

EFFECT OF HIIT AND MICT ON CARDIOVASCULAR INDICES IN WOMEN WITH PCOS

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Abstract

Polycystic ovary syndrome is one of the most prevalent endocrine dysfunction affecting women in their reproductive age. Women with PCOS are at a higher risk of cardiovascular complications due to central adiposity, dyslipidemia, insulin resistance and alterations in cardiovascular autonomic function. Exercise Interventions such as High and Moderate intensity training can help in enhancing cardiovascular health and effectively mitigating the metabolic and vascular dysfunction seen in PCOS. An extensive Literature search was performed through five databases namely PubMed, Scopus, Cochrane Library, Science direct and PeDro (from 2010 to 2024) using the appropriate keywords. Study selection followed the PRISMA flow diagram, and data extraction and quality assessment were performed independently by two authors. The Cochrane Risk of Bias tool was used for evaluating risk of bias for RCTs, PeDro and Newcastle-Ottawa Scale were used for quality assessment of RCTs and Non-RCTs respectively. This review included nine studies. Cohen's d and Hedges' g were used in order to calculate effect size of all the outcome measures. Results indicated that VO₂ max was considerably increased by both interventions, with HIIT being more effective in improving the maximal aerobic capacity. In contrast, MICT was more effective in enhancing endothelial function which was measured by Flow-mediated dilation. The study concluded that MICT efficiently improves vascular function whereas HIIT seems to offer more advantages in improving maximal aerobic capacity. More research in this field is needed to determine the best exercise strategy for enhancing cardiovascular health in PCOS women.

Keywords: Cardiovascular health; Heart Rate Variability; High-Intensity Interval Training; Moderate-Intensity Continuous Training; Polycystic ovary syndrome; VO₂ max

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List of Abbreviations

AE: *GC-Aerobic Exercise: Group Counselling*
GC: *AE-Group counselling: Aerobic exercise*
CAD - Coronary Artery Disease
CG - Control Group
COM - Combined (Resistance and Endurance Training)
CIMT - Carotid Intima-Media Thickness
CVDs - Cardiovascular Diseases
ES - Effect Size
FMD - Flow Mediated Dilation
HF - High Frequency
HIIT - High-Intensity Interval Training
HV-HIIT - High Volume HIIT
HRV - Heart Rate Variability
LF - Low Frequency
LV-HIIT - Low Volume HIIT
MAV - Maximal Aerobic Velocity
MICT - Moderate-Intensity Continuous Training
MISS - Moderate-Intensity Steady State Exercise
PCOS - Polycystic Ovarian Syndrome
RCT - Randomized Control Trial
ST - Strength Training Group

Introduction

Around 13% of women are affected by PCOS in their reproductive age and experience clinical symptoms like menstrual dysfunction, infertility, hirsutism, acne, and obesity (Bozdag *et al.*, 2016; Asghari *et al.*, 2022). The increased prevalence of PCOS amongst women is concerning as it leads to impaired insulin sensitivity, weight gain, and alteration in cardiovascular autonomic function, which can lead to an increased susceptibility to type 2 diabetes and CVDs (Philbois *et al.*, 2022).

Regular physical activity can be considered a preventative therapeutic intervention that can reduce the risk of comorbidities of PCOS (Norman *et al.*, 2007; Fauser *et al.*, 2011; Teede *et al.*, 2018). As per the 2020 guidelines, WHO recommends that adults should engage in 150 - 300 minutes of moderate physical activity or 75 to 150 minutes of intense aerobic activity weekly. (Bull *et al.*, 2020). HIIT combines short bursts of activities at a very high intensity followed by low-intensity activities or periods of rest (MacInnis & Gibala, 2016).

In exercise training prescription, moderate-intensity exercise is typically defined as endurance training - also known as moderate-intensity continuous training (MICT) - that is characterized by exercising at a moderate intensity for a prolonged duration (Binder *et al.*, 2008; Hofmann & Tschakert, 2017; Iannetta *et al.*, 2019). Both types of exercise modalities have been shown to enhance

cardiovascular health but through different kinds of mechanisms.

Some cardiovascular and metabolic parameters including insulin resistance, dyslipidemia, hypertension, and BMI have been studied deeply in PCOS but extensive research has not been conducted on some cardiovascular indices such as Heart rate variability, Carotid Intima-Media Thickness, Flow Mediated Dilation. Most of the evidence about the benefits of HIIT and MICT concerning cardiovascular health comes from studies in the general population and not in PCOS women. Hence, this systematic review aims to compile available research on the effects of HIIT versus MICT program on cardiovascular indices in PCOS women.

Methodology

1. Protocol and registration

The protocol for this systematic review was registered with PROSPERO in November 2024 (CRD42024616091) and it was conducted and reported in compliance with the PRISMA guidelines.

2. Study eligibility criteria

To optimize the search process effectively, eligibility criteria for the study were formulated according to the PICOS design (Population, Intervention, Comparison, Outcomes, and Study Design).

1. **Population:** Women aged 18-45 years old diagnosed with PCOS, based on recognized criteria (e.g., Rotterdam, NIH, AES). Studies with non-PCOS populations, or other metabolic/endocrine disorders were excluded.

2. **Intervention:** Studies utilizing HIIT or MICT, or both, and the details of the exercise protocol were clearly described (namely the frequency, duration, and intensity). Any trial that did not involve HIIT or MICT as the main form of exercise was excluded from this analysis.

3. **Comparison:** Studies that compared HIIT and MICT with each other, against control groups (e.g., no exercise) and other types of exercise like strength training, resistance training, or combined exercise training programs.

4. **Outcomes:** Studies assessing at least one cardiovascular outcome-HRV, FMD, CIMT, or VO₂ max-were included. Studies that didn't measure at least one of these parameters were excluded.

5. **Study Design:** Randomized control trials, clinical trials, pilot studies and observational studies including, cohort and case control studies.

6. Only English language studies were considered in this review.

3. Search Strategy

The search for articles was conducted in October 2024 across five databases: PubMed, SCOPUS, Science Direct, PeDro, Cochrane Library, whereby the search was limited to English-language publications and articles published between the years 2010 and 2024. The search strategy involved the use of keywords such as Polycystic ovary syndrome, Moderate-Intensity Continuous Training, High-Intensity Interval Training, Heart Rate Variability, Cardiovascular health, VO₂ max), Medical Subject Headings (MeSH terms), TIAB terms, and combinations of (MeSH) terms and TIAB terms. The Boolean operators 'OR' and 'AND' were used. The search strategy is listed in the Supplementary material.

4. Study Selection

The flow diagram of PRISMA shows the process of identification of records along with the number of articles screened, included and rejected at each stage and the reasons for exclusion mentioned at the last stage. Databases such as PubMed, Scopus, ScienceDirect, PeDro, and the Cochrane Library were used to obtain relevant articles, which were then imported into Mendeley for deduplication. Potentially relevant articles were first identified based on title and abstract screening, following which the remaining articles full texts were retrieved, and their eligibility was evaluated. In accordance with PRISMA, the flowchart illustrating the search strategy is presented in Figure 1.

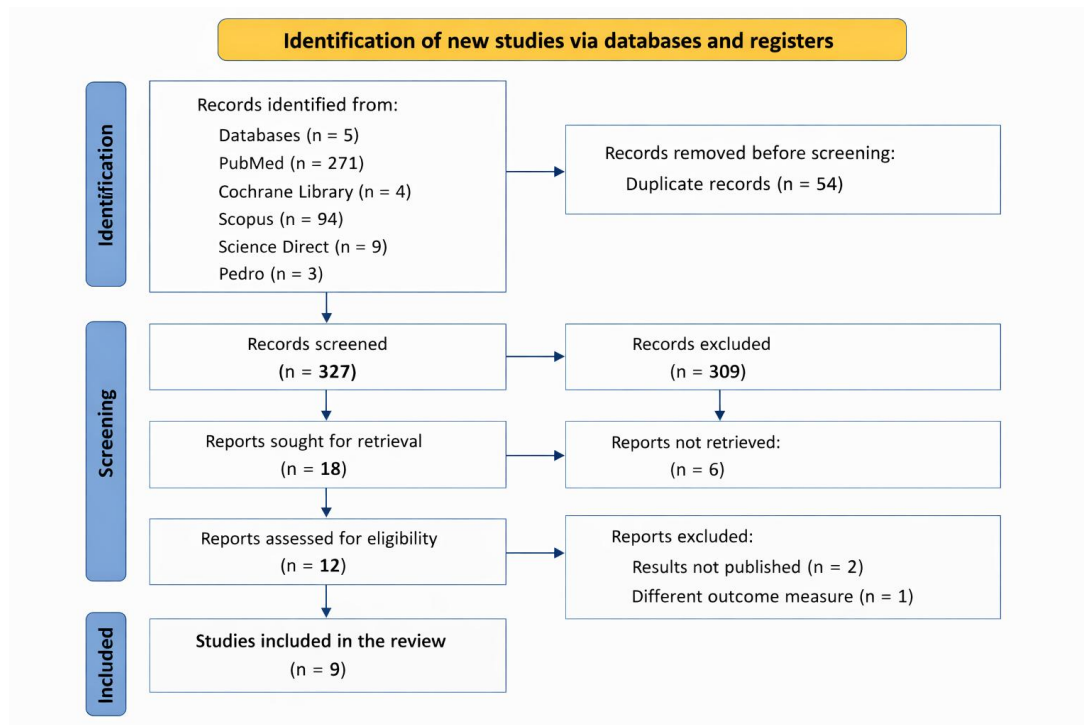


Figure 1. shows Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram

5. Methodological Quality Evaluation and Risk of bias

PeDro scale, which stands for Physiotherapy Evidence Database was used to assess the quality of the included RCTs. Two researchers (VS and AR) independently rated all the studies, excluding the criterion related to eligibility specification. Each criterion was scored as either “yes” (1) or “no” (0), resulting in a total score out of 10. According to the scoring, studies were graded as poor (<4), fair (4-5), good (6-8), or excellent (>8). Quality scoring for RCTs is presented in Table 1.

For a two-center RCT, case-control study, and another non-randomized controlled trial, the Newcastle-Ottawa Quality Assessment Scale (NOS) was used which focuses on the domains namely selection, comparability, and exposure or outcome for case-control and cohort studies respectively. Two versions of NOS were used for a cohort and a case-control study and are given in Table 2. Scores range from 0 to 9 stars, with 7 or higher considered high quality and below 7 low qualities.

VS and AR evaluated the risk of bias in Randomized Controlled Trials (RCTs) using the Cochrane Collaboration's Risk of Bias 2.0 tool and it is shown in Figure 2. It has five aspects; Bias

arising from the randomization process, Bias due to deviations from intended interventions, Bias due to missing outcome data, Bias in measurement of the outcome, and Bias in the selection of the reported result. Each domain was characterized as having either: low risk, some concerns and low risk of bias, high risk of bias (Sterne *et al.*, 2019; McGuinness & Higgins, 2020).

6. Data collection process-

6.1 Data Items and Extraction: Data extraction was done according to the PICO criteria. Participant characteristics including (sample size, age range, and mean), diagnostic criteria used to identify individuals with PCOS, exercise intervention type, control/comparator group details, interventional group details, outcomes (VO₂ max, flow-mediated dilation, heart rate variability and carotid intima-media thickness), and study characteristics (author, study design, year, program duration, data collection details) were extracted and are summarized in Table 3. VS and AR, two independent researchers extracted the data. Cohen's d and hedge's g were used to determine the effect sizes of all outcome measures. The effect size was defined as small (ES = 0.2), moderate (ES = 0.5), and large (ES = ≥ 0.8).

Table 1. shows Quality Assessment of included RCTs using PeDro scale

Study	References							
	Roessler <i>et al.</i> (2013)	Almenning <i>et al.</i> (2015)	Philbois <i>et al.</i> (2022)	Kiel <i>et al.</i> (2022a)	Kiel <i>et al.</i> (2022b)	Patten <i>et al.</i> (2022)	Nasiri <i>et al.</i> (2022)	Mohammadi <i>et al.</i> (2023)
Eligibility Criteria	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Random Allocation	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Concealed Allocation	No	No	Yes	Yes	No	No	Yes	Yes
Group Similarity at Baseline	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Blinding of Subjects	No	No	No	No	No	No	No	No
Blinding of Therapist	No	No	No	No	No	No	No	No
Blinding of Assessor	No	No	No	Yes	Yes	No	No	No
Adequate Follow-up	No	No	No	Yes	Yes	No	Yes	Yes
Intention to Treat Analysis	No	No	No	Yes	Yes	Yes	Yes	No
Between-group Difference Reported	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Point Estimate and Variability Reported	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Total Score	4/10	4/10	5/10	8/10	7/10	5/10	6/10	6/10
Quality	Fair	Fair	Fair	Good	Good	Fair	Good	Good

Table 2. shows NOS Quality assessment tool for included cohort and case-control studies

NOS Domain	Criteria	Score
Newcastle-Ottawa Assessment Scale (NOS for cohort studies) Sprung <i>et al.</i> (2013)		
Selection	1. Representativeness of the exposed cohort	1
	2. Selection of the non-exposed cohort	1
	3. Ascertainment of exposure	1
	4. Demonstration that outcome was not present at start	1
Comparability	1. Comparability of cohorts on the basis of the design or analysis	1
Outcome	1. Assessment of outcome	1
	2. Was follow-up long enough for outcomes to occur?	1
	3. Adequacy of follow-up of cohorts	1
Total Score		8/9
Newcastle-Ottawa Assessment Scale (NOS for case control studies) Kiel <i>et al.</i> (2022b)		
Selection	1. Case definition: Yes, with independent validation (clear definition of PCOS in women)	1
	2. Representativeness of the cases: Potential for selection biases, not described as consecutive	1
	3. Selection of Controls: Hospital controls (controls from clinics)	1
	4. Definition of Controls: No history of disease (controls without cardiovascular disease)	1
Comparability	1. Comparability of cases and controls: Controls for age and BMI	1
Exposure	1. Ascertainment of exposure: Structured interview, blind to case/control status	1
	2. Same method of ascertainment for cases and controls: Yes	1
	3. Non-response rate: Same rate for both groups, no dropouts mentioned	1
Total Score		8/9

Table 3. shows Sample and study characteristics

Author (Year)	Sample size	Study design	Age (Range and mean)	PCOS criteria used	Duration of exercise program	Intervention	Data collection	Outcomes	Intervention group	Control group/Comparator group
Roessler <i>et al.</i> (2013)	n=17(AE:GC=8, GC:AE=9)	Cross-over RCT	19- 46 years (mean 31.6 years)	Rotterdam criteria	8 weeks	High-intensity aerobic exercise	Pre-, cross-over, and post-intervention	VO ₂ max	High-intensity aerobic exercise (ramp-up period of two weeks)	Group counselling
Sprung <i>et al.</i> (2013)	n=17 (Exercise = 10, Conventional care = 7)	Non-RC	25-31 years (mean 28 years)	Rotterdam criteria	16 weeks	Moderate-intensity exercise training	Pre- and post-intervention	Flow-mediated dilation, VO ₂ max	Moderate-intensity aerobic exercise	Lifestyle advice
Almenning <i>et al.</i> (2015)	n=31 (HIIT = 10, ST = 11, CG = 10)	Three-arm parallel pilot RCT	21.7-32.7 years (mean 27.2 years)	Rotterdam criteria	10 weeks	High-intensity interval training, Strength training	Pre- and post-intervention	Flow-mediated dilation, VO ₂ max	High-intensity interval training, Strength training (both had 3 sessions per week for 16 weeks)	≥150 minutes of weekly moderate-intensity exercise
Philbois <i>et al.</i> (2022)	n=75 (HIIT = 25, MICT = 25, CG = 25)	RCT	18-39 years (mean not given)	Rotterdam criteria	16 weeks	MICT, HIIT	Pre- and post-intervention	HRV, VO ₂ max	High-intensity interval training, Moderate-intensity continuous training (both had 3 sessions per week for 16 weeks)	No exercise training
Kiel <i>et al.</i> (2022b)	n=79 (PCOS-HIIT = 41, PCOS non-ex = 23, Non-PCOS-HIIT = 15)	Two-center RCT and case-control study	PCOS: 25-35 years (mean 30 years), Non-PCOS: 25-37 years (mean 31 years)	Rotterdam criteria	16 weeks	LV-HIIT, HV-HIIT	Pre- and post-intervention	CIMT, FMD	LV-HIIT, HV-HIIT (three weekly sessions for 16 weeks)	Habitual daily physical activity and diet
Kiel <i>et al.</i> (2022a)	n=64 (HV-HIIT n=20, LV-HIIT n=21, CG=23)	Two-center RCT	CG: 23.0 to 33.6 (mean 28.3 years) LV-HIIT: 25.4 to 35.4 (mean 30.4 years) HV-HIIT: 25.2 to 35.0 (mean 30.1 years)	Rotterdam criteria	16 weeks	HIIT	Pre-post intervention, 12-month follow-up	VO ₂ max	LV-HIIT, HV-HIIT	≥150 mins/week of moderate-intensity physical activity or 75 minutes rigorous physical activity.
Patten <i>et al.</i> (2022)	n=29 (MICT=14, HIIT=15)	Two-armed RCT	HIIT: 24.9 to 34.5 (mean 29.7 years) MICT: 26.3 to 38.7 (mean 32.5 years)	Rotterdam criteria	12 weeks	HIIT, MICT	Pre- and post-intervention	Aerobic capacity (VO ₂ peak)	MICT/HIIT (three times per week for 12 weeks)	MICT(60–75% peak heart rate)
Nasiri <i>et al.</i> (2022)	n=45 (HIIT=15, COM=15, CG=15)	Randomized controlled clinical trial	CG: 18.0 to 28.2 years (mean 23.1 years) COM: 18.7 to 30.1 years (mean 24.4 years) HIIT: 19.5 to 30.3 years (mean 24.9 years)	Rotterdam criteria	08 weeks	High-intensity interval training, combined (resistant and endurance) training	Pre- and post-intervention	VO ₂ max	HIIT (combined resistant and endurance training)	≥150 minutes of weekly moderate-intensity exercise
Mohmmandi <i>et al.</i> (2023)	n=28 (HIIT=14, CG=14)	RCT	18.5 to 29.1 years (mean 23.8 years)	Rotterdam criteria	08 weeks	HIIT	Pre- and post-intervention	VO ₂ max	HIIT (three weekly sessions for 08 weeks)	No exercise training

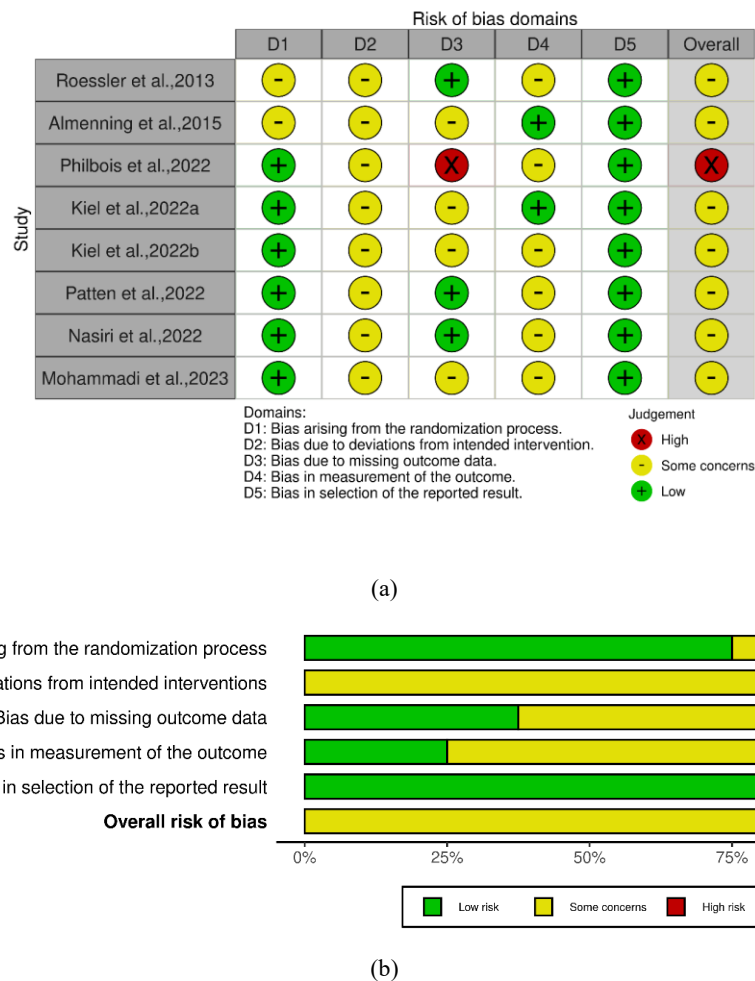


Figure 2. (a) shows Risk of Bias assessment of included RCTs using Cochrane RoB 2 tool, presented via a traffic light plot and (b) shows Weighted plot showing the distribution of overall risk of bias across each study

Results

1. Study selection

The database search identified a total of 381 articles. After the removal of 54 duplicates, 327 articles were screened for further stages. Out of these, 309 articles were excluded while screening through title and abstract. Following which full text of the remaining 18 articles was sought, of which 6 could not be accessed due to full text being unavailable. Out of the 12 articles evaluated for eligibility, 3 were excluded: 2 for results not published and 1 for using a different outcome measure. This review included nine studies in total (Figure 1).

2. Sample and study characteristics-

Nine studies were included in this systematic review. Among these, two were published in 2013,

one in 2015, five studies in 2022, and one in 2023. The participants' mean age was between 23.1 to 32.5 years and the sample size varied from $n=17$ to $n=79$. Rotterdam consensus criteria were used as a means of diagnosing PCOS in all the included studies. In terms of comparisons, One study included comparison between HIIT and MICT, while another compared HIIT with both MICT and a control group (CG). Two studies compared HIIT to a control group, and one study compared MICT to a control group. Additionally, one study examined the differences between HIIT and strength training (ST) along with a control group, while another compared HIIT to combined training (COM) and a control group. Furthermore, one study examined low-volume HIIT (LV-HIIT) versus high-volume HIIT (HV-HIIT) alongside a control group, and one study compared PCOS-HIIT with Non-PCOS-HIIT and PCOS non-exercise (Non-ex). The intervention

period for these studies ranged from eight to sixteen weeks. Sample and study characteristics are summarized in Table 4.

3. Methodological quality

Out of Nine studies, four were rated as good quality (score 6 -8) and four as fair quality (score 4-5) according to the PeDro scale. Two studies scored 4 out of 10, two scored 5, two received 6, one received 7, and one received 8 out of 10 points (Table 2).

The risk of bias assessment was done for eight studies. Seven of them were rated as having some concerns regarding the overall risk of bias, while one was identified with high risk of bias. All studies were rated as having some concerns in the “Bias due to deviations from intended interventions” category, but exhibited a low risk in the Bias in selection of the reported results “category”. The risk of bias evaluation can be visualized in Figure 2.

4. Overview of Results: The result findings are shown in Table 4.

4.1 Effect of Exercise Interventions On Cardiovascular Outcomes:

- **VO₂ max:** Eight studies evaluated VO₂ max and employed different training specifics. One study employed indirect calorimetry, while two employed bicycle ergometers, four employed treadmill ergometers, and one used direct analysis of expired gases. In comparing HIIT with Other exercise groups such as MICT and CG, these studies revealed that HIIT at 90-100% HRpeak or MAV benefitted VO₂ max in appreciable ways. The effect size for VO₂ max ranged from moderate to large and included $g = 0.82$ (HIIT vs MICT), $g = 0.52$ (low-volume HIIT vs CG and) $g = 1.26$ (high-volume HIIT vs CG), indicating substantial improvements in aerobic capacity due to high-intensity exercise (Table 4).

Table 4. shows Overview of results

Study Author	Sprung <i>et al.</i> (2013)	Roessler <i>et al.</i> (2013)	Patten <i>et al.</i> (2022)	Nasiri <i>et al.</i> (2022)
Program Characteristics	Exercise, CC	AE:GC, GC:AE	HIIT, MICT	HIIT, COM, CG
Frequency	3 times per week initially progressed to 5 times per week	3 days per week	3 days per week	3 days per week
Intensity	Moderate (30% Heart Rate Reserve initially progressed to 60% Heart Rate Reserve at week 12	Moderate (first 2 weeks)	Moderate (30% Heart Rate Reserve initially progressed to 60% Heart Rate Reserve at week 12	Moderate (first 2 weeks)
Time	30 minutes till week 11,45 mins from week 12 onwards	Ramp-up period (first 2 weeks): Cycling: 30 mins, Walking/Running: 25 minutes, Week 3-8: Cycling: 60 mins, Walking/Running: 45 minutes	MICT-45 mins HIIT-variable duration for each session	Variable duration for each session for both groups.
Duration	16 weeks	8 weeks	12 weeks	08 weeks
Type	Aerobic exercise	High intensity Aerobic activities - indoor cycling and outdoor brisk walking/running	Stationary cycle ergometer	combined aerobic (endurance) and resistance (strength) training, HIIT
Cardiovascular Outcome measures	Vo2 max FMD (in percentage)	VO ₂ max	VO ₂ max	VO ₂ max
Measurement of the outcomes	treadmill ergometer, high-resolution ultrasound machine	Monark ergometer 818E testing cycle	incremental maximal graded exercise test conducted on a cycle ergometer.	Treadmill
Effect Size Of Outcome Measures (using Hedges' g or Cohen's d)	VO ₂ max($g^a=4.55$) FMD($g^a=2.85$)	$g^a=3.10$	$g^a=0.82$	ES(b/w HIIT,COM group) $g^a=1.08$.

• **Flow-Mediated Dilation:** Three studies assessed flow-mediated dilation (FMD). Two studies employed high-resolution ultrasonography, while one used a 12-MHz ultrasonic Doppler probe. In the study by Sprung *et al.* (2013), a moderate-intensity aerobic exercise program was conducted

over sixteen weeks. The intervention initially consisted of three sessions per week and was gradually increased to five sessions per week by the twelfth week. The effect size ($g = 2.85$) was large, indicating that moderate-intensity aerobic exercise significantly improved vascular function (Table 4).

Table 4. shows Overview of results (continued)

Study Author	Mohammadi <i>et al.</i> (2023)	Kiel <i>et al.</i> (2022a)	Kiel <i>et al.</i> (2022b)	Philbois <i>et al.</i> (2022)	Almenning <i>et al.</i> (2015)
Program Characteristics	HIIT, CG	LV-HIIT, HV-HIIT, CG	PCOS HIIT(LV+HV), Non PCOS-HIIT (LV+HV), PCOS non -ex	HIIT, MICT, CG	HIT, ST, CG
Frequency	3 days per week	3 days per week	3 days per week	3 days per week	3 days per week
Intensity	High intensity during interval sprints at 100% MAV, recovery at 50% MAV.	LV-HIIT=Maximal intensity HV-HIIT=90%-95% HRmax	HV-HIIT: 90-95% HRmax; LV-HIIT: Maximal intensity they can sustain	MICT=50-65% (warm-up), 70-80% (main), 40-50% (cool-down) HIIT=50-65% (warm-up), 85-90% (work), 65-70% (recovery), 40-50% (cool-down)	HIT= 90-95% HRmax (4x4 mins), Max intensity (1 min) ST= 75% of 1RM (resistance exercises)
Time	30-40 minutes	LV-HIIT = 29 minutes HV-HIIT = 35 minutes	HV-HIIT = 41 minutes LV-HIIT = 33 minutes	MICT=60 min HIIT=35-45 min	HIT=25,19 mins ST=30 mins
Duration	08 weeks	16 weeks	16 weeks	16 weeks	10 weeks
Type	Interval running on treadmill	Treadmill running or walking	Treadmill walking/running	Aerobic exercise (Treadmill)	HIT=Treadmill, running, or cycling ST= Dynamic strength exercises (resistance training)
Cardiovascular Outcome measures	VO ₂ max	VO ₂ max	CIMT(in mm),FMD(in %)	HRV, VO ₂ max	FMD(in %), VO ₂ max
Measurement of the outcomes	Multistage Fitness Test (MSFT) on a treadmill.	Indirect calorimetry	high-resolution B-mode ultrasound machine.	VO ₂ max-submaximal exercise test conducted on a treadmill HRV-RR intervals (RRi) from ECG records.	12-MHz ultrasound Doppler Probe, direct analyses of expired gas (Oxycon Pro)
Effect Size Of Outcome Measures (using Hedges' g or Cohen's d)	$g^a=2.22$	ES(b/w LV-HIIT,CG) $g^a=0.52$ ES b/w(HV-HIIT,CG) $g^a=1.26$	CIMT-ES(b/w PCOS-HIIT,PCOS-non ex) $g^a=0.072$ ES(b/w PCOS-HIIT,Non-PCOS HIIT) $g^a=0.37$ FMD-appt.data to calculate ES not given.	VO ₂ max ES(b/w HIIT,CG) $d^b=0.97$ ES (b/w MICT,CG) $d^b=0.77$ HRV-ES(b/w HIIT ,CG) RR Interval (RRi)($d^b=0.3$) 2UV% ($d^b=0.48$) ES(b/w MICT,CG) RR Interval(RRi) ($d^b= 0.42$) 2UV%($d^b=0.48$)	VO ₂ max ES(HIT,CG) $g^a=0.89$ ES(ST,CG) $g^a=0.54$ FMD-ES(b/w HIT,CG) $g^a=0.57$ ES(b/w ST,CG) $g^a=0.77$

Almenning *et al.* (2015), examined the benefits of both high-intensity and strength training by a 10-week comparison of HIIT, ST, CG. In comparison with the control group, the HIIT group had a large effect size for the improvement of FMD, $g = 0.89$. Strength training performed for 30 minutes at 75% of 1 RM produced a moderately significant effect size for FMD when compared to the control group ($g = 0.54$). The computation of effect size was not done for the study by Kiel *et al.* (2022b), since the necessary data was lacking (Table 4).

- **Heart Rate Variability:** HRV was assessed in one study using RR intervals obtained from ECG records. Philbois *et al.* (2022) evaluated the implication of 16-week HIIT and MICT programs on HRV. Each of these exercise programs took place thrice a week on the treadmill. The MICT sessions were one hour long; intensity was set up in increasing order. The HIIT sessions lasted 35-45 minutes, including warm-up (50-65% HR_{max}), work intervals (85-90% HR_{max}), recovery (65-70% HR_{max}), and cool-down (40-50% HR_{max}) (Rissanen *et al.*, 2016). In terms of the RR interval (RRi), both HIIT and MICT groups exhibited a small effect size when compared to the control group ($d = 0.3$ and $d = 0.42$) respectively, which indicates that both moderate and high-intensity training regimens led to small improvements in HRV. Additionally, both training regimens demonstrated small to medium effect sizes ($d = 0.48$ each) in comparison to CG for the HRV measure (2UV%), indicating that both aerobic training approaches improved autonomic regulation to a similar degree (Table 4).

- **Carotid Intima-Media Thickness:** In a study done by Kiel *et al.* (2022b), CIMT was assessed by High-resolution B-mode ultrasonography. Participants were split into groups based on their PCOS status and then given either High Volume HIIT at 90-95% of their HR_{max}, Low Volume HIIT at their maximal sustainable effort, or no exercise, for 16 weeks. Sessions took place on a treadmill three times a week. The small ES value of 0.072, when comparing CIMT outcomes between the PCOS-HIIT and the PCOS non-exercise groups implies that HIIT had minimal effect on CIMT in women with PCOS compared to their sedentary counterparts. This infers that HIIT may not significantly impact CIMT in this population. A small to moderate effect size ($ES = 0.37$), suggested a more favorable response in non-PCOS participants when comparing CIMT across PCOS-HIIT and non-PCOS HIIT groups. (Table 4).

Discussion

This systematic review examined the effect of HIIT and MICT on cardiovascular indices in women with PCOS, using nine previously published studies. While many studies have explored the effects of exercise interventions on metabolic and reproductive outcomes in women with PCOS, there is a significant lack of research focusing on effect of physical activity on cardiovascular indices such as VO₂ max, flow-mediated dilation, carotid intima-media thickness, and heart rate variability. Given the increased long-term cardiovascular risk in this population due to underlying metabolic and hormonal abnormalities, understanding how specific exercise interventions influence cardiovascular structure and autonomic function is essential for effective risk reduction. To our knowledge, this systematic review is the first that attempts to evaluate the effects of HIIT and MICT on cardiovascular indices among PCOS women aged between 18-45 years.

The key findings from this review are: (i) High-intensity interval training significantly increases VO₂ max; (ii) Moderate-intensity aerobic exercise enhances FMD; (iii) Both HIIT and MICT have similar, mild effects on HRV; (iv) Neither HIIT nor MICT training led to significant changes in CIMT.

1. EFFECT OF HIIT, MICT, ST AND COM INTERVENTION ON VO₂ max:

According to Kodama *et al.* (2009), a 15% reduction in the risk of CVD-related mortality can be achieved by increasing VO₂ max by 1 MET which is equivalent to 3.5 ml per kg per min. Low levels of VO₂ max can be due to cardiac dysfunction and impaired exercise cardiac output or higher concentration of inflammatory markers and excessive visceral fat (Giallauria *et al.*, 2009; Rissanen *et al.*, 2016).

In our analysis, while post-intervention VO₂ max was higher than baseline in both high and moderate intensity protocols, Patten *et al.* (2022) showed that the improvement of VO₂ max in HIIT group was superior as compared to the MICT group. This result contradicts the works of Richards *et al.* (2021) who reported an increment in the VO₂ max following the MISS(Moderate- intensity steady state) interventions, the potential cause for which can be the enhanced volume and density of mitochondria following MISS exercise which subsequently results in increased mitochondria respiratory capacity and from the fact that higher mitochondrial oxidative capacity has a direct link with improvements in VO₂ max (Holloszy & Coyle, 1984; Van Der Zwaard *et al.*, 2016).

We found that HIIT proved to be superior in enhancing VO_2 max when compared with other types of training programs, such as strength training or combined training, by observing the effect sizes in studies by Nasiri *et al.* (2022) and Kiel *et al.* (2022a). Additionally, these studies had similar frequencies, durations (8-10 weeks), and intensities for the strength program (70-75%), which, when combined with recent data showing that endurance training with moderate intensity reduces cardio-metabolic risk factors in PCOS, supports the effectiveness and superiority of HIIT in enhancing VO_2 peak in PCOS individuals. Our findings suggest that optimal FITT for VO_2 max improvement in PCOS may involve exercising 3-4 days per week at a high-intensity ($\geq 85\%$ max HR), with 20-30-minute sessions of aerobic activities (e.g., cycling, running) following HIIT protocols.

2. EFFECT OF LOW AND HIGH VOLUME HIIT, STRENGTH TRAINING AND MICT ON FMD:

Endothelial dysfunction is an early marker of atherosclerosis when there is no structural abnormality or clinical symptoms, often seen in women with PCOS (Sprung *et al.*, 2013). Nitric oxide influences the FMD response seen in conduit vessels (Doshi *et al.*, 2001), and exercise training reduces oxygen free radicals while upregulating endothelial NO synthase in CAD patients (Hambrecht *et al.*, 2003).

MICT was found to have a notable impact on FMD (Sprung *et al.*, 2013) with a large effect size, while HIIT intervention yielded better improvement in FMD than the Control group (Kiel *et al.*, 2022b). This may be explained by the fact that MICT (moderate-intensity continuous training) provides a more consistent and sustained stimulus on the cardiovascular system resulting in enhanced improvement in dilation of the blood vessels.

Consequently, according to the findings outlined above, MICT is the exercise modality of choice for increasing FMD. This aligns with the findings of the study carried out by Sprung *et al.* (2013) which focused on a subgroup of women with PCOS who fulfilled all the diagnostic criteria, suggesting a more pronounced and severe phenotype that may impact cardiovascular outcomes.

3. EFFECT OF MICT, HIIT ON HRV AND CIMENT:

Mirzohreh *et al.* (2024) suggested that identifying low HRV as an initial sign of autonomic dysfunction helps in the prevention and management of cardiovascular complications in PCOS patients. This could help in identifying subgroups within PCOS populations that are at an

increased risk of cardiovascular complications based on HRV parameters. Yildirim *et al.* (2006) and Lee *et al.* (2010) found that women with PCOS had increased LF and LF/HF ratios, and reduced HF values which led to higher sympathetic activity and lower parasympathetic control of HRV.

In a study by Philbois and colleagues, HRV was assessed in two groups; the MICT group and the HIIT group. The study revealed that symbolic analysis had higher sensitivity in identifying alterations in cardiac autonomic regulation, seen as a rise in vagal modulation (2UV%) in both groups. Additionally, no significant difference was observed in intergroup comparison (Philbois *et al.*, 2022). The currently available literature reveals that there are few studies done on the effects of exercise interventions like HIIT and MICT on HRV women with PCOS, and since the current findings highlight that both HIIT and MICT elicit similar improvements in HRV, it cannot be inferred which intervention is superior to the other.

Calderon-Margalit *et al.* (2014) and Meyer *et al.* (2012) reported a positive association between PCOS and increased carotid intima-media thickness (CIMENT), likely due to characteristic metabolic abnormalities such as insulin resistance, dyslipidemia, and central obesity. However, most studies reviewed indicate that neither high-intensity interval training (HIIT) nor moderate-intensity continuous training (MICT) leads to significant improvements in CIMENT among women with PCOS. In contrast, research conducted in other populations points to a more favorable effect of aerobic exercise on vascular health. For example, in healthy adults, aerobic, resistance, and combined exercise regimens have been associated with CIMENT reduction, with aerobic workouts showing the most substantial benefits-likely due to their ability to lower pro-inflammatory cytokines such as tumor necrosis factor- α (TNF- α) and interleukins (Wang *et al.*, 2022).

In the context of PCOS, the absence of CIMENT improvement might be due to underlying metabolic disturbances, including persistent inflammation, insulin resistance, and abnormal lipid levels. Similarly, Kiel *et al.* (2022b) found no meaningful difference in CIMENT between women with PCOS and healthy controls after a 16-week HIIT intervention, implying that such training may have limited influence on vascular remodeling in this group. Conversely, Ghardashi-Afousi *et al.* (2020) demonstrated a significant decline in CIMENT following a 12-week HIIT regimen in individuals with type 2 diabetes, suggesting that exercise-induced vascular benefits are more apparent in populations with more pronounced cardiovascular or metabolic risk profiles.

Limitations

Several limitations should be acknowledged. The small sample sizes of the included studies may limit the generalizability of the findings to the broader PCOS population. The inclusion of both experimental and non-experimental research designs may have contributed to heterogeneity and data variability, and the overall methodological quality of the included studies was moderate. Variations in exercise parameters, such as intensity, frequency, and duration, may have resulted in differing cardiovascular outcomes, thereby complicating direct comparisons across studies. Furthermore, the absence of long-term follow-up limits the ability to assess the sustained effects of exercise interventions on cardiovascular outcomes.

Conclusion

Both high-intensity interval training (HIIT) ($\geq 85\%$ HR_{max}, 3-4 sessions/week, 20-30 minutes/session) and moderate-intensity continuous training (MICT) (50-70% HR_{max}, 3-5 sessions/week, 30-45 minutes/session) provide clinically meaningful benefits for women with PCOS. HIIT appears to be more effective in improving cardiorespiratory fitness, whereas MICT demonstrates greater enhancement of endothelial function. However, current evidence does not indicate significant effects of either modality on carotid intima-media thickness or heart rate variability. Further research is warranted to examine the impact of longer-duration exercise interventions and to establish optimal training protocols for improving structural and autonomic cardiovascular outcomes in this population.

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Competing Interests

The authors declare that they have no competing interests related to this systematic review.

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Ethical Approval

This study did not involve any research with human or animal participants conducted by the authors.

Data Availability

All data included in this study are available within the article and its supplementary materials.

Author Contributions

Vandana Sharma: Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing.

Anushree Rai: Project administration, Supervision, Visualization, Writing – review & editing.

Siddhartha Sen: Conceptualization, Formal analysis, Investigation, Resources.

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