association, NSCA.

tion was based on the result of the Wilks' Lambda and Greenhouse-Geisser tests, respectively, for the multivariate and univariate analysis. Likewise, partial eta squared (ηp^2) values were reported for selected variables as indicators of effect size for the repeated measures GLM. Values of 0.02, 0.13 and 0.26 were considered small, medium and large, respectively [26]. Additionally, a Δ (post-test – pre-test) analysis was performed to determine the 95 % confidence interval (95 % CI) for the mean. A 95 % CI of the mean value fully above or below the initial value (value 0) was interpreted as a significant change. The normality of the data was assessed using the Shapiro-Wilk test. A 95 % confidence level was established for all tests. The statistical procedures were performed with the Statistical Package for the Social Sciences (SPSS 24.0, SPSS Inc., Chicago, USA) and the Δ figures were prepared with GraphPad Prism version 7.03 (GraphPad Software, California, USA).

Results

Participants in the OC group reported continuous contraceptive use during a minimum of 6 months prior to the study. All participants reported a regular cycle of 28–30 days.

The multivariate analysis revealed a difference with a large effect size after the intervention (Time: $p < 0.05$; $\eta p^2 = 0.94$) but no effect of the Time × Group interaction ($p = 0.27$; $\eta p^2 = 0.32$). The univariate analysis revealed differences in body mass (BM) by Time ($p < 0.05$; $\eta p^2 = 0.37$), but there was no effect of Group or the Time x Group interaction variable. Regarding body composition indicators, there was no effect of Time, Group or the Time × Group interaction variable on fat mass (FM); there was an effect of Time ($p < 0.05$; $\eta p^2 = 0.389$) on FFM, but the Group and Time × Group interaction variables had no effect (▶ **Table 3**).

With regard to muscle strength indicators, Time had an effect on both BP and SQ ($p < 0.05$; $\eta p^2 = 0.821$ and $p < 0.05$; $\eta p^2 = 0.877$, respectively). No effect of Group or the Time × Group interaction variable was observed. There was no effect of any of the variables on the CMJ test results (▶ **Table 4**).

The Δ values for each of the measured outcomes are shown in ▶ **Table 5**. A significant change in BM and FFM was observed for the OC but not for the NOC group, whereas FM did not show a significant change in either group (▶ **Fig. 2**). Similarly, significant changes were recorded in BP and SQ in both groups; however, no difference was found between the two groups (▶ **Fig. 3**).

Discussion

Our study compared changes in strength levels and body composition over the course of an 8-week RT protocol in a cohort of resistance-trained women using OCs since at least 6 months prior to study entry versus a group not using a contraceptive method. The results showed no significant differences in markers of strength or body composition between the groups, although only OC significantly increased FFM post-study. These findings are in agreement with the findings of Nichols et al. [15], who evaluated measures of 1 RM BP, 10 RM leg extension and isokinetic peak torque in female water polo and softball college athletes performing free weight exercises three days a week for 12 weeks. In this study, subjects who used contraceptives that included only progesterone were excluded, however, all combinations incorporated ethinylestradiol, such

▶ **Table 3** Results in BM and body composition.

Group		Before	After	ES	Time p (ηp^2)	Time × Group p (ηp^2)	Group p (ηp^2)
BM (kg)	NOC	61.9 ± 5.8	62.9 ± 6.4	0.16	0.003 (0.375)	0.297 (0.057)	0.571 (0.017)
	OC	59.1 ± 9.3	60.9 ± 10.0 *	0.18			
FM (kg)	NOC	18.3 ± 4.3	18.7 ± 4.5	0.07	0.079 (0.153)	0.616 (0.013)	0.309 (0.054)
	OC	16.1 ± 5.3	16.6 ± 5.0	0.08			
FFM (kg)	NOC	43.5 ± 2.8	44.2 ± 3.4	0.21	0.003 (0.389)	0.251 (0.069)	0.931 (0.000)
	OC	43.0 ± 5.1	44.4 ± 5.6 *	0.25			

Data are means ± SD. Greenhouse-Geisser univariate p-levels are presented for each variable. $p < 0.05$ is considered significant. NOC = no oral contraceptives group; OC = oral contraceptives group; BM = body mass; FM = fat mass; FFM = fat-free mass; ES = Effect Size (Cohen's d); * Denotes a significant difference from baseline.

▶ **Table 4** Results in strength.

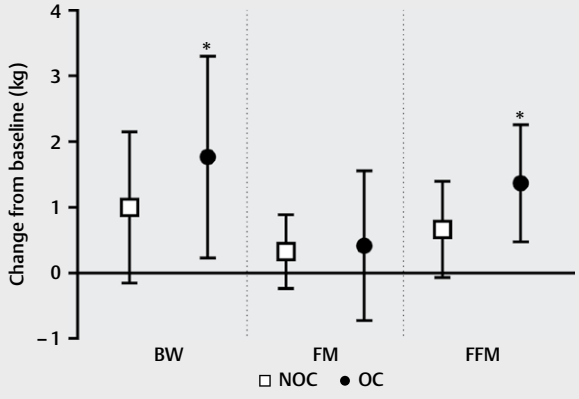
Group		Before	After	ES	Time p (ηp^2)	Time × Group p (ηp^2)	Group p (ηp^2)
BP (kg)	NOC	39.8 ± 7.1	44.6 ± 7.4 *	0.66	< 0.001 (0.821)	0.249 (0.069)	0.975 (0.000)
	OC	37.8 ± 7.6	44.5 ± 7.4 *	0.88			
SQ (kg)	NOC	64.5 ± 11.3	80.1 ± 10.8 *	1.41	< 0.001 (0.877)	0.311 (0.054)	0.564 (0.018)
	OC	68.2 ± 8.5	81.2 ± 9.3 *	1.46			
CMJ (kg)	NOC	24.0 ± 5.0	24.6 ± 4.8	0.14	0.279 (0.061)	0.314 (0.053)	0.405 (0.037)
	OC	25.2 ± 4.4	25.3 ± 3.4	0.01			

Data are means ± SD. Greenhouse-Geisser univariate p-levels are presented for each variable. $p < 0.05$ is considered significant. NOC = no oral contraceptives group; OC = oral contraceptives group; BP = Bench Press; CMJ = countermovement jump. ES = Effect Size (Cohen's d); * Denotes a significant difference from baseline.

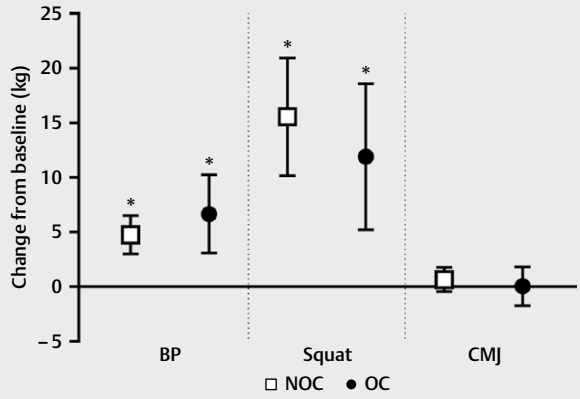
▶ **Table 5** Results of the change of the variables after the intervention.

Group	NOC	OC
BM (kg)	1.0 ± 1.7 (−0.2–2.1)	1.8 ± 2.4 * (0.2–3.3)
FM (kg)	0.3 ± 0.8 (−0.2–0.9)	0.4 ± 1.8 (−0.7–1.5)
FFM (kg)	0.7 ± 1.1 (−0.1–1.4)	1.4 ± 1.4 * (0.5–2.3)
BP (kg)	4.8 ± 1.8 * (3.6–5.9)	6.7 ± 3.6 * (4.4–8.9)
SQ (kg)	15.6 ± 5.4 * (11.7–19.4)	13.0 ± 5.8 * (9.1–16.9)
CMJ (cm)	0.7 ± 1.1 (−0.1–1.4)	0.1 ± 1.8 (−1.1–1.2)

Data are means ± SD (95 % IC, lower bound – upper bound); NOC = no oral contraceptives group; OC = oral contraceptives group; p = difference between groups (ANCOVA); * Denotes a significant difference from baseline; * * differences between groups.



▶ **Fig. 2** Changes in body mass, body mass index and body composition. Mean changes with 95 % CI's completely above or below the baseline are significant changes. NOC = no oral contraceptives group; OC = oral contraceptives group; BW = body weight; FM = fat mass; FFM = fat-free mass; * Denotes a significant difference from baseline (p < 0.05); ‡ Denotes a significant difference between groups.



▶ **Fig. 3** Changes in in muscle strength. Mean changes with 95 % CI's completely above or below the baseline are significant changes. NOC = no oral contraceptives group; OC = oral contraceptives group; BP = Bench Press; CMJ = Countermovement Jump; * Denotes a significant difference from baseline (p < 0.05); ‡ Denotes a significant difference between groups.

as estrogen, without differentiating the type of pill, monophasic or triphasic, as with our research. Results showed similar strength increases between groups at the end of the study irrespective of contraceptive use. Likewise, research by Wikstrom-Frisen et al. [16] investigating the effects of 3 lower-limb RT protocols with different frequencies and periodization of variables found no significant differences in body composition (FFM) or strength levels (CMJ, squat jump, isokinetic peak torque) between women using OCs and those who did not. Nevertheless, it should be emphasized that more frequent RT during the first 2 weeks of the menstrual cycle resulted in greater improvements in FFM, strength and power compared to a protocol with similar frequency but implemented during the last 2 weeks of the cycle. In this case, the subjects who consumed contraceptive pills with monophasic and triphasic formulas in different groups were randomized. Our OC study protocol was also mixed; women used different combinations of hormones. More recently, Myllyaho et al. [27] found that OC use in physically active women did not alter strength gains, nor did it negatively influence other athletic performance-related parameters. In this study, combined monophasic pills, progesterone pills and even intrauterine systems were used.

Elliott et al. [13] concluded that OC use neither increased strength levels (dynamic or isometric) nor caused significant changes in body composition. In this case, the subjects exclusively consumed monophasic pills. However, this research was conducted in sedentary women and did not incorporate an exercise protocol. Moreover, these findings should be interpreted with caution since factors such as the type of progestogen used may influence the outcome. For example, antiandrogenic progestogens such as chlormadinone acetate can counteract fluid retention and even lead to a reduction in body fat [28]. Another study reported differences in young women using OCs, including decreased FFM and decreased levels of DHEA and Insulin-like growth factor-1 (IGF-1) after a 10-week RT program [14]. The authors speculated that the observed reduction in FFM (measured by hydrostatic weighing) may be related to the androgenicity caused by progestin, which can bind to the androgen receptor and therefore inhibit its function. Nevertheless, these results may vary depending on the level of the athlete, as the use of monophasic contraceptives in active women has been found to lead to an increase in BM, whereas the same contraceptive can decrease BM in sedentary women [12]. Methodological differences such as body composition measurement techniques and the RT program should be considered in order to correctly interpret these studies; such differences often explain the disparate results found in the literature to date. Similar to the abovementioned studies, our findings showed that FFM and strength levels in the OC group were not impaired, nor were they inferior to those of the NOC group; in fact, they improved after the intervention.

There is insufficient evidence in the present study to establish a relationship or to rule out an added advantage of using OCs in the women studied, especially if we consider that different results have

been reported despite the variation in hormones such as testosterone, growth hormone and DHEA [29, 30]. Thus, based on the findings reported in this study and in the current literature, it can be inferred that OC use during an eight-week RT protocol does not impair strength gains or increases in FFM.

It should be noted that estrogens play a vital role in women's health; in fact, its synthesis not only occur in reproductive tissues, but also in the liver, heart, muscles, bone and brain. Thus, estrogen synthesis is specific to each tissue, encompassing several actions [31] given the variety of forms that can be found endogenously; estrone, estriol and estradiol; the latter being the most important because of its high affinity for estrogen receptors [32].

A decrease in estrogen levels may produce mood swings and irritability, with variations in emotional and cognitive behavior. Interestingly, there are reports of therapeutic benefits of estrogen administration in women at the brain level, although they are not fully extrapolatable to men [33]. These authors highlight the evidence of beneficial effects on learning, memory and mood, which can have a positive social impact. Moreover, a lower mortality rate in cardiovascular diseases is related to estrogen replacement therapies in post-menopausal women; however, there are some reports of possible risk of thrombotic events, cancer or arrhythmias [34]. Thus, the conversion of endogenous testosterone into estrogens, through the aromatase enzyme, is being investigated as a possible replacement therapy that may offer greater safety [34]. Further research is needed to distinguish the effect of estrogen on different brain disorders.

In addition, skeletal muscle mass decreases with aging, a condition exacerbated in women due to the menopause-induced loss of estrogen. This estrogen deficiency is related to a decrease in muscle strength [35]. Therefore, adequate levels of estrogen can enhance the increase in muscle strength in post-menopausal women [36] and in estrogen-deficient rodents [37]. It is hypothesized that the mechanism underlying the effect of estrogen on muscle strength is due to the action of nuclear estrogen receptors, which can cause an improvement in myosin function [38], specifically phosphorylation of myosin and the function of satellite cells. In this sense, an estrogen deficiency is associated with the generation of apoptosis in the skeletal muscle, which would generate a loss of mass, and therefore of strength [35].

Limitations

The results of this study should be interpreted cautiously due to limitations in the methodology. First, groups with a larger number of participants are required to reduce the possible interindividual difference. In addition, the results obtained in our study have been obtained in groups of women with several years of resistance training experience. Different responses have been found between active and sedentary women (Burrows et al. 2007), so results cannot be extrapolated to other populations. Second, the inclusion requirement for the contraceptive group was the use of combined contraceptives, regardless of their dose or formulation. This is an important limiting factor, since differences have been observed in the type of contraceptive (monophasic vs triphasic) and in the dose/progestin used [6, 28]. Therefore, more studies are needed on the topic to confidently provide recommendations for different population groups. Third, measures of FFM constitute all non-fatty tissues, and thus do not necessarily represent changes in muscle mass; it remains possible that differences in water retention may have influenced this outcome between groups, despite our attempts to control for variances in the menstrual cycle. Finally, the design of the study mandated a quasi-experimental design; the lack of randomization may have confounded results based on the inherent characteristics of those who either choose to use or not use OCs.

Conclusion

Within the framework of a supervised nonlinear RT program in conjunction with a supervised diet, OC use does not impair strength gains nor body composition in resistance-trained young adult women. Rather, there were increases in FFM (without a concomitant increase in FM), BP and SQ after the intervention, and these changes were similar compared to the group not using OCs. Additional randomized clinical studies are required to further clarify the influence, positive or negative, of OCs on performance variables associated with strength and body composition.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

[1] Richters J, Fitzadam S, Yeung A, Caruana T, Rissel C, Simpson JM, de Visser RO Contraceptive practices among women: The second Australian study of health and relationships. Contraception 2016; 94: 548–555

[2] Brody SA, Turkes A, Goldzieher JW. Pharmacokinetics of three bioequivalent norethindrone/mestranol-50 micrograms and three norethindrone/ethinyl estradiol-35 micrograms OC formulations: Are "low-dose" pills really lower? Contraception 1989; 40: 269–284

[3] Woutersz TB. A new ultra-low-dose combination oral contraceptive. J Reprod Med 1983; 28: 81–84

[4] Collins DC. Sex hormone receptor binding, progestin selectivity, and the new oral contraceptives. Am J Obstet Gynecol 1994; 170: 1508–1513

[5] Rabe T, Runnebaum B. Progestins and carbohydrate metabolism. Int J Fertil 1986; 31: SU [UPDATE] 31–45

[6] Sitruk-Ware R, Nath A. Characteristics and metabolic effects of estrogen and progestins contained in oral contraceptive pills. Best Pract Res Clin Endocrinol Metab 2013; 27: 13–24

[7] Bermon S, Garnier PY. Serum androgen levels and their relation to performance in track and field: mass spectrometry results from 2127 observations in male and female elite athletes. Br J Sports Med 2017; 51: 1309–1314

[8] Bermon S. Androgens and athletic performance of elite female athletes. Curr Opin Endocrinol Diabetes Obes 2017; 24: 246–251

[9] Longcope C. Adrenal and gonadal androgen secretion in normal females. Clin Endocrinol Metab 1986; 15: 213–228

[10] Aden U, Jung-Hoffmann C, Kuhl H. A randomized cross-over study on various hormonal parameters of two triphasic oral contraceptives. Contraception 1998; 58: 75–81

[11] Zimmerman Y, Eijkemans MJ, Coelingh Bennink HJ et al. The effect of combined oral contraception on testosterone levels in healthy women: a systematic review and meta-analysis. Hum Reprod Update 2014; 20: 76–105

[12] Burrows M, Peters CE. The influence of oral contraceptives on athletic performance in female athletes. Sports Med 2007; 37: 557–574

[13] Elliott KJ, Cable NT, Reilly T. Does oral contraceptive use affect maximum force production in women? Br J Sports Med 2005; 39: 15–19

[14] Lee CW, Newman MA, Riechman SE. Oral contraceptive use impairs muscle gains in young women. FASEB J 2009; 23: 955.25

[15] Nichols AW, Hetzler RK, Villanueva RJ, Stickley CD, Kimura IF. Effects of combination oral contraceptives on strength development in women athletes. J Strength Cond Res 2008; 22: 1625–1632

[16] Wikstrom-Frisen L, Boraxbekk CJ, Henriksson-Larsen K. Effects on power, strength and lean body mass of menstrual/oral contraceptive cycle based resistance training. J Sports Med Phys Fitness 2017; 57: 43–52

[17] Harriss DJ, Macsween A, Atkinson G. Standards for ethics in sport and exercise science research: 2018 update. Int J Sports Med 2017; 38: 1126–1131

[18] Loucks AB. Energy availability, not body fatness, regulates reproductive function in women. Exerc Sport Sci Rev 2003; 31: 144–148

[19] Reed JL, De Souza MJ, Mallinson RJ, Scheid JL, Williams NIT. Energy availability discriminates clinical menstrual status in exercising women. J Int Soc Sports Nutr 2015; 12: 11.

[20] Wooding DJ, Packer JE, Kato H, West DWD, Courtney-Martin G, Pencharz PB, Moore DR. Increased protein requirements in female athletes after variable-intensity exercise. Med Sci Sports Exerc 2017; 49: 2297–2304

[21] Teixeira V, Voci SM, Mendes-Netto RS, da Silva DG. The relative validity of a food record using the smartphone application MyFitness-Pal. Nutr Diet: The Journal of the Dietitians Association of Australia 2018; 75: 219–225

[22] Rosenfeld R, Livne D, Nevo O, Dayan L, Milloul V, Lavi S, Jacob G. Hormonal and volume dysregulation in women with premenstrual syndrome. Hypertension 2008; 51: 1225–1230

[23] Stachenfeld NS. Sex hormone effects on body fluid regulation. Exerc Sport Sci Rev 2008; 36: 152–159

[24] Sung E, Han A, Hinrichs T, Vorgerd M, Manchado C, Platen P. Effects of follicular versus luteal phase-based strength training in young women. SpringerPlus 2014; 3: 668

[25] McGuigan M, Administration, scoring, and interpretation of selected tests. In Haff G, Triplett T., eds. Essentials of Strength Training and Conditioning. Champaign, IL: Human Kinetics; 2016: 265–266

[26] Dalton RL, Sowinski RJ, Grubic TJ, Collins PB, Coletta AM, Reyes AG, Sanchez B, Koozehchian M, Jung YP, Rasmussen C, Greenwood M, Murano PS, Earnest CP, Kreider RB. Hematological and hemodynamic responses to acute and short-term creatine nitrate supplementation. Nutrients 2017; 9: E1359

[27] Myllyaho MM, Ihalainen JK, Hackney AC, Valtonen M, Nummela A, Vaara E, Häkkinen K, Kyröläinen H, Taipale RS. Hormonal contraceptive use does not affect strength, endurance, or body composition adaptations to combined strength and endurance training in women. J Strength Cond Res 2018, doi:10.1519/jsc.0000000000002713.

[28] Uras R, Orru M, Etzi R, Peppi G, Marotto MF, Pilloni M, Zedda P, Lello S, Melis GB, Paoletti AM. Evidence that in healthy young women, a six-cycle treatment with oral contraceptive containing 30 mcg of ethinylestradiol plus 2 mg of chlormadinone acetate reduces fat mass. Contraception 2009; 79: 117–121

[29] Graham CA, Bancroft J, Doll HA, Greco T, Tanner A. Does oral contraceptive-induced reduction in free testosterone adversely affect the sexuality or mood of women? Psychoneuroendocrinology 2007; 32: 246–255

[30] Rechichi C, Dawson B, Goodman C. Athletic performance and the oral contraceptive. Int J Sports Physiol Perform 2009; 4: 151–162

[31] Cui J, Shen Y, Li R. Estrogen synthesis and signaling pathways during aging: From periphery to brain. Trends Mol Med 2013; 19: 197–209

[32] Houtman CJ, Legler J, Thomas K, Effect-directed analysis of endocrine disruptors in aquatic ecosystems. In Brack W., ed. The Handbook of Environmental Chemistry: Effect-Directed Analysis of Complex Environmental Contamination. Berlin, Heidelberg: Springer Berlin Heidelberg; 2011: 237–265.

[33] Gillies GE, McArthur S. Estrogen actions in the brain and the basis for differential action in men and women: A case for sex-specific medicines. Pharmacol Rev 2010; 62: 155–198

[34] Iorga A, Cunningham CM, Moazeni S, Ruffenach G, Umar S, Eghbali M. The protective role of estrogen and estrogen receptors in cardiovascular disease and the controversial use of estrogen therapy. Biol Sex Differ 2017; 8: 33

[35] Collins BC, Laakkonen EK, Lowe DA. Aging of the musculoskeletal system: How the loss of estrogen impacts muscle strength. Bone 2019; 123: 137–144

[36] Samson MM, IBAE Meeuwsen, Crowe A, Dessens JA, Duursma SA, Verhaar HJ. Relationships between physical performance measures, age, height and body weight in healthy adults. Age Ageing 2000; 29: 235–242

[37] Greising SM, Baltgalvis KA, Lowe DA, Warren GL. Hormone therapy and skeletal muscle strength: A meta-analysis. J Gerontol A Biol Sci Med Sci 2009; 64: 1071–1081

[38] Lowe DA, Baltgalvis KA, Greising SM. Mechanisms behind estrogen's beneficial effect on muscle strength in females. Exerc Sport Sci Rev 2010; 38: 61–67