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Comparison of aerobic exercise capacity and muscle strength in overweight women with and without polycystic ovary syndrome

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Objective To assess maximal aerobic capacity ($\dot{V}O_{2max}$) and muscle strength in overweight and obese women with polycystic ovary syndrome (PCOS) and determine their relationship with metabolic and hormonal factors.

Design Cross-sectional study.

Setting Clinical Research Unit.

Population Overweight and obese women with PCOS (n = 10) and age-and weight-matched healthy controls (n = 16).

Methods $\dot{V}O_{2max}$ was measured during an incremental treadmill test and maximal isometric (ImS) and isokinetic knee extensor strength (IkS) (120°/second) were assessed by isokinetic dynamometry.

Main outcome measures $\dot{V}O_{2max}$, ImS, IkS, waist circumference, blood lipids, glucose, insulin, insulin resistance (homeostatic model assessment [HOMA2]), C-reactive protein (CRP), hormonal profile.

Results PCOS women had higher levels of testosterone and free testosterone ($P \leq 0.05$), but there were no significant differences in any cardiovascular disease (CVD) risk markers between the groups. $\dot{V}O_{2max}$ was similar in women with PCOS and healthy controls (PCOS 26.0 ± 4.1 ml/kg/minute, controls 25.7 ± 3.8 ml/kg/minute; P = 0.90), as was ImS (PCOS 1.50 ± 0.54 Nm/kg, controls 1.50 ± 0.47 Nm/kg; P = 0.96) and IkS (PCOS 1.04 ± 0.32 Nm/kg, controls 1.16 ± 0.23 Nm/kg; P = 0.32). $\dot{V}O_{2max}$ was inversely related to waist circumference, insulin, HOMA2 and CRP. Waist circumference was inversely associated with ImS and IkS. No significant associations between exercise parameters and hormonal variables were identified.

Conclusions Compared to age- and weight-matched healthy overweight and obese women with similar insulin resistance and CVD risk profiles, women with PCOS had similar aerobic capacity and muscle strength. This suggests PCOS, at least in the absence of an adverse metabolic profile is unlikely to limit physical function. Larger studies examining the effects of PCOS on exercise tolerance in a diverse range of PCOS phenotypes is required.

Keywords Cardiovascular risk, exercise tolerance, metabolic syndrome, obesity.

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Introduction

Polycystic ovary syndrome (PCOS), characterised by chronic anovulation, menstrual dysfunction and hyperandrogenism, is a common reproductive endocrine disorder[1] affecting ~7% of women of reproductive age.[2] PCOS is also associated with an increased prevalence of a number of metabolic risk factors including obesity, abdominal obesity, insulin resistance and compensatory hyperinsulinaemia, hypertension, dyslipidaemia and a higher risk of developing type 2 diabetes.[1,3,4] However, it is still to be confirmed whether women with PCOS have an increased incidence of cardiovascular disease (CVD).[5]

It is well established that cardiorespiratory fitness (CRF) or maximal aerobic capacity ($\dot{V}O_{2max}$) is a strong independent predictor of CVD and all-cause mortality in both men and women.[6–9] Even after adjustment for other known

contributors, the level of CRF remains a strong predictor of CVD and mortality,[7,8] indicating that impaired CRF may carry prognostic significance for cardiovascular events. In addition, $\dot{V}O_{2max}$ is probably the best predictor of functional capacity[10] and is a primary determinant of an individual's ability to sustain physical activity. Hence, the ability of the cardiorespiratory system to meet increased metabolic demands not only has implications for cardiovascular health but also influences the ability to perform activities of daily living and undertake exercise training; the latter being widely accepted as a cornerstone for PCOS management.[11,12]

Previous studies have demonstrated that CRF is inversely associated with insulin resistance in various patient groups with metabolic abnormalities.[13–16] Accordingly, case–control studies have shown that individuals with insulin resistance and/or type 2 diabetes have reduced $\dot{V}O_{2max}$ compared with healthy age, weight and physical activity-matched controls.[14,17,18] However, despite an increased prevalence of insulin resistance and hyperinsulinaemia in PCOS,[1,19] data evaluating the effect of PCOS on exercise capacity and tolerance are limited and inconclusive. Two previous studies reported no difference in $\dot{V}O_{2max}$ between overweight women with and without PCOS matched for age and BMI.[20,21] In contrast, Orio *et al.*[22] recently demonstrated that young overweight women with PCOS had impaired maximal and submaximal cardiopulmonary responses to exercise compared with age and BMI-matched healthy controls, with the magnitude of impairment being associated with the degree of insulin resistance. The reason for the discrepancy between the findings of these studies is not clear and debate continues to surround the effects of PCOS as a risk factor for impaired CRF and CVD.

In addition to CRF, muscle strength has shown to predict the risk of metabolic syndrome and all-cause mortality independently[23,24] and represents an important marker of exercise tolerance and physical function.[25,26] It has been reported that muscle strength is inversely associated with fasting insulin levels and insulin resistance,[27,28] an observation that is consistent with a recent study that showed muscle strength was lower in individuals with an adverse metabolic profile compared to healthy controls.[29] However to date, studies, which have evaluated the effects of PCOS on exercise function, have only investigated effects on CRF[20–22] and effects on muscle strength and its relationship with metabolic risk factors has not been examined.

The purpose of this study was to compare multiple facets of physical function, including CRF and muscle strength, in overweight and obese women with and without PCOS and to evaluate their relationship with insulin resistance and other metabolic risk factors.

Methods

Participants

Ten women with PCOS and 16 non-PCOS controls, matched for age, body weight and level of habitual activity, were recruited by public advertisement (Table 1). These participants were a subset of women who completed additional exercise testing from a previous study.[30] All participants were overweight or obese (body mass index [BMI]: 27–45 kg/m^2), premenopausal, sedentary women aged 25–44 years and had been weight stable (<2.0 kg weight change) for at least 3 months prior to enrolment. Presence of PCOS was diagnosed according to the Rotterdam criteria.[31] Menstrual irregularity was defined as cycle length <21 days or >35 days or variation between consecutive cycles of >3 days. Exclusion criteria included smoking, uncontrolled hypertension, cancer, liver, renal, haematological, CVD, diabetes, Cushing syndrome, androgen secreting tumours, late-onset 21-hydroxylase deficiency, thyroid dysfunction, hyperprolactinaemia or pregnancy. Participants with a history of angina or any other cardiac, pulmonary or physical symptom that would potentially limit exercise performance were also excluded. All women provided written informed consent and the study protocols

Table 1. Physical characteristics, cardiovascular disease risk factors and hormonal profiles of women with PCOS and healthy controls

Variable	PCOS (n = 10)	Control (n = 16)	P-value
Age (years)	33.6 ± 6.7	36.8 ± 4.8	0.22
Body weight (kg)	89.9 ± 11.3	96.5 ± 15.1	0.22
BMI (kg/m^2)	34.1 ± 5.5	35.5 ± 4.9	0.52
Waist circumference (cm)	108.7 ± 12.9	112.1 ± 12.8	0.56
Triglycerides (mmol/l)	1.5 ± 0.5	1.7 ± 0.7	0.44
Total cholesterol (mmol/l)	4.8 ± 0.7	5.2 ± 1.1	0.25
High density lipoprotein cholesterol (mmol/l)	1.4 ± 0.2	1.3 ± 0.3	0.16
Low density lipoprotein cholesterol (mmol/l)	2.7 ± 0.7	3.0 ± 0.6	0.30
Fasting glucose (mmol/l)	5.2 ± 1.0	5.2 ± 0.5	0.92
Fasting insulin (mu/l)	14.3 ± 11.2	11.5 ± 5.9	0.70
HOMA2	1.6 ± 0.9	1.5 ± 0.8	0.99
C-reactive protein (mg/l)	5.5 ± 3.7	4.2 ± 2.6	0.97
Testosterone (nmol/l)	3.2 ± 1.2	2.1 ± 0.5	0.03
Free testosterone (pmol/l)	66.4 ± 33.4	44.6 ± 14.4	0.05
Sex-hormone binding globulin (nmol/l)	23.9 ± 13.4	24.1 ± 9.2	0.96
Free androgen index	22.6 ± 24.2	11.2 ± 9.2	0.11

BMI, body mass index; HOMA2, homeostasis model of assessment.
Values are mean ± SD.
Subjects with CRP > 10 mg/l (n = 1 PCOS, n = 1 control) were excluded from the CRP analysis.

and procedures were approved by the Human Ethics Committee of the Commonwealth Scientific Industrial Research Organisation (Ref No. 03/09).

Study design

All women attended the clinic on three occasions, separated by at least 2 days for testing. At the first visit, after a minimum 3 hours fast, height, weight and waist circumference were measured before a graded maximal treadmill exercise test was performed to measure $\dot{V}O_{2max}$. At the second visit, following a minimum 3 hours fast, muscular strength was assessed. At the final visit, after an overnight fast, a blood sample was drawn for measurement of blood lipids, C-reactive protein (CRP), glucose, insulin and hormonal markers. Participants were advised not to consume any alcohol or participate in any vigorous physical activity 24 hours before each visit. Habitual daily physical activity levels were assessed using a validated questionnaire,[32,33] which provides an index of routine physical activity over the past 12 months, including occupational, sport and leisure time activities.

Height, body weight and waist circumference

Height was measured to the nearest 0.1 cm using a stadiometer (SECA, Hamburg, Germany) with participants in the free-standing position. Body weight was measured to the nearest 0.05 kg with participants wearing light clothing and no shoes, using calibrated electronic digital scales (Mercury; AMZ 14, Tokyo, Japan). Waist circumference was measured (in duplicate to the nearest 0.5 cm) at a point 3 cm above the iliac crest with participants in a standing position at the end of normal expiration. Waist circumference was taken to be the mean of the two measures.

Maximal exercise test

$\dot{V}O_{2max}$ was assessed during a graded exercise test to volitional exhaustion on an electronic treadmill (Trackmaster TMX425CP; Full Vision Inc., Newton, KS, USA) using the Bruce Protocol.[34] Participants were encouraged to exercise to volitional fatigue or until they reached symptom-limited exhaustion. Measurements of oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) with calculations of the respiratory exchange ratios (RER, $\dot{V}CO_2/\dot{V}O_2$) were measured from expired air as 30 seconds averages throughout the exercise test using indirect calorimetry. To collect expired air, participants breathed through a low resistance respiratory valve (Hans Rudolph 2700 series, Kansas City, MO, USA) with a pre-calibrated large flow turbine transducer (P.K. Morgan Mark 2, Seaford, Australia) attached to the inspiratory port to measure ventilatory volumes. Expired air was directed into a 2.6 l mixing chamber (Sportech, Canberra, ACT, Australia), from which dried gas was sampled continuously (~500 ml/minute) and passed to an oxygen analyser (Ametek S-31A/I, Pittsburgh, PA, USA) and a carbon dioxide analyser (Ametek CD-3A, Pittsburgh, PA, USA), both of which had been pre-calibrated with commercially available gases of known composition (BOC Gases, Adelaide, SA, Australia). The highest oxygen uptake value achieved over 30 seconds was taken to represent $\dot{V}O_{2max}$. Heart rate (HR) was recorded throughout the test as 5 seconds averages using a HR monitor and chest transmitter (Polar Accurex Plus; Polar Electro, Oulu, Finland). An electrocardiogram was monitored continuously (CardioLife Tec-7100 Defibrillator; Nihon Kohdenm Shinjuku-ku, Tokyo) and blood pressure was measured manually before exercise and during the last 30 seconds of each exercise stage to ensure volunteer safety. Participants were asked to report their rating of perceived exertion (RPE) according to the Borg Scale[35] at the end of each exercise stage and upon the cessation of exercise. $\dot{V}O_{2max}$ was deemed to have been reached and the test data included in the analysis, if the volunteer achieved the primary criteria of a plateau in $\dot{V}O_2$ (increase of <150 ml/minute) with increasing workload or at least two of the following three secondary criteria: 1) peak RER of ≥1.0, 2) peak HR of ≥85% of age-predicted maximum (220-age [years]) and 3) RPE ≥ 17.[36] Tolerance to exercise was assessed by expressing the measured $\dot{V}O_{2max}$ as a percentage of predicted $\dot{V}O_{2max}$ calculated according to the method of Wasserman *et al.*[37]

Skeletal muscle function assessment

Strength of the knee extensor muscles of the dominant leg was assessed using an isokinetic dynamometer (Kin-Com 125AP; Chattecx Corporation, Chattanooga, TN, USA). Prior to the muscle strength assessments, participants completed a warm-up consisting of 5 minutes of unloaded cycle ergometry (Repco Fitness Ergometer Air Bike, Repco Fitness, The Fitness Generation, Rowville, Vic., Australia) at a self-selected cadence at which they felt comfortable and would not induce fatigue. Participants were then seated on the dynamometer in a comfortable upright position and secured using thigh, pelvic and torso straps to minimise extraneous body movements. The lateral femoral epicondyle was used as the bony landmark for matching the axis of rotation of the knee joint with the axis of rotation of the dynamometer lever arm. The resistance pad of the dynamometer lever arm was positioned at a point on the lower leg at ~75% of the fibula length. Isometric muscle strength (ImS) was taken to be the highest peak torque achieved from three maximal contractions with the knee positioned at 90° of flexion, with a 2 minute rest between efforts. After a 5 minutes rest period, isokinetic muscle strength (IkS) was assessed from five consecutive maximal knee extension manoeuvres performed at a velocity of

120°/seconds. Peak torque, corrected for gravitational effects, was assessed for each contraction throughout a windowed range of motion from 10° to 60°.[38,39] The highest peak torque achieved across the five repetitions was taken as the measured value of IkS. During the testing, participants were given verbal encouragement as well as visual feedback from the dynamometer computer monitor in an attempt to facilitate maximal contractions.[40] Functional ImS and IkS were expressed per kg of body weight.

Biochemical analyses

Fasting blood samples were collected for measurement of serum sex hormone binding globulin (SHBG), testosterone, free testosterone, total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglycerides, high sensitivity C-reactive protein (CRP) and plasma glucose and insulin as previously described.[41,42] The free androgen index (FAI) was calculated as testosterone/SHBG X 100. The homeostatic model assessment (HOMA2), used as a surrogate measure of insulin resistance, was estimated using fasting glucose and insulin concentrations and the HOMA2 online calculator.[43]

Statistical analysis

Data were checked for normality and non-normally distributed variables (insulin, triglycerides, HOMA2, CRP, testosterone and FAI) were log transformed prior to analysis. Subjects with a CRP>10 mg/l (n = 1 PCOS, n = 1 control) were excluded from the CRP analysis. Group differences were determined using unpaired Student's t-tests. Chi-square test was used to compare categorical data. Pearson's correlation analysis was used to determine relationships between variables. Statistical analyses were performed using SPSS for Windows 14.0 (SPSS, Chicago, IL, USA). Data is presented as means ± SD and the level of statistical significance was set at $P \leq 0.05$.

Results

Participant characteristics, physical measurements, metabolic risk markers and hormonal parameters are presented in Table 1. The groups were well-matched for age and BMI. The groups were also well-matched for physical activity levels with no difference between the groups for any of the physical activity indices (PCOS versus Controls; total physical activity score, 7.2 ± 0.8 versus 7.2 ± 1.5, P = 0.91; work activity index, 2.8 ± 0.4 versus 2.6 ± 0.7, P = 0.47; sports activity index, 1.6 ± 0.2 versus 1.9 ± 0.8, P = 0.30; leisure-time activity index, 2.8 ± 0.5 versus 2.6 ± 0.7, P = 0.52). Testosterone and free testosterone were significantly higher in PCOS compared with controls ($P \leq 0.05$; Table 1). There were no significant difference between PCOS and controls for any of the CVD risk markers, including waist circumference, insulin, HOMA2, lipids, glucose or CRP ($P \geq 0.16$; Table 1).

Two participants in each group did not reach $\dot{V}O_{2max}$ based on the pre-defined criteria. Consequently, the exercise treadmill data was excluded for these participants and the analysis was based on the remaining 22 participants (PCOS, n = 8; controls, n = 14). There were no significant differences in exercise time required to reach exhaustion during the incremental treadmill test (TTE), nor were there any differences in absolute or relative $\dot{V}O_{2max}$ or percentage of predicted $\dot{V}O_{2max}$ achieved between the PCOS and control women ($P \geq 0.11$, Table 2). The proportion of participants that achieved predicted $\dot{V}O_{2max}$ was also similar in both groups (PCOS 5/8 (62.5%), versus controls 12/14 (85.7%); P = 0.21). Peak RER and HR and RPE at the cessation of exercise were also similar between the groups ($P \geq 0.18$). Similarly, RPE during submaximal exercise was not significantly different between groups (Workload 1, PCOS 9.0 ± 2.2, controls 10.3 ± 1.6; P = 0.13; Workload 2, PCOS 13.9 ± 2.9, controls 13.2 ± 1.4; P = 0.55). Correlation analysis indicated relative $\dot{V}O_{2max}$ was inversely correlated with waist circumference, fasting insulin, HOMA2 and CRP (Figure 1); but not with any other parameters.

There were no differences between PCOS and control women in ImS (PCOS 133.6 ± 43.1 Nm, Controls 142.7 ± 48.2 Nm; P = 0.64) or IkS (PCOS 93.8 ± 25.4 Nm, Controls 109.9 ± 19.3 Nm; P = 0.09). When these variables were expressed relative to body weight to provide a measure of functional strength, there was still no difference between the groups (ImS, PCOS 1.49 ± 0.54 Nm/kg, controls

Table 2. Cardiorespiratory fitness variables in women with PCOS and non-PCOS controls

Variable	PCOS (n = 8)	Control (n = 14)	P-value
Time to exhaustion (minutes)	11.1 ± 1.2	11.1 ± 1.1	0.99
$\dot{V}O_{2max}$ (l/minute)	2.26 ± 0.31	2.48 ± 0.31	0.13
$\dot{V}O_{2max}$ (ml/kg/minute)	26.0 ± 4.1	25.7 ± 3.8	0.90
% predicted $\dot{V}O_{2max}$	104.4 ± 12.4	113.2 ± 10.4	0.11
RER_{peak}	1.12 ± 0.11	1.13 ± 0.06	0.85
HR_{peak} (beats/minute)	182.8 ± 8.2	177.8 ± 7.8	0.18
RPE_{peak}	16.1 ± 1.6	16.7 ± 2.2	0.50

$\dot{V}O_{2max}$, maximal aerobic capacity; RER, respiratory exchange ratio; HR, heart rate.
Values are mean ± SD. No significant differences were found between the PCOS and control participants.
% predicted $\dot{V}O_{2max}$ is measured $\dot{V}O_{2max}$ as a percentage of the predicted $\dot{V}O_{2max}$ calculated according to the method of Wasserman *et al.*[37]
Data was excluded for four participants who did not reach the criteria for $\dot{V}O_{2max}$ (PCOS = 2, control = 2).[37]

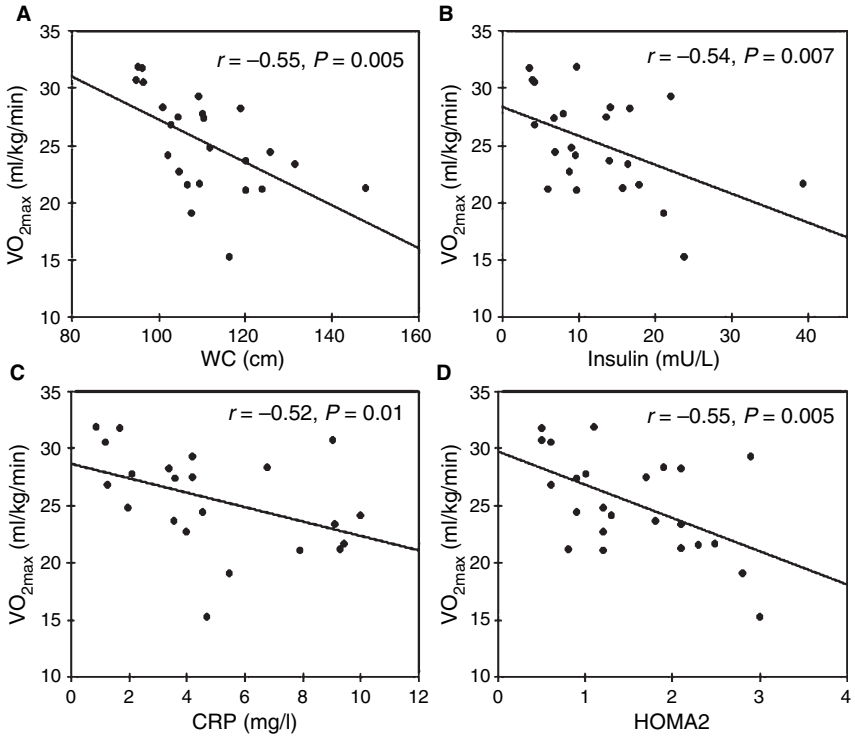

Figure 1. Relationship between cardiorespiratory fitness ($\dot{V}O_{2max}$) and (A) waist circumference (WC), (B) fasting insulin, (C) CRP and (D) HOMA2. Analysis was carried out on log-transformed data for insulin, HOMA2 and CRP.

1.50 ± 0.47 Nm/kg; $P = 0.96$; IkS, PCOS 1.04 ± 0.32, controls 1.16 ± 0.23 Nm/kg; $P = 0.32$). Absolute ImS or IkS did not correlate with any metabolic or hormonal parameters, but when expressed per unit body weight, both strength measures were inversely related to waist circumference (ImS r = −0.44, $P = 0.04$; IkS r = −0.58, $P = 0.004$) and ImS was inversely related to CRP (r = −0.45, $P = 0.04$). After controlling for waist circumference and surrogates of insulin resistance (fasting insulin and HOMA2), the relationship between ImS and CRP did not remain.

Discussion

This study showed that in overweight and obese women, the diagnosis of PCOS was not related to aerobic exercise capacity, perceptions of exertion during aerobic exercise or muscle strength compared to age and BMI matched controls with similar surrogate measures of insulin resistance. An inverse association between $\dot{V}O_{2max}$ and insulin resistance and waist circumference and muscle strength and waist circumference was also determined.

Maximal aerobic capacity ($\dot{V}O_{2max}$) is generally considered the best indicator of the capacity to perform aerobic exercise. Our results are in agreement with two previous studies that showed no difference in $\dot{V}O_{2max}$ between young overweight women with and without PCOS, matched for age and BMI.[20,21] In contrast Orio *et al.*[22] demonstrated a markedly impaired $\dot{V}O_{2max}$ in PCOS women compared with healthy controls (17 versus 27 ml/kg/minute). While the present study sample was small, we still had sufficient power (alpha>99%, $P < 0.05$) to detect a difference in $\dot{V}O_{2max}$ between the PCOS and control groups of the same magnitude as that reported by Orio *et al.*,[22] suggesting that the lack of a difference between groups in the current study was not a result of a Type II error. Instead, given that there was an inverse relationship between $\dot{V}O_{2max}$ and insulin resistance in both the study by Orio *et al.* and in ours, suggests that the discrepancy in findings between studies could be related to differences in the level of insulin resistance in the patients studied. While insulin resistance did not differ between PCOS women and controls in the present study, in the study by Orio *et al.*,[22] the PCOS women had markedly higher fasting insulin levels (20.2 mu/l versus 14.3 mu/l) and greater insulin resistance compared to their controls. Taken together this evidence suggests that the presence of insulin resistance rather than PCOS *per se* may be a key determinate of impaired CRF in PCOS. Hence, it is possible that the divergent findings between our study and those of Orio *et al.* in terms of CRF between PCOS women and controls could be explained by differences in the degree of insulin

resistance and the presence of CVD risk factors between the experimental groups. However, two previous studies[20,21] showed no difference in $\dot{V}O_{2max}$ between PCOS and control women despite marked differences in insulin resistance, suggesting that other unidentified factors could also be involved. It is also possible that the surrogate measures of insulin resistance used (fasting insulin and HOMA2) may not have been sensitive enough to assess insulin resistance in the small groups and more sensitive measures, such as hyperinsulinemic-euglycemic clamp or insulin tolerance tests may have been more informative. Alternatively, the presence of obesity may have influenced the performance of the treadmill test[44,45] and the higher BMI in both the control and PCOS groups may have suppressed any differences that were observed in previous studies at a lower BMI.[22] Further research investigating lean women with PCOS may assist in clarifying the effect of obesity.

Consistent with our findings, several previous studies have reported an inverse association between CRF and the degree of insulin resistance in patient groups with adverse CVD risk profiles, including PCOS.[13,15,22,46] Several mechanisms have been proposed, including impairment of mitochondrial function,[22] blunted insulin-induced endothelial nitric oxide synthase activity,[47] increased autonomic sympathetic tone, decreased vagal tone and impaired baroreflex activity,[48,49] suggesting that the presence of insulin resistance and hyperinsulinaemia may be central to the presence of cardiorespiratory impairment. Although insulin resistance and metabolic abnormalities are common in PCOS women, prevalent in 40–70%,[50,51] they are not universally present.[52] It has previously been shown that PCOS is a heterogeneous disorder with varying phenotypes that may present with diverse metabolic profiles and risk of CVD.[53,54] In the current study, the $\dot{V}O_{2max}$ values achieved and the CVD risk profiles of the women with and without PCOS were similar and relatively normal.[55,56] In particular, the degree of insulin resistance was not considered high,[57] suggesting that our PCOS participants with a normoinsulinemic phenotype may not have any greater CVD risk. Hence, further studies are required that directly compare CRF and CVD risk in normoinsulinemic and hyperinsulinemic women with PCOS to better understand the interrelationships between insulin resistance and CRF in this patient group.

As there was no difference in $\dot{V}O_{2max}$ between PCOS women and controls in the present study and a direct relationship has been previously established between RPE and $\dot{V}O_{2max}$[58] that was also present in our results (data not shown), it was not unexpected that endurance exercise performance (i.e. TTE during treadmill exercise) and the perception of effort during exercise did not differ between the groups. This suggests that the presence of PCOS does not necessarily impact negatively on perceived effort or fatigability, which could alter the tolerance or ability to sustain, aerobic exercise. Previous studies have demonstrated that endurance exercise training in PCOS women is effective for increasing exercise capacity and has a beneficial effect on many metabolic risk factors.[59,60] However, studies are still required to evaluate the perception, tolerance and effectiveness to a regular exercise programme in women with PCOS with varying degrees of insulin resistance compared to healthy controls.

In the present study, CRP negatively correlated with $\dot{V}O_{2max}$. This is consistent with a number of previous studies[61–63] including in women with PCOS.[64] CRP, an inflammatory molecule directly implicated in the atherosclerotic process, has been identified as an independent predictor of future cardiac events[65,66] and is modifiable in PCOS women through aerobic exercise training.[59,67] This suggests that apart from improving aerobic fitness, regular exercise might also be useful for preventing the development of vascular inflammation and subsequent atherosclerosis in women with PCOS through reductions in CRP.

Distinct from previous studies, we also assessed the effects of PCOS on muscle strength. We found muscle strength was similar in women with PCOS compared to healthy controls. Previous studies have shown inverse relationships between muscular strength and insulin resistance in a number of populations, including obese sedentary women[68] and impaired muscle strength in patients with metabolic disturbances, including type 2 diabetes.[23,29] Obesity and impaired physical functioning are associated with low-grade systemic inflammation,[69,70] which may explain the observed relationships between muscle strength and waist circumference and CRP. Hence, in the present study, it is possible that the similar insulin resistance, metabolic and inflammatory profiles between the PCOS and control women could explain the lack of any difference in muscle strength between the groups. Further investigation should be undertaken in PCOS women with high levels of insulin resistance and metabolic disturbances. Previous studies have also shown that testosterone replacement in men improves muscle strength without exercise training.[71,72] However, since no difference in muscle strength between groups was observed and strength was not associated with hormonal variables suggests that hyperandrogenism in PCOS is not an influential factor.

Muscle strength is an important marker of exercise tolerance[25] and has been associated with disability and self-reported function difficulties in obese women.[73] This highlights the importance of this physical domain in the functional ability to undertake everyday activities, including physical exercise. As muscle strength was not affected by the presence of PCOS, it suggests that women with PCOS compared to healthy controls with similar insulin resistance do not appear to experience functional limitations that would

limit their ability to maintain an active lifestyle. This is supported by a previous study that reported no difference in free-living physical activity levels between PCOS and non-PCOS women, [74] suggesting that PCOS may not alter participation in physical activity and active daily living tasks.

In conclusion, in the overweight and obese women studied, PCOS status did not adversely affect CRF, muscle strength or exercise tolerance compared to age- and weight-matched controls that showed similar insulin resistance and metabolic profiles. These results suggest that the presence of PCOS itself is unlikely to limit an individual's ability to participate in active daily living tasks or tolerate physical exercise that is considered a cornerstone in the management of PCOS. However, the fact that $\dot{V}O_{2max}$ and muscle strength correlated inversely with markers of insulin resistance suggests that physical capacity may be linked to insulin resistance and that PCOS women with more insulin resistance than controls (as is commonly observed), may have impaired CRF and muscle strength that may impact tolerance to exercise; although this could not be determined in the present study. Further research is required to confirm these findings in PCOS women with greater levels of insulin resistance and to assess CRF and muscle strength in lean and normal weight women with PCOS. Based on the current level of evidence and existence of metabolically diverse PCOS phenotypes, unequivocal conclusions regarding the effects of PCOS on CRF and muscle strength and subsequent effects on exercise tolerance and CVD risk cannot be made.

Disclosure of interests

RT, JB, LM, PC, RN and GB have nothing to disclose. MN has received lecture fees from Meat and Livestock Australia.

Contribution to authorship

RT was responsible for the analysis and interpretation of data and drafting of the manuscript. GB was responsible for the conception and design of the study, acquisition of data and contributed to the analysis and interpretation of data and the writing of the manuscript. JB, LM, MN, PC, and RN contributed to the design of the study, interpretation of the data and drafting of the manuscript. Each author revised critically the manuscript and provided final approval of the version to be published.

Details of ethics approval

All women provided written informed consent and the study protocols and procedures were approved by the Human Ethics Committee of the Commonwealth Scientific Industrial Research Organisation (Ref No. 03/09).

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