

# Effects of three treatment modalities (diet, myoinositol or myoinositol associated with D-chiro-inositol) on clinical and body composition outcomes in women with polycystic ovary syndrome

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**Abstract. – OBJECTIVE:** To evaluate, in overweight/obese PCOS women, which of three distinct treatment modalities achieved the greatest clinical benefits in terms of clinical and body composition outcomes.

**PATIENTS AND METHODS:** Forty-three polycystic ovary syndrome (PCOS) overweight/obese patients were randomly treated for 6 months with: only diet (Group 1, n = 21); diet and myo-inositol (MI) 4 g + folic acid 400 µg daily (group 2, n = 10); diet in association with MI 1.1 g + D-chiroinositol (DCI) 27.6 mg + folic acid 400 µg daily (group 3, n = 13). Menstrual cycle, Ferriman-Gallwey score, body mass index (BMI), waist circumference, hip circumference, waist-hip ratio (WHR), and body composition by bioimpedentiometry were measured at baseline, 3 and 6 months.

**RESULTS:** Body weight, BMI, waist and hip circumferences decreased significantly in all groups. There was a significant difference between the 3 groups regarding the restoration of menstrual regularity ( $p = 0.02$ ) that was obtained in all patients only in-group 3.

**CONCLUSIONS:** MI+DCI in association with diet seems to accelerate the weight loss and the fat mass reduction with a slight increase of percent lean mass, and this treatment contributes significantly in restoring the regularity of the menstrual cycle.

## Key Words:

Polycystic ovary syndrome, Myo-inositol, D-chiroinositol, Body composition, Bioelectrical impedance analysis.

## Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in females in reproductive age, with a prevalence of about 6-10%<sup>1</sup>. PCOS is characterized by two of these three conditions according to the Rotterdam criteria: hyperandrogenism, chronic anovulation and polycystic ovarian morphology<sup>1-3</sup>. The frequent association between PCOS, hyperandrogenism, insulin resistance (IR) and hyperinsulinemia, justifies the metabolic syndrome<sup>4-6</sup>. Obesity (mostly android and present in 30-70%), increased levels of triglyceride, low density lipoprotein (LDL) and insulin with associated IR and frequent metabolic syndrome<sup>4-10</sup>, result in possible long-term complications such as type 2 diabetes, dyslipidemia, hypertension, atherosclerosis and cardiovascular events, including acute myocardial infarction and stroke<sup>8-13</sup>. The more frequent cardiovascular disease observed in PCOS, is mostly mediated through increased total and abdominal adiposity, and perhaps interacting with PCOS-related hyperandrogenism<sup>13</sup>. Weight loss through a balanced diet and regular physical activity is considered the first therapeutic intervention to restore ovarian function and fertility and to prevent metabolic-vascular complications, reducing abdominal fat, androgenic-

ty and IR and improving dyslipidemia<sup>13-16</sup>. Body composition assessment studies in PCOS patients have shown that the increase in fat mass (FM) and its predominantly abdominal distribution are present regardless of obesity/overweight<sup>17-19</sup>. Data on lean muscle mass in PCOS are few and contradictory<sup>20-22</sup>. Carmina et al<sup>23</sup> showed that lean mass is more represented in women with PCOS than normal women even in obesity or overweight. Although the increased lean mass (LM) observed in post-menopausal women<sup>24</sup> is associated with hyperinsulinemia and hyperandrogenemia that increase lean mass<sup>25,26</sup>, prior studies on body composition in PCOS have yielded conflicting results<sup>27</sup>. The increase in LM in classic PCOS appears to be associated with IR and central obesity rather than with energy intake, physical activity or androgens<sup>28</sup>. Myo-inositol (MI) is a polyol (cyclohexane-1,2,3,4,5,6-hexol) synthesized from glucose-6-phosphate (G-6-P), and the most abundant of five naturally occurring stereoisomers (scyllo-, muco-, D-chiro-, and neo-inositol), MI and D-chiro-inositol (DCI) being those most represented in the human body<sup>29,30</sup>. MI is not only the precursor of DCI (a conversion catalyzed by an insulin-dependent epimerase) but also the precursor of a number of inositol phosphates, which act in the Ca-dependent intracellular signaling pathways<sup>30,31</sup>. Numerous studies<sup>31,32</sup> have shown that the administration of DCI, whose deficiency in diabetics and subjects with PCOS can contribute to insulin resistance, improves glucose tolerance and insulin sensitivity, reduces androgens and restores ovulation in patients with PCOS. Also the other inositol isoform, the MI precursor of DCI, and very common in nature, reduces blood levels of insulin and testosterone, restores normal ovarian function, controls metabolic syndrome<sup>16,33,34</sup>. Similar beneficial effects on IR, metabolic syndrome, androgens and ovulation were reported for DCI<sup>35</sup>. The combined administration of MI and DCI in a 40 to 1 ratio, which is the physiological plasma ratio, ensures better clinical results in the setting of treatment of PCOS women<sup>36,37</sup> and improves the glucose metabolism and the lipid profile of obese PCOS women thus reducing the cardiovascular risk<sup>38</sup>. The purpose of this study was to evaluate, in overweight/obese women with PCOS, which of three distinct treatment modalities achieved the greatest clinical benefits in terms of clinical and body composition outcomes when administered for 6 months to three corresponding groups of patients.

## Patients and Methods

Of 92 consecutive overweight or obese patients who came to our observation between November 2015 and June 2016, 43 were selected for the study. Inclusion criteria were: diagnosis with PCOS according to Rotterdam criteria: age between 16 and 45 years; BMI  $\geq 25\text{kg/m}^2$ ; no hormone therapy for less than 6 months; no concurrent medical disease and taking no medications or over-the-counter products at baseline with commitment not to take any throughout the 6-month duration of the study. Should medications/supplementations, other than those prescribed in this study, be needed for the *de novo* appearance of some disease, the patient had to drop out from the study. Of these, 43 women (age  $26.7 \pm 8.8$  years), 19 (44%) were unemployed or housewives, 15 (33%) employed, and 9 (21%) students. Nine women (21%) were smokers, and none (0/43) performed regular physical activity. The 43 patients were randomly divided into 3 groups, based on treatment. Group 1 (n = 21) was treated with diet only; group 2 (n = 10) treated with diet and MI; group 3 (n = 12) was treated with diet and an association of two inositols (MI + DCI). The treatment duration was 6 months for all groups. The diet (1200 Kcal) administered to all three groups was the same as in a previous study on other patients<sup>15</sup>. It was according to Italian guidelines, Livelli di Assunzione di Riferimento di Nutrienti (LARN)<sup>39</sup> and consisted of 25% fats, 15-18% proteins and the remaining portion glucids; low glycemic index (IG) foods were recommended. The MI administered to group 2 is manufactured by Lo.Li.Pharma (Rome, Italy), and each sachet contains 2000 mg MI and 200  $\mu\text{g}$  folic acid. The product administered to group 3 is manufactured by Lo.Li.Pharma (Rome, Italy), and each softgel capsule contains 550 mg MI, 13.8 mg DCI and 200  $\mu\text{g}$  folic acid. Group 2 was treated with 2 sachets per day, and group 3 with 2 softgel capsules per day. Women enrolled were blind to the treatment. At time of enrolment (baseline) and two time-points (90 days and 180 days) while on treatment, all women underwent a thorough anamnesis and physical examination. During the physical examination, pertinent indices were recorded: height, weight, waist circumference, hip circumference and degree of hirsutism using the Ferriman-Gallwey score. In addition, bioimpedentiometry analysis (BIA) was performed, using the BIO 101 instrument by Akern s.r.l (Pontassieve, Italy), to evaluate indices of body composition. These indices are fat mass (FM) in kg

and %, lean mass (LM) in kg and %, total body water (TBW) in lt. Written informed consent was obtained from all participants; the protocol and other materials were in accord with the Helsinki Declaration of 1975 and approved by Institutional Review Boards.

### Statistical Analysis

The statistical analysis was performed by a parametric approach after having verified the normality of the examined variables by Kolmogorov Smirnov test. The numerical parameters were expressed as mean and standard deviation; the categorical variables as number and percentage. The ANOVA test was applied in order to assess the existence of statistically significant differences at baseline and at six months between the 3 groups, and to compare baseline, 3 and 6 months numerical variables in each of the 3 groups; for the same purpose chi square for trend was applied for the categorical variable (number and percentage of oligomenorrhoeic patients). Student *t*-test was applied to perform two by two comparison between group 1 vs. group 2; group 1 vs. group 3; group 2 vs. group 3. All tests were two-tailed, and the threshold for statistical significance was set at a *p*-value < 0.05. *p*-values comprised between 0.5 and 0.10 were considered to indicate borderline statistical significance.

## Results

Table I summarizes the pertinent data at baseline in the three groups of women. The three groups of women did not differ significantly (*p* > 0.05)

for any index, including the frequency of irregular cycles (*df* = 2,  $\chi^2 = 4.25$ , *p* = 0.12). Not shown in Table I, but inferable from Table II, is that the rate of oligomenorrhea was 33/43 (76.7%), with this distribution: 14/21 (66.7%, group 1), 10/10 (100%, group 2), 9/12 (75%, group 3). Regarding body composition, as expected, based on previous literature<sup>15,22,33</sup>, indices of body composition (FM and LM) deviated from normality<sup>40</sup>; the FM mean levels were higher than those recommended by Lhoman et al<sup>40</sup>; and LM levels were higher than those of FM in both kg and %. The fat-lean mass in kg (F/L) ratio was high at basal conditions in all groups. Table II shows changes in the evaluated indices over the 6 months of treatment, except for indices associated with body composition, which are summarized in Table III. Overall, the greatest changes, and in the favorable direction (decrease), occurred in group 3. The weight loss was significant in all groups after six months and highest in group 3 (8.1, 8.5 and 9.8 kg, respectively). Noteworthy, group 3 was the only group in which regularization of the menstrual cycle had a 100% success rate (Table II). Table III illustrates how body composition is significantly altered after six months in all 3 groups. The FM in % was significantly reduced in group 1 and borderline significantly reduced in groups 2 and 3; in groups 1 and 2, it falls within the acceptable limits (< 35%), above which the risk of health increases for women in reproductive age, according to Lohman's classification<sup>40</sup>. The FM in kg, was significantly reduced in groups 1 and 3, and borderline significantly in group 2. The LM in % significantly increased in group 2 (*p* = 0.01) and to a lesser extent in group 3 (*p* = 0.03). After six months, the

**Table I.** Descriptive indices of the 43 women with polycystic ovary syndrome (PCOS) at baseline\*.

	Group 1 (n = 21)	Group 2 (n = 10)	Group 3 (n = 12)	<i>p</i> -value
Age (years)	29.7 ± .8	25.5 ± 3.4	24.1 ± 5.1	0.09
Ferriman-Gallwey score	8.1 ± 5.5	9.9 ± 6.6	7.7 ± 4.2	0.48
Body Mass Index	31.9 ± 5.2	32.4 ± 5.5	31.8 ± 6	0.99
Waist circumference (cm)	98.6 ± 15.1	92.8 ± 16.1	91.7 ± 13.7	0.31
Hip circumference (cm)	110.2 ± 8.7	113 ± 4.6	107.3 ± 9.7	0.52
Waist Hip ratio	0.89 ± 0.1	0.82 ± 0.1	0.87 ± 0.1	0.10
Fat Mass (%)	38.2 ± 4.9	42.8 ± 7.4	39 ± 7.5	0.67
Fat Mass (kg)	30.7 ± 8.6	35.2 ± 9.2	34.1 ± 12	0.50
Lean Mass (%)	60.2 ± 7.1	50.6 ± 8.3	55.4 ± 11.1	0.07
Lean Mass (kg)	48.9 ± 6.3	46.9 ± 8.5	49.8 ± 7.9	0.97
Total Body Water (lt)	35.9 ± 4.7	35 ± 4.2	40.2 ± 5.9	0.14

Footnote. \*The 43 PCOS women were assigned randomly to these three groups, based on a 6-month duration treatment: only diet (Group 1, n = 21); diet and myo-inositol (MI) 4g + folic acid 400 µg daily (group 2, n = 10); diet in association with MI 11 g + D-chiroinositol (DCI) 27.6 mg + folic acid 400 µg daily (group 3, n = 13). Data are mean ± SD.

**Table II.** Changes at 3 and 6 months of the evaluated indices in the three treatment groups of 43 PCOS patients.

	Group 1 (n = 21)			Group 2 (n = 10)			Group 3 (n = 12)					
	Basal	3 months	6 months	p-value	Basal	3 months	6 months	p-value	Basal	3 months	6 months	p-value
Oligomenorrhic patients n° (%)	14 (66.7)	11 (52.4)	9 (42.8)	<b>0.022</b>	10 (100)	9 (90)	2 (20)	<b>0.001</b>	9 (75)	2 (20)	0 (0)	<b>0.001</b>
Ferriman Gallwey score (% variation)	8.1 ± 5.5	7.4 ± 4.6 (-9.4%)	7 ± 3.9 (-15.7%)	<b>0.001</b>	9.9 ± 6.6	7.8 ± 5.1 (-26.9%)	7.8 ± 5.1 (-26.9%)	<b>0.004</b>	7.7 ± 4.2	5.2 ± 3.4 (-48.1%)	5.2 ± 3.4 (-48.1%)	<b>0.001</b>
Weight kg (% variation)	80.1 ± 13.5	73.1 ± 11.9 (-9.6%)	72 ± 10.2 (-11.2%)	<b>0.000</b>	80.9 ± 17	76.5 ± 16.5 (-5.7%)	72.4 ± 14.2 (-11.7%)	<b>0.000</b>	80.5 ± 14.4	74.9 ± 14.6 (-7.5%)	70.7 ± 15.1 (-13.9%)	<b>0.000</b>
Body Mass Index kg/m <sup>2</sup> (% variation)	31.9 ± 5.2	29.1 ± 4.8 (-9.6%)	28.6 ± 3.7 (-11.5%)	<b>0.000</b>	32.4 ± 5.5	30.6 ± 5.2 (-5.9%)	29 ± 4.4 (-11.7%)	<b>0.000</b>	31.8 ± 6	29.9 ± 5.3 (-6.7%)	28.2 ± 5.4 (-12.8%)	<b>0.000</b>
Waist circumference cm (% variation)	98.6 ± 15.1	89.5 ± 11.5 (-10.2%)	85.5 ± 11.6 (-15.3%)	<b>0.000</b>	92.8 ± 16.1	86.5 ± 13.2 (-7.3%)	81.7 ± 12.1 (-13.6%)	<b>0.000</b>	91.8 ± 13.7	87.2 ± 12.1 (-5.3%)	83 ± 10.4 (-10.6%)	<b>0.000</b>
Hip circumference cm (% variation)	110.2 ± 8.7	101.7 ± 8.2 (-8.3%)	102.8 ± 6.3 (-7.2%)	<b>0.000</b>	113 ± 4.6	108 ± 4.8 (-4.6%)	105 ± 5.1 (-7.6%)	<b>0.000</b>	107.3 ± 9.7	102.1 ± 11.1 (-5.1%)	98.6 ± 11.7 (-8.8%)	<b>0.000</b>
Waist/Hip ratio (% variation)	0.89 ± 0.1	0.88 ± 0.11 (-1.1%)	0.82 ± 0.1 (-8.5%)	<b>0.029</b>	0.81 ± 0.1	0.79 ± 0.1 (-2.5%)	0.78 ± 0.1 (-3.8%)	<b>0.011</b>	0.87 ± 0.1	0.84 ± 0.06 (-3.6%)	0.83 ± 0.06 (-4.8%)	<b>0.376</b>

Footnote. \*For definition of the three groups see footnote of Table I. Data are number (oligomenorrhic patients) and mean ± SD.

**Table III.** Body composition at baseline, and after 3 and 6 months of treatment in the 3 PCOS groups.

	Group 1 (n = 21)			Group 2 (n = 10)			Group 3 (n = 12)			
	Basal	3 months	6 months	Basal	3 months	6 months	Basal	3 months	6 months	p-value
FM % (% variation)	38.2 ± 4.9	33.3 ± 5.8 (-14.7%)	33.5 ± 4.3 (-14%)	42.8 ± 7.4	39.3 ± 7.3 (-8.9%)	36.6 ± 7 (-16.9%)	39 ± 7.5	34.5 ± 7.1 (-13%)	32.8 ± 7.9 (-18.9%)	<b>0.008</b>
FM kg (% variation)	30.7 ± 8.6	24.5 ± 7.7 (-25.3%)	25.9 ± 7.3 (-18.5%)	35.2 ± 9.2	31.9 ± 8.6 (-10.3%)	31.8 ± 13.3 (-10.7%)	34.1 ± 12	27.7 ± 11 (-23.1%)	25.8 ± 10.7 (-32.2%)	<b>0.000</b>
LM % (% variation)	60.2 ± 7.1	62.5 ± 9.5 (+3.7%)	56.7 ± 7.1 (-6.2%)	50.6 ± 8.3	53.5 ± 9.2 (+5.4%)	54.5 ± 8.6 (+7.1%)	55.4 ± 11.1	52.3 ± 14.2 (-5.9%)	55.5 ± 13.4 (+0.2%)	<b>0.032</b>
LM kg (% variation)	48.9 ± 6.3	47.4 ± 5.6 (-3.2%)	48.7 ± 6 (-0.4%)	46.9 ± 8.5	50.1 ± 9 (+6.2%)	50.9 ± 9.3 (+7.8%)	49.8 ± 7.9	44.4 ± 11.2 (-12.2%)	45.8 ± 9.3 (-8.7%)	<b>0.264</b>
TBW lt (% variation)	35.9 ± 4.6	37.2 ± 6.4 (+3.2%)	43.1 ± 8 (+16.7%)	35 ± 4.2	36.7 ± 4.2 (+4.6%)	37.4 ± 4.1 (+6.7%)	40.2 ± 5.9	35.8 ± 5.3 (-12.6%)	45.2 ± 8.4 (+11.1%)	<b>0.165</b>
F/L kg (% variation)	0.62 ± 0.12	0.51 ± 0.12 (-21.6%)	0.53 ± 0.13 (-17%)	0.76 ± 0.24	0.64 ± 0.11 (-18.7%)	0.62 ± 0.2 (-22.6%)	0.68 ± 0.21	0.63 ± 0.22 (-7.9%)	0.57 ± 0.23 (-19.3%)	<b>0.005</b>

Footnote. \*For definition of the three groups see footnote of Table I. Data are mean ± SD. Abbreviations: FM = Fat mass; LM = Lean mass; TBW = Total body water; F/L = Fat /Lean kg ratio.

LM in kg slightly significantly decreased only in group 1, while it increased in group 2 and 3. The F/L ratio decreased significantly in all groups ( $p = 0.02$ ,  $p = 0.015$ ,  $p = 0.005$  respectively). TBW increased in all groups with a significant difference after six months in groups 1 and 2. No significant differences were found between the 3 groups at six months regarding Ferriman-Gallwey score, weight, BMI, waist and hips, waist-hip ratio (WHR) and bioimpedentiometry data; the only significant difference between the 3 groups was found in oligomenorrhea rate ( $p = 0.02$ ) (Table IV). Regarding two by two comparison between group 1 vs. group 2, group 1 vs. group 3 and group 2 vs. group 3, at 6 months (Table IV) there was a significant difference in TBW between group 2 vs. group 3 ( $p = 0.03$ ) and borderline significant difference was found in Ferriman-Gallwey score between group 1 vs. group 3 ( $p = 0.09$ ) and in WHR between Group 2 vs. group 3 ( $p = 0.09$ ).

### Discussion

Our results show, in agreement with the literature, that the weight loss in PCOS improves the metabolic and hormonal framework facilitating the restoration of physiological conditions<sup>13-16</sup>. There was a significant difference between the 3 groups regarding the restoration of menstrual regularity, that was obtained in 80% of cases in group 2 and in all patients of group 3. Comparing these data between group 2 and 3 with the results of our previous study<sup>16</sup>, it is evident that the addition of MI plus DCI to the diet contributes even

more in restoring the regularity of the menstrual cycle with a success rate of 100% vs. 66.6% with only MI integration. These data are in agreement with those of other researchers<sup>34,36,38</sup> and suggest that the combination MI/DCI in a physiological plasma ratio of 40:1, might be more effective than the supplementation with single MI, because of the imbalance in the MI/DCI ratio present in the PCOS ovary, possibly due to enhanced epimerase activity<sup>36</sup>. No significant difference was found between the 3 groups regarding the improvement of the Ferriman-Gallwey score, that was more apparent in group 1 and 3. Many authors<sup>1-5</sup> have shown that increased abdominal fat is an important determinant of increased cardiovascular and metabolic disease. However, there is paucity of data on other components of body structure and their possible effects on cardiovascular risk in PCOS. It has been shown that obese women also tend to have increased LM<sup>6</sup>; this trend may be higher in women with PCOS where other factors such as obesity, IR, and androgen excess may also contribute to increasing LM. Since lean muscle mass contributes significantly to metabolism and represents one of the major targets of both insulin and androgen action<sup>15</sup>, this determinant may be an important parameter of body composition to assess in PCOS. The importance of determining muscle mass in PCOS has been further increased by the finding that changes in LM appear to correlate with changes in some cardiovascular parameters, including a correlation between small increases in carotid intima-media thickness (IMT) with larger muscle mass<sup>23</sup>. The increased F/L ratio observed in Ezech et al<sup>27</sup> work, indicates a di-

**Table IV.** Two by two comparisons between group 1 vs. group 2; group 1 vs. group 3; group 2 vs. group 3, at six months.

	<i>p</i> -value Group 1 vs. 2	<i>p</i> -value Group 1 vs. 3	<i>p</i> -value Group 2 vs. 3	<i>p</i> -value among all groups
Oligomenorrhic patients (n <sup>2</sup> )	0.21	0.01	0.10	0.02
Ferriman Gallwey score	0.81	0.09	0.16	0.19
Body Mass Index (kg/m <sup>2</sup> )	0.74	0.60	0.53	0.79
Waist circumference (cm)	0.29	0.40	0.76	0.52
Hip circumference (cm)	0.44	0.24	0.14	0.26
Waist Hip ratio	0.33	0.79	0.09	0.30
Fat Mass (%)	0.54	0.96	0.64	0.84
Fat Mass (kg)	0.55	0.86	0.54	0.79
Lean Mass (%)	0.54	0.82	0.64	0.82
Lean Mass (kg)	0.31	0.53	0.16	0.34
Total Body Water (lt)	0.22	0.33	0.03	0.11
Fat/Lean ratio (kg)	0.55	0.5	0.94	0.75

Footnote. \*For definition of the three groups see footnote of Table I.

sproportional change in FM relative to LM, and suggests a decreased ability of LM to increase proportionately with the changes in FM in PCOS. In our study, in all PCOS groups treated either with diet alone, in combination with MI, or with MI plus DCI, there was a significant reduction in BMI; despite the significant reduction in waist and hip circumference obtained in the 3 groups, the WHR was significantly improved only in groups 1 and 2 with more significant trend in group 2. Regarding the body composition, it was improved after six months in all groups without significant differences between the 3 groups. The % FM was significantly reduced by diet alone, and borderline significantly by diet plus MI and diet plus MI and DCI. The FM in kg was more reduced by diet in combination with MI plus DCI. The % LM was increased by diet in cotreatment with MI, while it was reduced by diet alone; in the group treated with diet in association with MI and DCI, the % LM was reduced after 3 months and then reached baseline levels at six months. The LM (kg) was significantly reduced only by diet. There was a significant difference in TBW between group 2 vs. group 3.

Our data confirm those of literature that overweight or obese PCOS women as well as having higher levels of FM predominantly distributed abdominally, also have a higher LM rate as a result of IR<sup>17-22</sup>. It has been shown that during the treatment of obese PCOS women with insulin-sensitizing pioglitazone in addition to decreasing fasting insulin levels, significantly reduced lean body mass without modifying testosterone levels<sup>41</sup>. The high F/L ratio at basal condition was significantly reduced in all groups after 6 months within acceptable levels, without significant difference between the 3 groups. According to Ezech et al<sup>27</sup> the F/L ratio predicts metabolic dysfunction more effectively than WHR and the deleterious effects of excess body fat therefore overrides the beneficial effects of LM in the scenario of increased F/L ratio. The presence of obesity is accompanied by an increase in muscle mass<sup>42,43</sup>. However, the increased F/L ratio indicates a disproportional change in FM relative to LM, suggesting a decreased ability of LM to increase proportionately with the changes in FM in PCOS<sup>27</sup>. The data from our study, although limited by the low number of subjects enrolled, suggest that both MI such as MI plus DCI can positively influence body composition in obese PCOS patients, by improving glucose tolerance and insulin sensitivity.

## Conclusions

Weight loss through diet undoubtedly improves the symptoms of PCOS; moreover, the addition of MI plus DCI to the diet seems to accelerate the weight and FM reduction with a slight increase of LM% and contributes even more in restoring the regularity of the menstrual cycle. In agreement with Ezech et al<sup>27</sup>, our data suggest that BIA could be used to assess F/L ratio, that could possibly represent an alternative to WHR as a marker of metabolic dysfunction in clinical practice. Further studies are needed to confirm the role of MI and DCI on improving body composition, with particular regard to lean muscle mass also correlated to some cardiovascular parameters<sup>23</sup>.

## Conflict of Interest

The Authors declare that they have no conflict of interests.

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