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**UWARUNKOWANIA ŻYWIENIOWE, STAN ODŻYWIENIA
I ZABURZENIA METABOLICZNE U KOBIET Z ZESPOŁEM
POLICYSTYCZNYCH JAJNIKÓW (PCOS)**

**NUTRITIONAL DETERMINANTS, NUTRITION STATUS AND
METABOLIC DISORDERS IN WOMEN WITH POLYCYSTIC OVARY
SYNDROME (PCOS)**

ROZPRAWA DOKTORSKA

UNIWERSYTET PRZYRODNICZY W POZNANIU

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2 WYKAZ PUBLIKACJI W CYKLU:

2.1 PUBLIKACJA 0: ARTYKUŁ PRZEGLĄDOWY

Bykowska-Derda A., Kolay E., Kałużna M., Człapka-Matyasik M. Emerging Trends in Research on Food Compounds and Women's Fertility: A Systematic Review. *Applied Sciences*. 2020; 10(13):4518. <https://doi.org/10.3390/app10134518>

Impact Factor: 2,921 pkt. MNiSW: 100

2.2 PUBLIKACJA 1: ARTYKUŁ ORYGINALNY

Bykowska-Derda, A., Człapka-Matyasik, M., Kałużna, M., Ruchała, M., & Ziemnicka, K. Diet quality scores in relation to fatness and nutritional knowledge in women with polycystic ovary syndrome: Case–control study. *Public Health Nutrition*. 2021; 24(11), 3389-3398. <https://doi:10.1017/S1368980020001755>

Impact Factor: 4,777 pkt. MNiSW: 70

2.3 PUBLIKACJA 2: ARTYKUŁ ORYGINALNY

Bykowska-Derda, A.; Kałużna, M.; Ruchała, M.; Ziemnicka, K.; Człapka-Matyasik, M. The Significance of Plant-Based Foods and Intense Physical Activity on the Metabolic Health of Women with PCOS: A Priori Dietary-Lifestyle Patterns Approach. *Applied Sciences*. 2023, 13, 2118. <https://doi.org/10.3390/app13042118>

Impact Factor: 2,921 pkt. MNiSW: 100

2.4 PUBLIKACJA 3: ARTYKUŁ ORYGINALNY

Bykowska-Derda, A.; Kałużna, M.; Garbacz, A.; Ziemnicka, K.; Ruchała, M.; Człapka-Matyasik, M. Intake of Low Glycaemic Index Foods but Not Probiotics Is Associated with Atherosclerosis Risk in Women with Polycystic Ovary Syndrome. *Life* 2023, 13, 799. <https://doi.org/10.3390/life13030799>

Impact Factor: 3,253 pkt. MNiSW: 70

Łączny Impact Factor: 13,872

pkt. MNiSW: 340

3 LISTA SKRÓTÓW UŻYTYCH W PRACY

AIP	indeks aterogenności w osoczu
AMH	hormon antymüllerowski
BMI	body mass index
DHEA-S	siarczan dehydroepiandrosteronu
FSH	hormon folikulotropowy
HDL	cholesterol o dużej gęstości
hGIDI-7	indeks/wskaźnik diety o wysokim indeksie glikemicznym
HOMA-IR	wskaźnik insulinooporności HOMA
hSDI-4	indeks/wskaźnik diety o wysokiej zawartości cukru
hSFDI-8	indeks/wskaźnik diety o wysokiej zawartości nasyconych kwasów tłuszczowych
IG	indeks glikemiczny
KON	grupa kontrolna
LDL	cholesterol o niskiej gęstości
IGIDI-4	indeks/wskaźnik diety o niskim indeksie glikemicznym
LH	hormon luteinizujący
nHDI-14	indeks/wskaźnik diety niezdrowej
OR	iloraz szans
PCOS	zespół policystycznych jajników
PDLP	rozważny wzór stylu życia i żywienia
pHDI-10	indeks/wskaźnik diety prozdrowotnej
pro-DI-4	indeks/wskaźnik probiotyczny diety
SHGB	globulina wiążąca hormony płciowe
TG	trójglicerydy
VAT	wisceralna tkanka tłuszczowa
WDLP	zachodni wzór stylu życia i żywienia
WHR	stosunek obwodu talii do obwodu bioder
WHtR	stosunek obwodu talii do wzrostu

4 STRESZCZENIE W JĘZYKU POLSKIM

Wstęp

Zespół policystycznych jajników (PCOS) jest chorobą endokrynną, która oprócz hiperandrogenizmu jest związana z częstszym występowaniem chorób metabolicznych, takich jak: insulinooporność, hiperlipidemia, hipercholesterolemia czy nadciśnienie tętnicze. Celem niniejszej pracy była analiza uwarunkowań żywieniowych, stanu odżywienia i zaburzeń metabolicznych u kobiet z zespołem PCOS oraz podjęcie próby doprecyzowania wskazań dietoterapii w celu poprawy zaburzeń metabolicznych.

Metody

Do badań zaproszono grupę kobiet z potwierdzoną diagnozą PCOS i grupę kontrolną (KON). Badania stanu odżywienia obejmowały: parametry antropometryczne, analizę składu ciała (pletyzmografię powietrzną) i rozmieszczenia tkanki tłuszczowej (podwójną wiązkę promieniowania rentgenowskiego). Ocenę spożycia prowadzono za pomocą pomiaru częstotliwości spożycia poszerzonej grupy produktów spożywczych, na podstawie których szacowano wskaźniki jakości diety tj. (1) pro-zdrowotny (*Pro-Healthy-Diet-Index*; pHDI-10), (2) niezdrowy (*Non-Healthy-Diet-Index*; nHDI-14), (3) o wysokim indeksie glikemicznym (*High-Glycemic-Diet-Index-7*; hGIDI-7), (4) o niskim indeksie glikemicznym (IG) (*Low-Glycemic-Diet-Index-4*; lGIDI-4), (5) o wysokiej zawartości cukrów prostych (*High-Sugar-Diet-Index-4* (hSDI-4), (6) o wysokiej zawartości nasyconych kwasów tłuszczowych (*High-Saturated-Fats-Diet-Index-8*; hSFDI-8). Nasilenie zaburzeń metabolicznych określono wykorzystując parametry biochemiczne krwi (glukoza i insulina na czczo, profil lipidowy: cholesterol całkowity, LDL, HDL, trójglicerydy). Indeks aterogenności w osoczu (AIP) został obliczony na podstawie stężenia trójglicerydów i HDL. Dodatkowo oszacowano poziom aktywności fizycznej i poziom wiedzy żywieniowej respondentek.

Wyniki

Przeprowadzone badania wykazały, że kobiety z PCOS charakteryzowały się większym całkowitym otłuszczeniem ciała i niższą wiedzą żywieniową, w porównaniu z kobietami z grupy KON. Ponadto, kobiety z PCOS charakteryzowały się niższym. Ponadto, wysokie natężenie spożycia produktów o niskim IG (lGIDI-4) było związane z obniżonym wskaźnikiem AIP wśród kobiet z PCOS (Publikacja 3).

Analiza składowych głównych pozwoliła na wyodrębnienie trzech wzorów stylu życia, żywienia i stanu odżywienia (DLP): zachodniego (WDLP), rozważnego (PDLP) oraz

aktywnego (ADLP). Wzór zachodni (WDLP) charakteryzował się wyższą zawartością wisceralnej tkanki tłuszczowej, wyższą częstotliwością spożycia: produktów odzwierzęcych, słodczy, słodzonych napojów, przetworzonych produktów zbożowych, produktów typu „fast-food” i produktów smażonych, a niższą częstotliwością spożycia produktów roślinnych. Wzór rozważny (PDLP) był natomiast związany z wysoką częstotliwością spożycia produktów roślinnych, nabiału, ilością spożywanych posiłków w ciągu dnia oraz częstszymi i dłuższymi intensywnymi ćwiczeniami fizycznymi. Aktywny wzór stylu życia i żywienia (ADLP) wiązał się z wysoką zawartością wisceralnej tkanki tłuszczowej częstotliwością spożycia produktów roślinnych, wysoką aktywnością fizyczną, a niską częstotliwością spożycia produktów typu „fast-food” i produktów smażonych. Kobiety z podwyższonym LDL >135 mg/dL i stężeniem trójglicerydów >150 mg/dL charakteryzowały się wyższą adherencją do WDLP (OR 7,73 CI95% 1,79; 33,2; p < 0,05) i (OR 3,70 CI95% 1,03; 13,27; p < 0,05). Niska adherencja do PDLP była związana z ponad trzykrotnie wyższym ryzykiem wystąpienia podwyższonego stężenia całkowitego cholesterolu (>200 mg/dL).

In conclusion, plant-based foods related to PDLP and intense physical activity offer a significantly higher chance of improving metabolic health in women with PCOS

Wnioski

Stan odżywienia, zachowania żywieniowe oraz poziom wiedzy żywieniowej różnią się pomiędzy grupą kobiet z PCOS a grupą kontrolną. Częste spożycie produktów o charakterze prozdrowotnym, o niskim IG, produktów roślinnych obniżają ryzyko wystąpienia zaburzeń metabolicznych u kobiet z PCOS. Intensywna aktywność fizyczna może być również ważnym czynnikiem obniżającym ryzyko występowania zaburzeń metabolicznych u kobiet z PCOS.

5 STRESZCZENIE W JĘZYKU ANGIELSKIM

Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disorder which, in addition to hiperandrogenism, is associated with metabolic diseases such as insulin resistance, hyperlipidemia, hypercholesterolemia, and hypertension. The aim of the doctoral thesis is to analyze the relationship between nutritional determinants and nutrition status and metabolic disorders in women with PCOS, and to develop appropriate recommendations in diet therapy.

Methods

A group of women with PCOS and a control group were invited to the study. The analysis of nutrition status included anthropometric parameters, body composition assessment (air plethysmography), and body fat distribution (dual-energy X-ray absorptiometry). Nutrition intake was analyzed by food frequency questionnaire based on which there were assessed diet quality scores: Pro-Healthy-Diet-Index (pHDI-10), Non-Healthy-Diet-Index (nHDI-14), High-Glycemic-Diet-Index-7 (hGIDI-7), Low-Glycemic-Diet-Index-4 (lGIDI-4), High-Sugar-Diet-Index-4 (hSDI-4), and High-Saturated-Fats-Diet-Index-8 (hSFDI-8). The severity of metabolic disorders was determined using blood biochemical parameters (fasting glucose and insulin, lipid profile: total cholesterol, LDL, HDL, triglycerides). Plasma Atherogenicity Index (AIP) was calculated from triglycerides and HDL. In addition, the level of physical activity and nutritional knowledge of the patients was estimated.

Results

The research showed that women with PCOS were characterized by higher total body fat and lower nutritional knowledge, compared to women from the KON group. In addition, women with PCOS were characterized by a lower intensity of consumption of pro-healthy products pHDI-10 and low GI products lGIDI-4. In addition, high consumption of low GI (lGIDI-4) products was associated with reduced AIP among women with PCOS (Publication 3).

Principal component analysis allowed to distinguish three patterns of lifestyle, nutrition and nutritional status (DLP): western (WDLP), prudent (PDLP) and active (ADLP). The Western pattern (WDLP) was characterized by a higher content of visceral adipose tissue, the frequency of consumption of: animal products, sweets, sweetened beverages, processed cereal products, "fast-food" and fried products, and a lower frequency of consumption of plant products. The prudent pattern (PDLP) was associated with a high frequency of consumption of plant products, dairy products, the number of meals consumed during the day, and more frequent and prolonged intense physical exercise. An active lifestyle and diet pattern (ADLP) was associated with high visceral fat content, frequency of plant-based foods, high physical activity, and low frequency of consumption of fast-food and fried foods. Women with elevated LDL >135 mg/dL and triglycerides >150 mg/dL had higher adherence to WDLP (OR 7.73 CI95% 1.79, 33.2; $p < 0.05$) and (OR 3.70 CI95% 1.03, 13.27, $p < 0.05$). Low adherence to PDLP was associated with a more than three-fold higher risk of elevated total cholesterol (>200 mg/dL).

Conclusion

Nutritional status, eating behavior and the level of nutritional knowledge differ between the group of women with PCOS and the control group. Frequent consumption of pro-healthy and low GI products of plant origin reduces the risk of metabolic disorders in women with PCOS. Intense physical activity may also be an important aspect reducing the risk of metabolic disorders in women with PCOS

6 CYKL PUBLIKACJI STANOWIĄCYCH PRACĘ DOKTORSKĄ

6.1 PUBLIKACJA 0: ARTYKUŁ PRZEGLĄDOWY

Bykowska-Derda A, Kolay E, Kałużna M, Człapka-Matyasik M. Emerging Trends in Research on Food Compounds and Women's Fertility: A Systematic Review. *Applied Sciences*. 2020; 10(13):4518. <https://doi.org/10.3390/app10134518>

Celem systematycznego przeglądu literatury była ocena aktualnego stanu wiedzy związanej z żywieniem i jego wpływem na płodność kobiet.

Metodyka

Artykuły poszukiwano za pomocą terminów: (bioactive OR nutrient OR food OR ingredient OR vitamin OR mineral OR antioxidant OR phytonutrient) AND (fertility)) w bazach naukowych: PubMed (National Institute of Health, USA), Web of Science (Clarivate Analytics, USA), Scopus (Elsevier, RELX Group plc), and Science Direct (Elsevier, RELX Group plc). Protokół przeglądu został zarejestrowany w bazie PROSPERO (International Prospective Register of Systematic Reviews) (numer: CRD42020160223).

Wyniki

Wstępna analiza obejmowała 4609 artykułów naukowych. Z tej grupy 29 artykułów poddano szczegółowej analizie jakościowej, w tym 25 artykułów dotyczyło badań obserwacyjnych, a 4 badań interwencyjnych. Analizowane artykuły dotyczyły: diety śródziemnomorskiej (n = 2), spożycia owoców, warzyw i produktów pełnoziarnistych (n = 2), ryb (n = 1), nabiału (n = 3), rodzajów kwasów tłuszczowych (n = 4), soi (n = 2), kawy (n=3), kwasu foliowego i witaminy B12 (n = 4), melatoniny (n = 1), koenzymu Q10 (n = 1), kombinacji mikroskładników diety (n = 4).

Wnioski

Spożycie produktów prozdrowotnych wpływa na płodność kobiet. Kobiety planujące ciążę powinny przede wszystkim zadbać o spożycie owoców, warzyw, kwasu foliowego oraz

witaminy D. Natomiast częste spożycie słodzonych napojów i kwasów tłuszczowych trans zmniejsza szansę zajścia w ciążę.

6.2 PUBLIKACJA 1: ARTYKUŁ ORYGINALNY

Bykowska-Derda, A., Człapka-Matyasik, M., Kałużna, M., Ruchała, M., & Ziemnicka, K. Diet quality scores in relation to fatness and nutritional knowledge in women with polycystic ovary syndrome: Case-control study. *Public Health Nutrition*, 24(11); 2021, 3389-3398. doi:10.1017/S1368980020001755

Celem pracy była analiza żywienia się kobiet z PCOS przy wykorzystaniu istniejących i zaprojektowanych indeksów jakości diety, a także ocena stopnia otluszczenia ciała i wiedzy żywieniowej.

Metody

Częstotliwość spożycia i indeksy jakości diety oszacowano w badaniach ankietowych za pomocą kwestionariusza KomPAN®. Analizowano sześć indeksów jakości diety: (1) prozdrowotny (*Pro-Healthy-Diet-Index*; pHDI-10), (2) niezdrowy (*Non-Healthy-Diet-Index*; nHDI-14), (3) o wysokim indeksie glikemicznym (*High-Glycemic-Diet-Index*; hGIDI-7), (4) o niskim indeksie glikemicznym (IG) (*Low-Glycemic-Diet-Index*; IGIDI-4), (5) o wysokiej zawartości cukrów prostych (*High-Sugar-Diet-Index* (hSDI-4), (6) o wysokiej zawartości nasyconych kwasów tłuszczowych (*High-Saturated-Fats-Diet-Index*; hSFDI-8). Otluszczenie ciała badano metodą pletyzmografii powietrznej (BodPod, Life Measurement Inc.). Wiedzę żywieniową oceniono na podstawie badań ankietowych, w części kwestionariusza KomPAN®.

Wyniki

Stwierdzono wyższe całkowite otluszczenie ciała i niższą wiedzę żywieniową u kobiet z PCOS, w porównaniu z grupą kontrolną. Kobiety z PCOS charakteryzowały się niższym spożyciem produktów z wskaźnikiem pHDI-10 oraz LGIDI-4, w porównaniu z grupą kontrolną. U kobiet z PCOS nie zaobserwowano istotnej korelacji pomiędzy wiedzą żywieniową a wskaźnikami diety (pHDI-10, nHDI-14, hGIDI-7, IGIDI-4, hSDI-4, hSFDI-8). Analiza statystyczna przeprowadzona dla grupy kobiet z grupy KON wykazała z kolei, że większe natężenie spożycia produktów prozdrowotnych (pHDI-10) i niższe natężenie spożycia źródeł nasyconych kwasów tłuszczowych (hSFDI-8), wiązało się z wysoką wiedzą żywieniową respondentek.

Wnioski

Wiedza żywieniowa, intensywność spożycia produktów o niskim IG LGIDI-4 oraz produktów prozdrowotnych pHDI-10 były niższe u kobiet z PCOS niż w grupie kontrolnej. Edukacja żywieniowa powinna być istotnym elementem wspierającym poprawę zwyczajów żywieniowych i w konsekwencji parametrów metabolicznych kobiet z PCOS.

6.3 PUBLIKACJA 2: ARTYKUŁ ORYGINALNY

Bykowska-Derda, A.; Kałużna, M.; Ruchała, M.; Ziemnicka, K.; Człapka-Matyasik, M. The Significance of Plant-Based Foods and Intense Physical Activity on the Metabolic Health of Women with PCOS: A Priori Dietary-Lifestyle Patterns Approach. *Appl. Sci.* **2023**, *13*, 2118. <https://doi.org/10.3390/app13042118>

Celem pracy była analiza wzorów stylu życia i żywienia (DLP) oraz ich związku z zawartością wisceralnej tkanki tłuszczowej i innymi parametrami metabolicznymi u kobiet z PCOS.

Metody

W badaniu brało udział 140 kobiet ze diagnozowanym PCOS. Analizę spożycia i stylu życia, w tym aktywności fizycznej, przeprowadzono na podstawie kwestionariuszy KomPAN[®] oraz Short IPAQ. Wisceralną tkankę tłuszczową mierzono za pomocą techniki podwójnej dawki promieniowania rentgenowskiego (DXA).

Wyniki

Analiza głównych składowych wyodrębniła trzy wzory stylu życia i żywienia (DLP): zachodni (WDLP), rozważny (PDLP) oraz aktywny (ADLP). Wzór zachodni WDLP charakteryzował się wysoką zawartością wisceralnej tkanki tłuszczowej, wysoką częstotliwością spożycia mięsa, słodczy, słodzonych napojów, przetworzonych produktów zbożowych, produktów typu „fast-food” i produktów smażonych, a niską częstotliwością spożycia produktów roślinnych. Wzór rozważny PDLP był związany z wysoką częstotliwością spożycia produktów roślinnych, nabiału, dużą ilością spożywanych posiłków w ciągu dnia oraz intensywnymi ćwiczeniami fizycznymi. Z kolei wzór aktywny ADLP korelował z wysoką zawartością wisceralnej tkanki tłuszczowej, wysoką częstotliwością spożycia produktów roślinnych, intensywną aktywnością fizyczną, a niską częstością spożycia produktów typu „fast-food” i produktów smażonych. Kobiety z wysoką adherencją do WDLP, miały podwyższone stężenie trójglicerydów >150 mg/dL, (OR 7,73 CI95% 1,79; 33,2, $p < 0,05$) i cholesterolu LDL > 135 mg/dL (OR 3,70 CI95% 1,03; 13,27, $p < 0,05$) we krwi.

Wnioski

Większa intensywność spożycia produktów roślinnych i nabiału, ograniczenie częstotliwości spożycia mięsa i słodczy oraz intensywna aktywność fizyczna związana z rozważnym wzorem życia i żywienia PDLP pozwala na poprawę zdrowia metabolicznego u kobiet z PCOS.

6.4 PUBLIKACJA 3: ARTYKUŁ ORYGINALNY

Bykowska-Derda, A.; Kałużna, M.; Garbacz, A.; Ziemnicka, K.; Ruchała, M.; Człapka-Matyasik, M. Intake of Low Glycaemic Index Foods but Not Probiotics Is Associated with Atherosclerosis Risk in Women with Polycystic Ovary Syndrome. *Life* 2023, 13, 799.

Celem pracy była analiza związku między częstotliwością spożycia produktów o niskim indeksie glikemicznym (prebiotycznym) i produktów probiotycznych, a ryzykiem miażdżycy u kobiet z PCOS.

Metody

W badaniu, grupę 127 kobiet ze zdiagnozowanym PCOS podzielono na dwie podgrupy: kobiet z indeksem aterogennym (AIP) powyżej 0,11 (wysoki AIP) oraz kobiet z indeksem AIP $\leq 0,11$ (niski AIP). Indeks aterogenny AIP obliczono jako logarytm trójglicerydów i lipoprotein o dużej gęstości (HDL). Częstotliwość i jakość spożywanych przez kobiety produktów przeliczono, a ich wzorce zakwalifikowano do jednego z czterech wskaźników: (1) prozdrowotny (*Pro-Healthy-Diet-Index*; pHDI-10), (2) niezdrowy (*Non-Healthy-Diet-Index*; nHDI-14), (3) o niskim indeksie glikemicznym (IG) (*Low-Glycemic-Diet-Index*; IGIDI-4), probiotyczny (*probiotic foods dietary index* pro-DI-4). Skład ciała mierzono techniką pletyzmografii powietrznej (BodPod).

Wyniki

Badania wykazały, że grupa kobiet z PCOS z potwierdzonym wysokim indeksem AIP rzadziej wybierała produkty o niskim indeksie glikemicznym IGIDI-4, w porównaniu z grupą kobiet z niskim AIP. Grupa z wysokim AIP również rzadziej wybierała produkty takie jak: kasza gryczana, owies, makaron pełnoziarnisty lub kasze gruboziarniste. Zauważono tendencję do niższej częstotliwości spożycia prozdrowotnej żywności pHDI-10 w grupie kobiet, u których obserwowano wysoki indeks AIP, nawet po uwzględnieniu adjustacji na BMI i wiek.

Wnioski

Kobiety z PCOS o podwyższonym ryzyku miażdżycy spożywały mniej produktów o niskim IG, w porównaniu do grupy kobiet z niskim ryzykiem miażdżycy. Spożycie produktów bogatych w błonnik, o niskim IG może zapobiegać miażdżycy w grupie kobiet z PCOS; jednak wpływ probiotycznego indeksu diety pozostaje niejasny.

7 WSTĘP

7.1 DEFINICJA, DIAGNOZA I ETIOLOGIA PCOS

Zespół policystycznych jajników (PCOS) jest jednym z najczęściej występujących zaburzeń endokrynologicznych wśród kobiet w wieku rozrodczym ¹. Szacuje się, że cierpi na niego od 5 do 10% młodych kobiet ²⁻⁴. Schorzenie charakteryzuje się hiperandrogenizmem i podwyższoną ilością drobnych pęcherzyków w jajnikach. PCOS wiąże się z nadmiernym wytwarzaniem hormonu luteinizującego (LH) oraz hormonu antymullerowskiego (AMH). To z kolei, hamuje owulację i dojrzewanie pęcherzyków jajowych⁵. Tak więc, zespół PCOS może być związany z szerokim spektrum powikłań, m.in. obniżoną płodnością (zwiększenie stężenia poziomu hormonów androgennych, brak menstruacji, niepłodność, hirsutyzm) czy zaburzeniami metabolizmu (insulinooporność, cukrzyca, hipercholesterolemia, otyłość, nadciśnienie). Skutkuje to znacznym obniżeniem jakości życia, a może być nawet przyczyną problemów o podłożu psychicznym ⁶.

Pomimo szeregu dyskusji na temat diagnostyki PCOS, zalecanym aktualnie schematem są kryteria rotterdamskie^{3,7}. By zgodnie z nimi potwierdzić diagnozę konieczne jest stwierdzenie minimum dwu z trzech następujących symptomów: 1) oligo lub anowulacja, 2) hiperandrogenizm, 3) wielotorbielowate policystyczne jajniki (Tabela 1). Kryteria rotterdamskie pozwalają na rozróżnienie czterech fenotypów PCOS (fenotypy I, II, III, IV), których charakterystyki zestawiono w tabeli 2.

Tabela 1. Kryteria diagnostyczne zespołu policystycznych jajników (PCOS) ²

Kryteria rotterdamskie
Przynajmniej 2 z 3 kryteriów:
1. Oligo- lub anowulacja.
2. Hiperandrogenizm lub hiperandrogenizacja: - Oznaki kliniczne: hirsutyzm, trądzik, <i>acanthosis nigrans</i> , - Oznaki biochemiczne: całkowity testosteron > 70 ng/dL, wskaźnik wolnego testosteronu (FAI) > 5,5 (-).
3. Wielotorbielowate (policystyczne) jajniki ≥ 25 cyst na jajnikach.

Tabela 2. Fenotypy PCOS na podstawie kryteriów diagnostycznych

<p>Fenotyp I (klasyczny):</p> <ul style="list-style-type: none"> -policystyczne jajniki, -hiperandrogenizm, -oligo- lub anowulacja. 	<p>Fenotyp II:</p> <ul style="list-style-type: none"> -hipersandrogenizm, -oligo- lub anowulacja, -brak policystycznych jajników.
<p>Fenotyp III:</p> <ul style="list-style-type: none"> -hiperandrogenizm, -policystyczne jajniki, -normo-owulacja. 	<p>Fenotyp IV:</p> <ul style="list-style-type: none"> -policystyczne jajniki, -oligo- lub anowulacja, -normo-androgenizm.

Etiologia PCOS jest bardzo złożona i nie do końca wyjaśniona, zależna od wielu czynników metabolicznych, genetycznych czy stylu życia ⁸. Stwierdzono, że mogą mieć znaczenie uwarunkowania środowiskowe, ekspozycja na androgeny w życiu płodowym, niska masa urodzeniowa czy otyłość ⁵. Znaczącym czynnikiem predysponującym do wystąpienia PCOS może być insulinooporność ⁹. Wysokie stężenie insuliny zwiększa bowiem miejscowy poziom wolnego testosteronu poprzez hamowanie syntezy globuliny wiążącej hormony płciowe (SHGB). To z kolei może zakłócić wzrost pęcherzyków jajnikowych ³. Hiperandrogenizm może również pojawić się w wyniku przewlekłego stanu zapalnego, spowodowanego nadmiarem glukozy i insuliny we krwi ¹⁰. Szacuje się, że występowanie insulinooporności u kobiet z PCOS w Polsce może być na poziomie około 23% biorąc pod uwagę wskaźnik HOMA-IR (Homeostatic Model Assessment-Insulin Resistance) ⁹. Leczenie insulinooporności w przypadku nadwagi lub otyłości, polega przede wszystkim na zmianie stylu życia i obniżeniu masy ciała oraz dietę o niskim IG^{11,12}.

7.2 ŻYWIENIE W PCOS

Obecnie, poza leczeniem - głównie farmakologicznym, podstawowymi zaleceniami dla osób z PCOS, są dieta o obniżonej gęstości energetycznej, obniżenie masy i poprawa składu ciała oraz odpowiednia aktywność fizyczna^{3,4}. Zaleceniem dietetycznym, wymienianym najczęściej, jest obniżenie IG diety, którego skuteczność potwierdzają wg niektórych autorów parametry diagnostyczne PCOS¹²⁻¹⁵. Wiadomo, że spożycie produktów o wysokim IG obniża insulinooporność, a nasila hiperandrogenizm^{12,15,16}. Należy tu jednak podkreślić,

że uproszczenie zaleceń dietetycznych tylko do produktów o obniżonym IG niesie ze sobą ryzyko mniejszego urozmaicenia diety, restrykcyjnego ograniczenia spożycia owoców, czy częstego spożycia produktów o niskim IG, ale z wysoką zawartością nasyconych kwasów tłuszczowych. Zapobiegając niekorzystnemu działaniu produktów z wysokim IG, wystarczy umiejętnie łączyć produkty żywnościowe w jeden posiłek, co także skutecznie obniży tempo wchłaniania glukozy, a co za tym idzie wyrzut insuliny we krwi¹⁷. Znajdujące się w grupie produkty o niskim IG takie jak mięso czerwone są wysokim źródłem nasyconych kwasów tłuszczowych, przyczyniających się do zaburzeń metabolicznych. Nadmiar nasyconych kwasów tłuszczowych, zwłaszcza palmitynowego, wpływa na zwiększenie białej tkanki tłuszczowej i apoptozę spowodowaną stresem oksydacyjnym retikulum endoplazmatycznego, wytwarzaniem ceramidów i reaktywnych form tlenu oraz poprzez sygnalizację kinazy białkowej C¹⁸. Ponadto ograniczenia związane z listą produktów o niskim GI mogą redukować spożycie owoców o zarówno wysokim potencjale antyoksydacyjnym i indeksie glikemicznym. Przykładem może być tutaj arbuz, dynia lub buraki. Posiadają one wysoki IG, ale również są bogate w fitozwiązki¹⁹.

Dieta śródziemnomorska to dieta obfitująca w oliwę z oliwek, owoce, warzywa, orzechy oraz ryby i owoce morza²⁰. Jej wysoka zawartość związków bioaktywnych, w tym nienasyconych kwasów tłuszczowych czyni ją dietą o wysokim potencjale antyoksydacyjnym. Wykazano, że dieta śródziemnomorska ma związek z obniżeniem markerów prozapalnych u kobiet z PCOS²¹. Dlatego też, biorąc pod uwagę sezonowość klimatu w Europie Środkowej i wzory spożycia z tym związane, dodatkowa restrykcja poszczególnych grup owoców z powodu indeksu glikemicznego, musi być przeprowadzona ze szczególną ostrożnością²².

Jednym z częstych schorzeń dotyczących kobiety w okresie prokreacyjnym jest niepłodność²³. Jej etiologii jest szeroka niemniej badania wskazują, że zespół PCOS jest najczęstszą przyczyną (około 70%) niepłodności związanej z brakiem owulacji²⁴. Spożycie produktów prozdrowotnych wpływa na płodność kobiet. Przygotowując publikację przeglądową (Publikacja 0), zauważono, że spożycie owoców, warzyw, kwasu foliowego oraz witaminy D podwyższa szanse zajścia w ciążę zarówno u kobiet z PCOS, kobiet z innymi przyczynami niepłodności jak i u kobiet zdrowych. Natomiast częste spożywanie słodzonych napojów i kwasów tłuszczowych trans zmniejsza szansę zajścia w ciążę²⁵. Spożycie słodzonych napojów i kwasów tłuszczowych trans jest charakterystyczne dla zachodniego wzoru żywienia,

którego elementami są żywność o wysokiej gęstości energetycznej, jednocześnie uboga w składniki odżywcze²⁶.

W 2019 roku naukowcy z grupy EAT-Lancet opracowali pierwsze na świecie cele naukowe dotyczące zdrowych i zrównoważonych systemów żywnościowych, w tym „zdrowej diety planetarnej” z określonymi dziennymi zaleceniami spożycia dla każdej grupy żywności²⁷. Jednym z celów diety planetarnej jest ograniczenie produktów mięsnych. Wysokie spożycie mięsa wiąże się również z „zachodnim” wzorem żywienia²⁶. Produkty mięsne często oprócz nasyconych kwasów tłuszczowych zawierają wysoką zawartość sodu (w przypadku wędlin), co może przyczyniać się do podwyższonego ryzyka występowania chorób kardiometabolicznych²⁸. Obecnie nie ma badań wykazujących, że spożycie produktów mięsnych może negatywnie wpływać na zdrowie kobiet z PCOS.

7.3 ANALIZA A PRIORI I A POSTERIORI W IDENTYFIKOWANIU WZORÓW ŻYWIENIOWYCH

Wzory stylu życia i żywienia (DLP) to zbiór czynności i zachowań okoł żywnościowych określonych poprzez częstotliwość z jaką są praktykowane, ilość, proporcje, lub różnorodność doboru produktów spożywczych. W badaniach nad modelami żywienia przyjmuje się, że są one opisem szeregu zachowań populacji, w której je zidentyfikowano i dają podstawę do wnioskowania na temat potencjalnego ryzyka chorób dietozależnych.

Zbiór takich czynności i zachowań oceniany jest jako pojedyncza ekspozycja żywieniowa²⁹. Metodyka określania wzorów żywienia może mieć charakter *a priori* lub *a posteriori*. *A priori* to analiza według już wcześniej określonych wzorów lub indeksów jakości diety względnie spożycia, takich jak np. indeks prozdrowotny diety. Analiza wzorów żywienia, *a posteriori* bazuje na analizie żywienia i zachowań zebranych danych, wykorzystując analizę czynnikową lub analizę głównych składowych (PCA)³⁰. Analiza *a posteriori* wzorów żywieniowych kobiet z PCOS była wielokrotnie wykorzystywana w ocenie sposobu żywienia populacji, w tym także kobiet z PCOS^{31,32}. Autorzy tych badań porównywali grupę kobiet z PCOS z grupą kontrolną. Analiza wzorów żywienia wyodrębniona tylko między kobietami z grupy PCOS, pozwoliłaby na znalezienie najbardziej i najmniej korzystnych, ale specyficznych wzorów żywienia dla kobiet z PCOS.

7.4 ZNACZENIE SKŁADU CIAŁA I ROZMIESZCZENIA TKANKI TŁUSZCZOWEJ W ROZWOJU CHORÓB METABOLICZNYCH I PCOS

Analiza literatury w Publikacji 0 wykazała brak wystarczających badań analizujących skład ciała i rozmieszczenie tkanki tłuszczowej w aspekcie sposobu żywienia się kobiet z PCOS oraz jego wpływu na płodność²⁵. Jak wskazuje piśmiennictwo u kobiet charakteryzujących się zawartością tkanki tłuszczowej w ciele powyżej 35%, jednocześnie prawidłowym lub podwyższonym BMI, obserwuje się podwyższone ryzyko kardiometaboliczne³³. W badaniach przeprowadzonych przez nasz zespół zauważono, że kobiety z PCOS miały wyższą zawartość tkanki tłuszczowej wisceralnej (VAT) od kobiet w grupie kontrolnej, dopasowanej pod względem wieku i BMI³⁴. Należy podkreślić, że VAT jest tkanką o funkcjach endokrynych, walnia między innymi prozapalne związki: adiponektynę, leptynę, czynnik martwicy nowotworów, rezystynę i interleukinę 6 (IL-6)^{35,36}. Wysoka zawartość VAT jest zatem związana z występowaniem zespołu metabolicznego, chorób układu krążenia, czy raka piersi i jelita grubego³⁵. Zawartość VAT można obniżyć przede wszystkim za pomocą ćwiczeń, diety z ujemnym bilansem energetycznym i niskim udziałem nasyconych kwasów tłuszczowych³⁷. Co warto podkreślić, kobiety z PCOS mogą mieć podwyższoną zawartość VAT przez zaburzenia endokryne, dlatego też przestrzeganie zaleceń diety i ćwiczeń fizycznych może mieć szczególne znaczenie terapeutyczne³⁴. Publikacja 2 była pierwszą publikacją analizującą współzależności pomiędzy VAT a wzorami stylu życia i żywienia i ich wpływem na markery metaboliczne kobiet z PCOS.

7.5 RYZYKO WYSTĘPOWANIA MIAŻDŻYCY U KOBIET Z PCOS W ASPEKCIE SPOSOBU ŻYWIENIA

Kobiety z PCOS charakteryzuje podwyższone ryzyko kardiometaboliczne. Wśród szeregu przyczyn wymienia się z występowanie zaburzeń metabolizmu kwasów tłuszczowych, takich jak dyslipidemia, czy hipercholesterolemia². Kobiety z PCOS charakteryzuje podwyższony indeks aterogenności osocza (AIP)³⁸. Wskaźnik AIP jest bardzo dobrym markerem ryzyka występowania miażdżycy³⁹. Zalecenia wskazują, że dieta w profilaktyce miażdżycy powinna być uboga w produkty pochodzenia zwierzęcego, o obniżonej zawartości soli, bogata w żywność pochodzenia roślinnego – produkty pełnoziarniste, owoce, warzywa, rośliny strączkowe i orzechy²⁸. Zauważono również, że suplementacja synbiotykami obniża ryzyko miażdżycy⁴⁰. Synbiotyki to kombinacja probiotyków i prebiotyków. Badania przeprowadzone na różnych populacjach wykazały, że zarówno pro- jak i prebiotyki wykazują

działania antymiażdżycowe⁴¹⁻⁴⁴. *Lactobacillus* i *Bifidobacterium*, które naturalnie znajdują się w jogurtach mogą poprawić mikrobiotę, a co za tym idzie również obniżyć ryzyko występowania zaburzeń metabolicznych⁴⁵. Dodatkowo, błonnik rozpuszczalny występujący w produktach typu ciemne pieczywo, kasze gruboziarniste, owies, czy warzywa strączkowe i warzywa szczególnie takie jak cykoria szparagi, czy buraki, nie tylko działa jako prebiotyk, ale również obniża cholesterol poprzez usuwanie go wraz z kwasami żółciowymi z jelit^{46,47}. Powyższa analiza pozwala na stwierdzenie, że odpowiedź na pytanie, czy wysokobłonnikowe, niskoglikemiczne i probiotyczne produkty są związane z obniżonym markerem AIP u kobiet z PCOS, byłoby niezwykle pomocne w ustalaniu zaleceń żywieniowych.

7.6 UWARUNKOWANIA STYLU ŻYCIA A PCOS I CHOROBY METABOLICZNE

Oprócz czynników żywieniowych, choroby metaboliczne są związane ze wzorami stylu życia, aktywnością fizyczną, siedzącym trybem życia, stresem, regularnością snu, czy wiedzą żywieniową. Wyniki wielu badań wskazują na pozytywny wpływ aktywności fizycznej o różnorodnym natężeniu, na zdrowie kobiet z PCOS⁴⁸. Zauważono również, że wiedza żywieniowa jest związana z jakością żywienia w wielu populacjach⁴⁹, a nawet ze wskaźnikiem BMI⁵⁰. Jednakże większość prac dotyczących PCOS i zaburzeń metabolicznych przedstawia pojedyncze czynniki ryzyka.

Publikacja nr 1 wchodząca w skład pracy doktorskiej obejmuje analizę wiedzy żywieniowej w aspekcie otluszczenia ciała u kobiet z PCOS. Brakuje niestety badań analizujących wiele czynników wpływających na zaburzenia metaboliczne, takie jak wzory stylu życia i żywienia a posteriori wśród kobiet z PCOS, w aspekcie wisceralnej tkanki tłuszczowej i markerów metabolicznych (Publikacja 2). Publikacja nr 3 natomiast po raz pierwszy analizuje natężenie spożycia produktów probiotycznych i ryzyko zachorowania na miażdżycę.

8 CELE I HIPOTEZY BADAWCZE

8.1 CEL PRACY

Celem pracy doktorskiej była analiza uwarunkowań żywieniowych, stanu odżywienia i zaburzeń metabolicznych oraz opracowanie dodatkowych wskazań w dietoterapii kobiet z zespołem PCOS.

8.2 CELE SZCZEGÓŁOWE

1. Analiza *a priori* i porównanie jakości diet w aspekcie stopnia otłuszczenia ciała i wiedzy żywieniowej kobiet z grupy PCOS na tle grupy KON (publikacja nr 1);
2. Wyodrębnienie i analiza *a posteriori* wzorów stylu życia i żywienia kobiet z PCOS, w spekcie wisceralnej tkanki tłuszczowej (publikacja nr 2);
3. Analiza zależności pomiędzy wzorami stylu życia i żywienia a markerami metabolicznymi u kobiet z PCOS (publikacja nr 2);
4. Analiza wskaźników jakości diety *a priori* w kontekście występowania ryzyka miażdżycy u kobiet z PCOS (publikacja nr 3);
5. Analiza zależności pomiędzy częstotliwością spożycia produktów probiotycznych i prebiotycznych a ryzykiem kardiometabolicznym u kobiet z PCOS (publikacja nr 3).

8.3 HIPOTEZY BADAWCZE

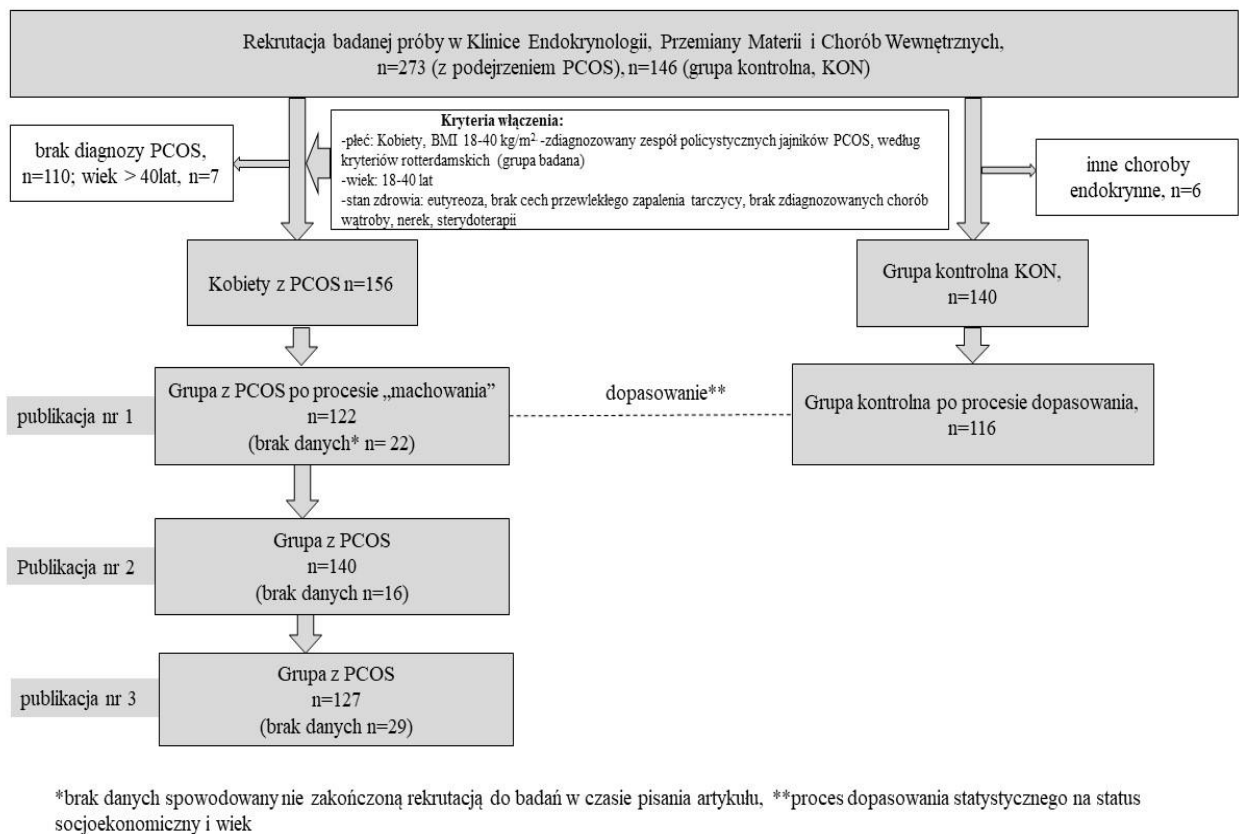
1. Wskaźniki jakości diety, stopień otłuszczenia ciała oraz poziom wiedzy żywieniowej kobiet z PCOS różnią się od kobiet z grupy KON (publikacja nr 1).
2. Wyodrębnione *a posteriori* wzory stylu życia i żywienia kobiet z PCOS wykazują współzależności w zakresie zawartości wisceralnej tkanki tłuszczowej i sposobu żywienia się kobiet z zespołem PCOS (publikacja nr 2).
3. Wzory stylu życia i żywienia rzutują na wartości markerów metabolicznych u kobiet z zespołem PCOS (publikacja nr 2).
4. Wskaźniki jakości diety wiążą się z występowaniem ryzyka miażdżycy w badanej grupie kobiet z PCOS (Publikacja nr 3).

9 BADANA PRÓBA I METODY

9.1 BADANA PRÓBA

W badaniach uczestniczyło 273 kobiet z podejrzeniem PCOS i 146 kobiet w grupie kontrolnej (KON). Badania diagnostyczne wykonano w Katedrze i Klinice Endokrynologii,

Przemiany Materii i Chorób Wewnętrznych, Uniwersytetu Medycznego im. Karola Marcinkowskiego w Poznaniu. Po wstępnej diagnozie, kobiety zgłaszały się do Ośrodka Badań Żywnościowych, Katedry Żywienia Człowieka i Dietetyki Uniwersytetu Przyrodniczym w Poznaniu (Rycina 1). PCOS diagnozowano przy pomocy kryteriów rotterdamskich (Tabela 1). Badanie zostało przeprowadzone zgodnie z wytycznymi Deklaracji Helsińskiej, a wszystkie procedury z udziałem pacjentek zostały zatwierdzone przez lokalną komisję bioetyczną Uniwersytetu Medycznego im. Karola Marcinkowskiego w Poznaniu (numer 552/16). Świadomą i pisemną zgodę na udział w badaniach uzyskano od wszystkich pacjentek.



Rycina 1.: Schemat rekrutacji uczestników badania

9.2 KRYTERIA WŁĄCZENIA I WYŁĄCZENIA

9.2.1 KRYTERIA WŁĄCZENIA:

1. Płeć: Kobiety
2. BMI 18-40 kg/m²
3. Zdiagnozowany zespół policystycznych jajników PCOS, według kryteriów rotterdamskich (grupa badana)

4. Wiek: 18-49 lat
5. Stan zdrowia: eutyreoza, brak cech przewlekłego zapalenia tarczycy, brak zdiagnozowanych chorób wątroby, nerek, sterydoterapii

9.2.2 KRYTERIA WYŁĄCZENIA:

1. Wiek: <18 i >49 lat
2. BMI <18 i >40 kg/m²
3. Cięża

9.3 ANALIZA BIOCHEMICZNA KRWI

Próbki krwi pobierano po uprzednim całonocnym poście. Poziom insuliny, FSH, LH, DHEAS zostały analizowane za pomocą urządzenia Cobas 6000 (Roche Diagnostics, GmbH, Mannheim, Niemcy) przy użyciu zestawów producenta. Całkowity cholesterol (TC), lipoproteiny o wysokiej gęstości (HDL) i trójglicerydy (TG) oceniano za pomocą metody enzymatyczno kolometrycznej. Lipoproteiny o niskiej gęstości (LDL) zostały oszacowane za pomocą wzoru Friedwalda (mg/dl):

$$LDL = TC - \left(HDL + \frac{TG}{5} \right)^{51} .$$

Glukozę w surowicy krwi analizowano za pomocą metody heksokinazy (Roche Diagnostics) ze współczynnikiem wariacji (CV) 3%. Wskaźnik insulinooporności został obliczony za pomocą wzoru (-):

$$HOMA - IR = \frac{glukoza\ na\ czczo\ \left(\frac{mg}{dL}\right) * insulina\ na\ czczo\ \left(\frac{mU}{L}\right)}{405}^{52} .$$

Indeks aterogenności w osoczu określono wg wzoru (-):

$$AIP = \log \frac{trójglicerydy}{HDL}^{39}$$

AIP poniżej 0,11, określono jako niskie ryzyko występowania miażdżycy a 0,11 lub wyższe, jako podwyższone ryzyko występowania miażdżycy^{39,53}.

9.4 SKŁAD CIAŁA I ROZMIESZCZENIE TKANKI TŁUSZCZOWEJ

9.4.1 BADANIE SKŁADU CIAŁA

Do oszacowania procentowej zawartości tkanki tłuszczowej i beztłuszczowej masy ciała użyto techniki pletyzmografii powietrznej (BodPod Cosmed Inc, Concord, California, model: 2007A, rok produkcji: 2013, numer seryjny 3959)⁵⁴. Badania składu ciała były przeprowadzone

na czczo w godzinach porannych po uprzedniej kalibracji według zaleceń producenta. Pacjentki nie miały na sobie biżuterii i metalowych akcesoriów, a w badaniu uczestniczyły w białym białym stroju kąpielowym i czepku pływackim, według zaleceń producenta, w stałej temperaturze pomieszczenia 21 °C. Przeprowadzano minimum dwa pomiary na pacjentkę, trwające 60 sekund. W razie niejednoznacznych wyników, pomiary powtórzono kolejny raz.

9.4.2 ANALIZA ROZMIESZCZENIA TKANKI TŁUSZCZOWEJ

Analiza rozmieszczenia tkanki tłuszczowej obejmowała technikę densytometrii podwójną wiązką promieniowania rentgenowskiego (DXA) analizatorem Prodigy (GE Medical Systems Lunar, Madison, Wisconsin, USA, model: 8743, rok produkcji: 2013, numer seryjny 79450GA). Kontrolę jakości według zaleceń producenta wykonywano każdego dnia badań. Tkanka tłuszczowa wisceralna (VAT) została oszacowana za pomocą oprogramowania enCORE™ (version 17) i CoreScan™ (GE Healthcare®, Madison, WI, USA).

9.4.3 ANTROPOMETRIA

Masa ciała, wzrost, obwody talii i bioder zostały zmierzone przez wykwalifikowanego dietetyka, według zaleceń WHO ⁵⁶, a następnie przeliczono WHR i WHtR.

9.5 AKTYWNOŚĆ FIZYCZNA

Analiza aktywności fizycznej obejmowała walidowany skrócony międzynarodowy kwestionariusz aktywności fizycznej (Short IPAQ). Wartości aktywności fizycznej podawane są jako współczynniki intensywności w jednostkach Metabolic Equivalent of Work MET-min/tydz ⁵⁷. Każdy rodzaj aktywności fizycznej (chodzenie = 3,3, aktywność umiarkowana = 4,0, aktywność intensywna = 8,0) można wyrazić w jednostkach MET-min./tydzień, mnożąc współczynnik przypisany tej aktywności, przez liczbę dni jej wykonywania w tygodniu oraz czas trwania w minutach na dzień. Np. dla osób, które wykonywało wysiłki intensywne przez 3 dni w tygodniu, przeciętnie przez 30 minut, całkowita wartość MET-min./tydzień = $8,0 \times 3 \times 30 = 720$ ⁵⁷.

9.6 ANALIZA SPOSOBU ŻYWIENIA

Analizę sposobu żywienia wykonano za pomocą kwestionariusza do badania poglądów i zwyczajów żywieniowych (KomPAN®). Wywiad był przeprowadzony przez wykwalifikowanego dietetyka. Trzydzieści trzy pytania dotyczyły częstotliwości spożycia różnych grup żywności. Użyto sześciu kategorii częstości spożycia w ciągu roku: 1)

Nigdy, 2) 1-3 razy w miesiącu, 3) raz w tygodniu, 4) 2-3 razy w tygodniu, 5) raz dziennie, 6) kilka razy dziennie. Każda odpowiedź została przeliczona na wartości liczbowe przedstawiające częstotliwość spożycia, gdzie: 1) Nigdy = 0,00 punktów; 2) 1-3 razy w miesiącu = 0,06; 3) Raz w tygodniu = 0,14; 4) 2-3 razy w tygodniu = 0,5; 5) raz dziennie = 1,00; 6) kilka razy dziennie = 2,00⁵⁸.

9.6.1 ANALIZA SPOŻYCIA A PRIORI

Różnice w częstości spożycia pomiędzy grupą badaną kobiet z PCOS a grupą KON analizowano za pomocą indeksów jakości diety, które informowały o intensywności spożycia produktów o cechach prozdrowotnych (pHDI-10), niezdrowych (nHDI-14), z niskim (IGDI-4) i wysokim indeksem glikemicznym (hGIDI-7), wysokiej zawartości cukrów prostych (hSDI-4) i tłuszczów nasyconych (hSFDI-8). Składowe poszczególnych indeksów umieszczono w Tabeli 3. Indeksy pHDI-14 oraz nHDI-10 zostały zwalidowane⁵⁸, natomiast IGDI-4, hGIDI-7, hSDI-4 oraz hSFDI-8 są indeksami opracowanymi przez autorkę, przeliczonymi na zasadach wcześniej walidowanych indeksów⁵⁸. Indeksy przygotowano na podstawie wcześniejszych doniesień i rekomendacji w dietoterapii PCOS, dlatego też powstał indeks obejmujący produkty o niskim i wysokim IG, wysokiej zawartości kwasów nasyconych oraz cukrów prostych (Publikacja nr 1). Indeks probiotyczny powstał po analizie *a posteriori* po wykazaniu wysokiej współzależności między produktami mlecznymi a wskaźnikami metabolicznymi (Publikacja nr 2).

Tabela 3: Indeksy jakości diety oraz ich składowe

Nazwa indeksu	Składowe indeksu
pHDI-10 (<i>Pro-healthy dietary index</i>) Indeks prozdrowotnej diety	(1) pieczywo razowe; (2) kasza gryczana, płatki owsiane, makaron pełnoziarnisty lub inne kasze gruboziarniste; (3) mleko (w tym mleko smakowe, kakao, kawa na mleku); (4) fermentowane napoje mleczne, np. jogurty, kefir (naturalne lub smakowe); (5) sery twarogowe (w tym serki homogenizowane, desery twarogowe); (6) potrawy z tzw. mięsa białego; (7) ryby; (8) potrawy z nasion roślin strączkowych; (9) owoce; (10) warzywa.

<p>nHDI-14 (<i>Non-healthy dietary index</i>) Indeks niezdrowej diety</p>	<p>(1) pieczywo jasne; (2) ryż biały, makaron zwykły lub drobne kasze, np. kasza manna, kuskus; (3) żywność typu fast food; (4) mięsne lub mączne potrawy smażone; (5) masło; (6) smalec; (7) sery żółte (w tym serki topione, sery pleśniowe); (8) wędliny, kiełbasy lub parówki; (9) potrawy z tzw. mięsa czerwonego; (10) słodczyce, np. cukierki, ciastka, ciasta, batony czekoladowe, batony typu ‘musli’, inne wyroby cukiernicze; (11) konserwy mięsne; (12) słodzone napoje gazowane lub niegazowane; (13) napoje energetyzujące; (14) napoje alkoholowe.</p>
<p>lGIDI-4 (<i>Low Glycemic index</i>) Indeks/wskaźnik diety o niskim IG</p>	<p>(1) pieczywo razowe; (2) kasza gryczana, płatki owsiane, makaron pełnoziarnisty lub inne kasze gruboziarniste; (3) potrawy z nasion roślin strączkowych, np. fasoli, grochu, soi, soczewicy; (4) warzywa.</p>
<p>hGIDI-7 (<i>High Glycemic Index</i>) Indeks diety o wysokim IG</p>	<p>(1) pieczywo jasne, np. pszenne, żytnie, mieszane pszenno-żytnie, pieczywo tostowe, bułki, rogalce; (2) ryż biały, makaron zwykły lub drobne kasze, np. kasza manna, kuskus; (3) słodczyce, np. cukierki, ciastka, ciasta, batony czekoladowe, batony typu ‘musli’, inne wyroby cukiernicze; (4) słodzone napoje gazowane lub niegazowane typu Coca-Cola, Pepsi, Sprite, Fanta, oranżada, lemoniada; (5) napoje energetyzujące, np. 2 KC, Black Horse, Red Bull, Burn, Shot lub inne; (6) soki owocowe; (7) owoce.</p>
<p>hSDI-4 (<i>high sugar dietary index</i>) Indeks diety o wysokiej zawartości cukru</p>	<p>(1) słodczyce, np. cukierki, ciastka, ciasta, batony czekoladowe, batony typu ‘musli’, inne wyroby cukiernicze; (2) słodzone napoje gazowane lub niegazowane typu Coca-Cola, Pepsi, Sprite, Fanta, oranżada, lemoniada; (3) soki owocowe; (4) słodzone gorące napoje.</p>
<p>hSFDI-8 (<i>high saturated fatty acid dietary index</i>) Indeks diety o wysokiej zawartości</p>	<p>(1) żywność typu fast food, np. frytki, hamburgery, pizza, hot dogi, zapiekanki; (2) mięsne lub mączne potrawy smażone; (3) masło jako dodatek do pieczywa lub potraw, do smażenia, pieczenia itp.; (4) smalec jako dodatek do pieczywa lub potraw, do smażenia, pieczenia itp.; (5) sery żółte (w tym serki topione, sery pleśniowe);</p>

nasyconych kwasów tłuszczowych	(6) wędliny, kiełbasy lub parówki; (7) potrawy z tzw. mięsa czerwonego, np. wieprzowiny, wołowiny, cielęciny, baraniny, jagnięciny, dziczyzny; (8) konserwy mięsne.
proDI-4 (<i>probiotic foods dietary index</i>) Indeks probiotyczny diety	(1) fermentowane napoje mleczne, np. jogurty, kefir (naturalne lub smakowe); (2) konserwy warzywne, warzywa marynowane lub kiszone; (3) sery twarogowe (w tym serki homogenizowane, desery twarogowe); (4) sery żółte (w tym serki topione, sery pleśniowe);

Wszystkie wskaźniki jakości diety zostały przeliczone według wzoru:

$$Diet\ Index\ (\%) = \frac{\sum A * 100\%}{\sum B}$$

Gdzie A jest sumą raportowanego dziennego spożycia produktów specyficznych dla danego indeksu (Tabela 3.), a B jest maksymalną sumą spożycia na dzień.

Przykład dla IGIDI-4:

$$\sum A = 0 + 0,14 + 0,06 + 0,5;$$

$$\sum B = 2 + 2 + 2 + 2.$$

Indeksy jakości diety były klasyfikowane w skali procentowej w celu charakterystyki grupy badanej. Niskie natężenie indeksu to 0-33 %, umiarkowane: 34-66%, wysokie: 67-100%. Do porównania indeksów jakości diety z poziomem wiedzy żywieniowej użyto klasyfikacji według zakresów tercylu swoistych dla badanej grupy.

9.6.2 WZORY ŻYWIENIA I STYLU ŻYCIA A *POSTERIORI*

Do wyodrębnienia wzorów stylu życia i żywienia (DLP) metodą a posteriori użyto analizy głównych składowych z varimax normalizowanej rotacji. Wzory zidentyfikowano biorąc pod uwagę następujące kryteria: (1) wartości własne korelacji zmiennych >1,0; (2) wykres wartości własnych; oraz (3) wyjaśniona całkowita wariancja. Ładunki czynnikowe o wartości bezwzględnej $\geq |0,50|$ zostały uznane za specyficzne dla danego wzoru. Wyniki każdego wzoru i pacjenta obliczone jako iloczyn obciążenia czynnikowego i częstotliwości spożycia. Następnie dla każdego wzoru obliczono tercyle, aby oszacować adherencję do wzorów przez każdego pacjenta.

Analiza wielowymiarowa głównych składowych obejmowała ilość spożytych posiłków w ciągu dnia, wisceralną tkankę tłuszczową oraz częstotliwość spożycia 24 produktów. Spożywane produkty podzielono na następujące grupy: (1) produkty roślinne; (2) produkty mięsne; (3) jasne produkty zbożowe (4) ciemne produkty zbożowe; (5) nabiał; (6) słodczyce i słodzone napoje; (7) produkty typu „fast food” i produkty smażone.

9.7 STATYSTYKA

Do obliczenia wielkości próby wykorzystano oprogramowanie Sample Size Calculator Clinical Calc (ClinCalc, LLC). Przewidywane średnie pHDI-10 ustalono na 27 ± 15 (niski wynik) i 34 (wysoki wynik). Minimalną liczbę osób dla odpowiedniej mocy badania obliczono na 119 dla każdej grupy (PCOS i KON) przy współczynniku zapisów ustalonym na 1, błędzie typu I na poziomie 0,05 i mocy 95%.

W celu uzyskania jednorodnej grupy kontrolnej przeprowadzono dopasowanie uwzględniając status ekonomiczny i wskaźnik BMI⁵⁹. Normalność rozkładu sprawdzono testem Shapiro-Wilka.

Charakterystykę pacjentek, porównanie składu ciała i indeksów jakości diety opisano za pomocą testu t-studenta między dwoma niezależnymi zmiennymi, a dla zmiennych o rozkładzie innym niż rozkład normalny, użyto testu Mann-Whitney’a. Dla zmiennych nieparametrycznych użytych do charakterystyki grup zastosowano test χ^2 . Regresja logistyczna została wykorzystana w celu określenia współzależności między poziomem wiedzy żywieniowej a indeksami jakości diety, zarówno w grupie pacjentek z PCOS jak i KON. Regresja logistyczna została również użyta do przedstawienia współzależności między wysoką adherencją do wzorów stylu życia i żywienia a markerami metabolicznymi, endokrynologicznymi i fenotypami PCOS. Ilorazy szans (OR) i 95% przedziały ufności (95% CI) obliczono między górnymi tercylami wzorców żywieniowych i standardowymi wartościami parametrów metabolicznych. Analizę statystyczną przeprowadzono za pomocą oprogramowania Statistica v.13.1 (StatSoft Polska sp. z o.o., Kraków, Polska).

10 WYNIKI

10.1 HIPOTEZA 1: WSKAŹNIKI JAKOŚCI DIETY, STOPIEŃ OTŁUSZCZENIA CIAŁA ORAZ POZIOM WIEDZY ŻYWIENIOWEJ Kobiet z PCOS RÓŻNIĄ SIĘ OD Kobiet z GRUPY KONTROLNEJ (PUBLIKACJA NR 1).

Zarówno w grupie kobiet z PCOS jak i grupie KON opisano niskie natężenie spożycia produktów ogólnie znanych jako prozdrowotne. Ponadto, grupa kobiet z PCOS charakteryzowała się znamienne niższym niż grupa KON (średnia \pm SD PCOS: $23,5 \pm 10,0\%$ vs KON/: $26,1 \pm 10,0\%$, $p < 0,05$) natężeniem spożycia produktów uznawanych za prozdrowotne (pHDI-10). Natężenie spożycia produktów o niskim IG (IGIDI-4) było również obniżone w grupie PCOS w porównaniu do grupy KON (średnia \pm SD PCOS: $27,5 \pm 13,1\%$, KON: $30,5 \pm 12,7\%$, $p < 0,05$). Najniższą intensywnością spożycia u badanych z PCOS na tle grupy KON charakteryzowały się składowe prozdrowotnych indeksów spożycia tj. owoce, warzywa, oraz sery twarogowe.

Nie wykazano z kolei statystycznej różnicy w natężeniu spożycia produktów niezdrowych (średnia \pm SD nHDI-14 PCOS: $13,0 \pm 7,2\%$, KON: $13,4 \pm 8,2\%$), i produktów o wysokiej zawartości nasyconych kwasów tłuszczowych (średnia \pm SD hSFDI-8 PCOS: $11,9 \pm 7,6\%$, KON: $12,1 \pm 7,7\%$) pomiędzy kobietami z PCOS i grupy KON. Niemniej, zauważono większą tendencję spożycia produktów o wysokiej zawartości cukrów prostych hSDI-4 u kobiet z PCOS (średnia \pm SD $14,9 \pm 13,5\%$) w porównaniu do z grupy KON (średnia \pm SD $13,5 \pm 13,9\%$).

Kobiety z PCOS charakteryzowały się wyższymi parametrami antropometrycznymi od kobiet z grupy KON. Zawartość tkanki tłuszczowej różniła się średnio o $5,4\%$ (średnia \pm SD PCOS: $36,5 \pm 9,7\%$, KON: $31,1 \pm 8,6\%$, $p < 0,05$). Tym samym, 50% kobiet z PCOS charakteryzowało ponad 36% otłuszczenie ciała świadczące o otyłości metabolicznej⁶⁰. 44% kobiet z PCOS miało BMI oznaczające nadwagę i otyłość, natomiast tylko 19% KON kobiet miało BMI powyżej $24,9 \text{ kg/m}^2$. Obwód talii jak i również stosunek obwodu talii do wzrostu (WHtR) był wyższy u kobiet z PCOS (średnia \pm SD talia PCOS: $82,7 \pm 14,3 \text{ cm}$, KON: $75,7 \pm 10,7 \text{ cm}$; WHtR PCOS: $0,5 \pm 0,06$, KON: $0,45 \pm 0,06$, $p < 0,05$).

Poziom wiedzy żywieniowej był znamienne niższy u kobiet z PCOS na tle kobiet z grupy KON (średnia \pm SD PCOS: $15,0 \pm 4,9$ vs KON: $16,7 \pm 5,9$, $p < 0,05$). Wspomniany poziom wiedzy żywieniowej w grupie PCOS nie miał wpływu na wysokość żadnego z analizowanych indeksów jakości diety i otłuszczenia ciała. Natomiast kobiety z grupy KON o wysokiej wiedzy żywieniowej ponad dwa razy częściej miały wysokie natężenie częstotliwości spożycia pHDI-10 (OR 2,25 CI95% 1,0; 4,9), a o połowę niższe natężenie częstotliwości

spożycia hSFDI-8 (OR 0,46 95% 0,2; 1,0). U kobiet z grupy KON zauważono również nieznaczną statystyczną współzależność pomiędzy wysoką wiedzą żywieniową a natężeniem spożycia produktów: nHDI-14 (OR 0,49 CI95% 0,2; 1,0, p=0,07), IGIDI-4 (OR 1,90; CI95% 0,9; 4,2, p=0,09), hGIDI-7 (OR 0,54; CI95% 0,2; 1,1, p=0,10), hSDI-4 (OR 0,58 CI95% 0,3; 1,3, p=0,17).

10.2 HIPOTEZA 2: WYODRĘBNIONE A POSTERIORI WZORY STYLU ŻYCIA I ŻYWIENIA KOBIEC Z PCOS WYKAZUJĄ WSPÓLZALEŻNOŚCI W ZAKRESIE ZAWARTOŚCI WISCERALNEJ TKANKI TŁUSZCZOWEJ A SPOSOBEM ŻYWIENIA SIĘ KOBIEC Z ZESPOŁEM PCOS (PUBLIKACJA NR 2).

Analiza głównych składowych wyodrębniła trzy wzory żywieniowe: zachodni (WDLP), rozważny (PDLP), oraz aktywny (ADLP). WDLP charakteryzował się wysoką zawartością wisceralnej tkanki tłuszczowej, podwyższoną częstotliwością spożycia produktów odzwierzęcych, słodczy, słodzonych napojów, przetworzonych produktów zbożowych, produktów typu „fast-food” i produktów smażonych, a niską częstotliwością spożycia produktów roślinnych. PDLP był związany z wysoką częstotliwością spożycia produktów roślinnych, nabiału, spożywanych posiłków w ciągu dnia oraz intensywnymi ćwiczeniami fizycznymi. ADLP natomiast charakteryzował się wysoką wisceralną tkanką tłuszczową, częstotliwością spożycia produktów roślinnych, aktywnością fizyczną, a niską częstotliwością spożycia produktów typu „fast-food” i produktów smażonych.

10.3 HIPOTEZA 3: WYODRĘBNIONE WZORY STYLU ŻYCIA I ŻYWIENIA RZUTUJĄ NA WARTOŚCI MARKERÓW METABOLICZNYCH U KOBIEC Z ZESPOŁEM PCOS (PUBLIKACJA NR 2).

Kobiety z wysoką adherencją do WDLP, posiadały ponad siedmiokrotnie wyższe ryzyko stężenia trójglicerydów powyżej 150 mg/dL, (OR 7,73 CI95% 1,79; 33,2) i blisko czterokrotne cholesterolu LDL powyżej 135 mg/dL (OR 3,70 CI95% 1,03; 13,27). Niska adherencja do WDLP zmniejszyła ryzyko BMI powyżej 30 kg/m² o 70%, jak również WHtR powyżej 0,5 (OR 0,40 CI95% 0,19; 0,88), HDL poniżej 50 mg/dL (OR 0,19 CI95% 0,04;0,89). Niska adherencja do WDLP obniżyła również ryzyko występowania insulinooporności (HOMA > 2,5) (OR 0,44 CI95% 0,20; 0,99). Kobiety z wysoką adherencją do PDLP miały prawie 58% niższe ryzyko BMI powyżej 25 kg/m² i o 54% niższe ryzyko tkanki tłuszczowej powyżej 35%. Niska adherencja do PDLP była związana z ponad trzy razy wyższym ryzykiem wystąpienia całkowitego cholesterolu powyżej 200mg/dL (OR 3,27 CI95% 1,28; 8,39). Wysoka i niska adherencja do ADLP nie była związana z ryzykiem wystąpienia podwyższonych

markerów metabolicznych. Kobiety z wysoką adherencją do WDLP miały ponad dwa razy wyższe ryzyko posiadania FSH powyżej górnego tercyla, o 65% obniżone ryzyko stężenia testosteronu całkowitego powyżej trzeciego tercyla, o 63% obniżone ryzyko posiadania androstenedionu powyżej trzeciego tercyla. Kobiety z wysoką adherencją do PDLP prawie dwa i pół razy częściej miały fenotyp II PCOS (OR 2,45 CI95% 0,98; 6,16), a kobiety z wysoką adherencją do ADLP posiadały ponad dwa razy wyższe ryzyko fenotypu I (OR 2,10 CI95% 1,00; 4,40).

10.4 **HIPOTEZA 4: WSKAŹNIKI JAKOŚCI DIETY SĄ WSPÓLZALEŻNE Z WYSTĘPOWANIEM RYZYKA MIAŻDŻYCY (PUBLIKACJA NR 3).**

Badania wykazały, że grupa kobiet z PCOS z potwierdzonym wysokim indeksem AIP rzadziej wybierała produkty o niskim indeksie glikemicznym IGIDI-4, w porównaniu z grupą kobiet z niskim AIP. Grupa z wysokim AIP również rzadziej wybierała produkty takie jak: kasza gryczana, owies, makaron pełnoziarnisty lub kasze gruboziarniste.. Nie zauważono współzależności pomiędzy poziomem wskaźnika AIP a natężeniem probiotycznego indeksu jakości diety. Kobiety o wysokim AIP charakteryzowały się również z nadwagą i otyłością (średnia \pm SD BMI highAIP 27.4 ± 5.7 ; lowAIP 23.5 ± 3.3 kg/m²), wysoką zawartością tkanki tłuszczowej (średnia \pm SD highAIP 45.8 ± 25.8 %; low AIP 37.2 ± 22.9 %, $p < 0,05$) oraz otyłością brzuszną (WHR high AIP 0.84 ± 0.10 ; low AIP 0.79 ± 0.06 (-), $p < 0,05$)

11 **MOCNE STRONY BADAŃ**

- Użycie nowych wskaźników jakości diety pozwalających na całościową jej analizę
- Pierwsze jak dotąd/opublikowane badanie analizujące jednocześnie dużą liczbę markerów metabolicznych, parametrów żywieniowych jak i stylu życia kobiet z PCOS;
- Użycie dokładnych, referencyjnych metod analizy składu ciała (pletyzmografia powietrzna) i rozmieszczenia tkanki tłuszczowej (DXA) w badaniach kobiet z PCOS;
- Grupa kontrolna dobierana według wieku i statusu socjoekonomicznego;
- Wykorzystanie wskaźnika ryzyka miażdżycy (AIP) i powiązanie go z zachowaniami żywieniowymi kobiet z PCOS;

12 **SŁABE STRONY BADAŃ**

- Uwzględnienie raportowanej częstotliwości spożycia i aktywności fizycznej, dlatego należy brać pod uwagę ryzyko niedoszacowań;

- Badania retrospektywne oceniały współzależność występowania a nie wpływ czynników, następnym krokiem byłoby podjęcie badań prospektywnych;

13 WNIOSKI

Badania pozwoliły na sformułowanie następujących wniosków:

1. Prozdrowotne wskaźniki jakości diety i wskaźnik diety o niskim IG kobiet z PCOS były na niższym poziomie, w porównaniu z kobietami z grupy KON (cel nr1; publikacja nr 1).
2. Połowa populacji kobiet z grupy z PCOS była otyła i charakteryzowała się wysoką zawartością całkowitej tkanki tłuszczowej (cel nr 1; publikacja nr 1).
3. Kobiety z PCOS miały niższą wiedzę żywieniową, w porównaniu do kobiet z grupy KON (cel nr 1; publikacja nr 1).
4. Analiza zachowań żywieniowych pozwoliła na wyodrębnienie trzech wzorów stylu życia i żywienia u kobiet z PCOS: zachodniego, rozsądnego i aktywnego (cel nr 2; publikacja nr 2).
5. Spożycie produktów roślinnych, nabiału i intensywna aktywność fizyczna związana z rozsądnym wzorem stylu życia i żywienia może istotnie obniżyć ryzyko występowania chorób metabolicznych u kobiet z PCOS (cel nr 3; publikacja nr 2).
6. Spożycie mięsa, słodczy i napojów słodzonych, siedzący tryb życia związany z zachodnim wzorem stylu życia i żywienia istotnie podwyższało ryzyko występowania chorób metabolicznych u kobiet z PCOS (cel nr 3; publikacja nr 2).
7. Wysokie spożycie produktów o niskim IG wiązało się z obniżonym ryzykiem kardiometabolicznym (cel nr 4; publikacja nr 3).
8. Wysoki i średni wskaźnik ryzyka miażdżycy był związany z podwyższonym BMI, wysokim otłuszczeniem ciała oraz otyłością brzuszną u kobiet z PCOS (cel nr 5; publikacja nr 3).

14 PODSUMOWANIE

Celem pracy doktorskiej była analiza uwarunkowań żywieniowych, stanu odżywienia i zaburzeń metabolicznych oraz opracowanie dodatkowych wskazań w dietoterapii kobiet z zespołem PCOS.

Cykl powyższych badań wykazał, że kobiety z PCOS charakteryzowały się zarówno podwyższonym BMI, odsetkiem tkanki tłuszczowej oraz zawartością wisceralnej tkanki

tłuszczowej w porównaniu do kobiet z grupy kontrolnej. Zastosowanie nowych zaprojektowanych wskaźników jakości diety (hGIDI-7, IGIDI-4, hSDI-4, hSFDI-8, pro-DI-4) w dietoterapii może ułatwić bilansowanie diety kobiet z PCOS i wspomóc poprawę parametrów metabolicznych w tej grupie. Wyodrębnienie poszczególnych wzorów stylu życia i żywienia (WDLP, PDLP, ADLP) wskazało na konkretne uwarunkowania żywieniowe w zaburzeniach metabolicznych kobiet z PCOS. Rekomendacje dietoterapii w PCOS do tej pory nie uwzględniały spożycia produktów pochodzenia zwierzęcego. Zalecenia obejmują ograniczenie produktów o wysokiej zawartości nasyconych kwasów tłuszczowych, w tym mięsa czerwonego i nabiału o wysokiej zawartości tłuszczu. Nasze badania po raz pierwszy wykazały, że niskie spożycie produktów mięsnych, zarówno drobiu jak i mięsa czerwonego, wpływa korzystnie na zaburzenia metaboliczne u kobiet z PCOS. Mając na uwadze, że najbardziej prozdrowotne dla kobiet z PCOS okazały się produkty roślinnego pochodzenia, takie jak warzywa, nasiona strączkowe) wprowadzenie zasad diety planetarnej jako dietoterapii u kobiet z PCOS może być zasadne i warte rozpatrzenia. Częstotliwość spożycia produktów o właściwościach prebiotycznych, takich jak kasze gruboziarniste, pełnoziarniste makarony czy płatki owsiane mogą skutecznie obniżać ryzyko występowania miażdżycy u kobiet z PCOS. Podsumowując, sposób żywienia i życia kobiet z PCOS jest ważnym czynnikiem obniżającym ryzyko wystąpienia chorób metabolicznych.

15 ZALECENIA DLA KOBIET Z PCOS NA PODSTAWIE CYKLU BADAŃ

W celu obniżenia ryzyka chorób metabolicznych, kobiety z pcos powinny:

- uwzględniać w zwyczajowej diecie produkty o charakterze prozdrowotnym i niskim indeksie glikemicznym (publikacja nr 1 i nr 3);
- spożywać produkty prebiotyczne, takie jak: kasze gruboziarniste, płatki owsiane, pełnoziarniste makarony i ryż przynajmniej dwa razy w tygodniu (publikacja nr 3);
- ograniczać spożycie produktów pochodzenia zwierzęcego, a jednocześnie zwiększyć spożycie produktów pochodzenia roślinnego (warzywa, owoce, warzywa strączkowe) (publikacja nr 2);
- wdrożyć aktywność fizyczną o wysokim natężeniu (np. aerobik, bieg, czy szybka jazda rowerem) i ograniczyć siedzący tryb życia do minimum (publikacja nr 2);
- być edukowane na temat sposobu bilansowania diety obejmującego cały wzór żywieniowy, a nie pojedynczych grup produktów (publikacja nr 1, nr 2 i nr 3).

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Review

Emerging Trends in Research on Food Compounds and Women's Fertility: A Systematic Review

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Featured Application: The application of this systematic review is a comprehensive study of food compounds, nutrition, food production, health and environmental sciences in improving female fertility.

Abstract: Pro-healthy behaviours, including the diet, are significant factors in maintaining women's fertility health. However, to improve the patient's nutrition management, it is important to seek food-derived bioactive compounds to support fertility treatment. This review analysed recent studies of food compounds related to fertility, using databases including PubMed, Web of Science and Science Direct as well as PRISMA (preferred reporting items for systematic reviews) to ensure complete and transparent reporting of systematic reviews. This review lists foods associated with a higher birth rate, using original papers from the last five years (2015). The analysis included the impact of food compounds such as caffeine, fatty acids, folates and vitamin D, as well as the intake of fish, whole grains, dairy and soya. In addition, dietary patterns and total diet composition supporting women's fertility were also analysed. The results will encourage further research on the relationship between food components and fertility.

Keywords: female infertility; nutrient; vitamin D; folates; soy; antioxidants; minerals; vitamins; food research trends; environmental impact

1. Introduction

Fertility, known as the ability to establish a clinical pregnancy, is dependent on multiple factors, including female age, environmental pollution, diet, tobacco use, alcohol intake, as well as diseases affecting endocrine function and the anatomy of the reproduction system [1,2]. In turn, infertility is medically defined as a failure to establish a clinical pregnancy after 12 months of regular and unprotected sexual intercourse. It is estimated that infertility in women of child-bearing age is 1 in 7 couples in developed countries and 1 in 4 couples in developing countries, which is increasing significantly [1]. The demand for infertility services is still growing and can be improved thanks to technological advances and the development of medicine.

Factors influencing fertility may be unmodifiable, such as age and environment, or could be medically treated, such as health status—including endocrine disorders. Furthermore, some factors could be modifiable, such as health behaviours, dietary patterns and micronutrient intake.

It has been confirmed that in-vitro fertilisation success rate seems to be highest during the summer months when the pollution of particulate matter (PM) is at its lowest [3]. Phthalates, which may

negatively influence the fertility health of women [4], were found to affect the occupational health of hairdressers [5]. Some primary factors, such as excess body weight or underweight, also decrease the rate of fertility [6,7]. Body saturation with vitamin D was suggested to have a beneficial influence on fertility [8–12].

The recommendations by the Committee of the American Society for Reproductive Medicine in collaboration with the Society for Reproductive Endocrinology and Infertility American Society for Reproductive Medicine, advise females to follow a healthy diet, avoid alcohol and decrease caffeine intake to a moderate level [13]. It is also advisable for women to supplement folate (400 µg/day) to decrease the chance of neural tube defects [13]. However, there is some evidence showing that some food ingredients and specific dietary patterns in women may be positively associated with pregnancy and live birth rates [14–16].

One of the food ingredients widely discussed in the context of fertility is sugar. It was shown that its presence in the diet reduces nutritional density and worsens its nutritional quality [17]. The possible mechanism between sugar-sweetened beverages and fertility was explained by increased insulin resistance, leading to oxidative stress. This relation may deleteriously affect semen quality and ovulatory function. Such a mechanism was hypothesised by Hatz, et al. [18], who studied a group of nearly five thousand women and found that fertility and the amount of sugar consumed in sugar-sweetened beverages (particularly sodas and energy drinks) was associated with lower fecundability [18].

A large group of compounds that are still being studied are bioactive compounds in food. Their roles in oxidative stress and fertility have been presented in many studies [19–22], including several studies on female animal models and bioactive food compounds [23–25]. Their role is hypothesised to diminish the effect on the endocrine system of disruptive chemicals. For example, there is some evidence that animals treated with BPA (Bisphenol A), after maternal supplementation of folate and a high phytoestrogen diet, influence oocyte growth and foetal methylation of DNA [26,27]. Other studies have highlighted that a low dose (but not a high dose) of ginger powder, improved the follicle counts of rats [23]. Therefore, it is not clear what dose will be as effective on humans. Additionally, human fertility is affected by complex and multiple factors which could be difficult to expose animals to.

The time of preconception may motivate couples to adopt healthier behaviours and to seek information on factors improving fertility. Even though medical consultation is still the most common source for seeking advice for fertility, social media and the internet also play significant roles [28]. The choice of supplement options is vast, as the fertility supplement market is continuously growing and it has been estimated to be worth USD 1.45 billion globally in 2018 [29]. The use of supplements is not always recommended by healthcare professionals, and their misuse may even pose a threat to health.

The literature related to food compounds and fertility has not been extensively collected, and there is no consensus on what the trends are in these studies or what groups of food ingredients should be considered as supportive or detrimental to fertility. In light of this evidence, an analysis of diet ingredients, food research (e.g., ginger, BPA) and fertility could lead to new supporting therapy strategies that affect the birth rate through the modulation of eating habits. Accordingly, this review provides an analysis of new food compound research influencing fertility and revises recent studies involving the impact of food bioactive compounds on women's fertility.

2. Materials and Methods

2.1. Search Strategy

A systematic search of literature published before December 2019 was performed in PubMed (National Institute of Health, USA) (<https://www.ncbi.nlm.nih.gov/pubmed>), Web of Science (Clarivate Analytics, USA) (<https://www.webofknowledge.com>), Scopus (Elsevier, RELX Group plc), (<https://www.scopus.com>) and Science Direct (Elsevier, RELX Group plc) (<https://www.sciencedirect.com>).

com/) to identify studies describing the association between bioactive food compound intake and women's fertility. The search strategy was restricted to English language original articles. The following types of documents were excluded: review, book and book chapters.

The search was based upon the following index terms, titles or abstracts listed below: ((bioactive OR nutrient OR food OR ingredient OR vitamin OR mineral OR antioxidant OR phytonutrient) AND (fertility)). The protocol was registered in the "PROSPERO International prospective register of systematic reviews" PROSPERO 2020: CRD42020160223 and is available on https://www.crd.york.ac.uk/prospERO/display_record.php?ID=CRD42020160223.

2.2. Inclusion and Exclusion Criteria

Studies on the influence of food compounds on infertility, signs and symptom changes in patients affected by infertility were included. Studies using different food components concerning changes in the concentration of biomarkers for the assessment of infertility and changes in symptoms were analysed. The systematic search included a population of women in the reproductive age 21–50 with diagnosed infertility or healthy women trying to conceive. All studies conducted on animals and case reports were excluded. The studies included were both qualitative and quantitative. A quality assessment of questionable articles was performed with a checklist described by Kmet et al. [30]. Articles written in a language other than English were excluded. Since the search included new trends in food research, it only included articles within the last five years (2015).

2.3. Study Extraction Process

The study selection process includes an assessment of articles based upon titles, abstracts and full text, which were performed by two independent researchers in parallel in each database. At each step of the assessment, all disagreements between the researchers were resolved after consultation with the review coordinator. Only in the case of disagreement during the title assessment process was the paper included in the next step. Full-texts of all records that were selected in the abstract review phase were searched for through the library of Poznan University of Life Sciences.

3. Results

A total of 4609 studies were screened for inclusion in this systematic review. After the elimination process (Figure 1), a total of 25 qualitative studies and 4 quantitative studies were included. The studies were performed internationally and included the following countries USA (n = 20) [15,31–45], Australia (n = 1) [46], New Zealand (n = 1) [46], Ireland (n = 1) [46], United Kingdom (n = 2) [46,47], China (n = 1) [48], Denmark (n = 4) [41,43,49,50], Greece (n = 1) [14], Iran (n = 2) [51,52], Brazil (n = 2) [53,54], Canada (n = 1) [43], Russia (n = 1) [55], Italy (n = 2) [56,57], Spain (n = 1) [58]. The articles concerned female fertility and the intake of a Mediterranean dietary pattern (n = 2) [51,57], fruit, vegetables and whole grain intake (n = 3) [38,46,53], fish (n = 1) [42], dairy (n = 3) [15,43,44], types of fatty acids (n = 4) [39–41], soy (n = 2) [32,33], caffeine (n = 3) [45,50,54], folate and B12 (n = 4) [34,35,59,60], melatonin (n = 1) [58], CoQ10 (n = 1) [48] as well as a combination of different compounds (n = 4) [37,47,52,55]. The women who participated in the studies were either planning pregnancy (n = 6) [36,40,41,45,46,55], infertile (n = 3) [49,51,55], undergoing or subjected to assistive reproductive technology (ART) therapy (n = 16) [14,15,31,34,35,39,42,44,50,52–54,57,58]. The main results of the studies have been summarized in Table 1 (qualitative studies) and Table 2 (quantitative studies).

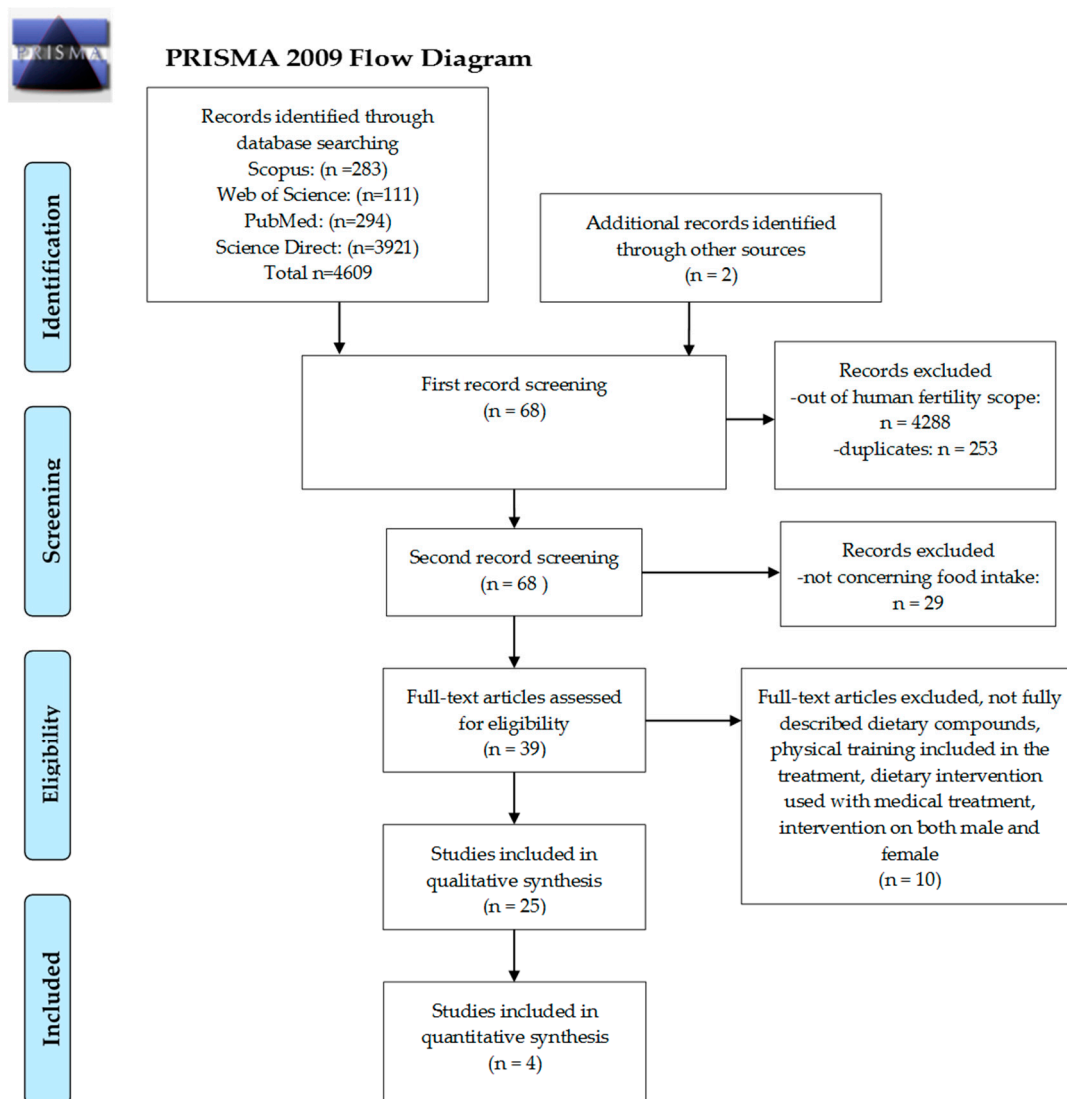


Figure 1. Preferred reporting items for systematic reviews (PRISMA) Study selection process diagram.

Table 1. Qualitative studies on bioactive food components and women’s fertility included in the review process.

Study	Sample	Assessment Tool	Results
Dietary Patterns			
Ricci et al. 2019 [57], Italy	n = 474 ART	FFQ	There were no consistent associations between adherence to a Mediterranean diet and successful obstetrics outcomes. There was an effect of the average adherence score on a Mediterranean diet on oocyte number and clinical pregnancy in women >35 years old but no effect on live birth.
Jahangirifar et al. 2019 [51], Iran	n = 140 infertile	FFQ	High adherence to the healthy dietary pattern was associated with a high average number of oocytes when compared with low adherence.
Karayiannis et al. 2018 [14], Greece	n = 244 non-obese ART	FFQ	Mediterranean diet score was positively related to clinical pregnancy and live birth among women <35 years old but not among women ≥35 years
Gaskins et al. 2019 [31], USA	n = 357 ART	FFQ	Pro-fertility dietary pattern (supplemental intake of folate, B12, low-pesticide residue produce, high intake of whole grains, seafood, dairy, soy foods) has a higher likelihood of live birth.

Table 1. Cont.

Study	Sample	Assessment Tool	Results
Fruits, Vegetables and Wholegrains			
Grieger et al. 2018 [46] Australia, New Zealand, Ireland, UK	n = 5628 nulliparous with low-risk singleton pregnancies	FFQ	Low intake of fruit and high intake of fast food was associated with an increase in time to pregnancy and infertility
Braga et al. 2015 [53], Brazil	n = 269 ART	FFQ	The intake of cereals, vegetables and fruits positively influenced the embryo quality at the cleavage stage. The intake of fruits influenced the likelihood of blastocyst formation. The intake of red meat had a negative effect on the implantation rate and the likelihood of pregnancy.
Gaskins et al. 2016 [38], USA	n = 273 ART	FFQ	High whole grain intake was related to a high probability of live birth.
Fatty Acids			
Eskew et al. 2017 [39], USA	n = 60 ART	Serum fatty acid index	Trans FA and elaidic FA had a negative correlation with IVF outcomes, other FA did not have any consistent correlations
Mumford et al. 2016 [40], USA	n = 259 regularly menstruating women	24h dietary record Serum reproductive hormones	Dietary docosapentaenoic acid (DPA) intake was associated with a reduced risk of anovulation
Wise et al. 2018 [41], USA, Denmark	n = 1290 (USA), n = 1126 (Denmark) attempting pregnancy	FFQ	High trans FA and low ω -3 FA intake was associated with reduced fecundity
Fish			
Nassan et al. 2018 [42], USA	n = 351 ART	FFQ	Fish intake was positively related to the proportion of cycles resulting in a live birth.
Dairy			
Wise et al. 2017 [43], USA, Denmark	n = 2426 attempting pregnancy	FFQ	High phosphorus and lactose intake was associated with high fecundability
Afeiche et al. 2015, [15], USA	n = 232 ART	FFQ	High dairy intake was associated with high chances of live birth
Souter et al. 2017 [44], USA	n = 265 ART	FFQ Antral follicle count (AFC)	High dairy protein intake was associated with lower AFC
Caffeine			
Setti et al. 2018 [54], Brazil	n = 524 ART	FFQ	≥ 3 servings of regular or diet soft drinks were associated with oocyte dysmorphism, lower embryo quality on 2–3 days of culture, and had a mild effect on blastocyst formation, implantation and pregnancy rate. Consumption of sweetened coffee was negatively associated with embryo quality.
Wesselink et al. 2016 [45], USA and Canada	n = 2135 pregnancy planner	FFQ	Preconception caffeine intake was not appreciably associated with pregnancy. Caffeinated coffee intake showed little association with pregnancy. Black tea, but not green tea, was associated with a slight decrease in pregnancy
Lyngsø et al. 2019 [50], Denmark	n = 1708 ART	FFQ	Intake of 1–5 cups of coffee versus none had a higher probability of achieving a pregnancy or a live birth when receiving IUI. No associations were found, between coffee consumption and achieving a pregnancy or a live birth from IVF/ICSI.
Soya			
Chavarro et al. 2016 [32], USA	n = 239 ART	FFQ Urinary BPA	BPA was inversely associated with live birth rate unless women had a high intake of soy.
Vanegas et al. 2015 [33], USA	n = 315 ART	FFQ	Dietary soy intake was positively related to the probability of live birth.

Table 1. Cont.

Study	Sample	Assessment Tool	Results
Folate			
Gaskins et al. 2019 [34], USA	n = 304 ART	FFQ residence-based daily nitrogen dioxide (NO ₂), ozone, fine particulate, and black carbon concentrations	Supplemental folate intake modified the association of NO ₂ exposure and livebirth
Mínguez-Alarcón et al. 2016 [35], USA	n = 178 ART	FFQ Urinary BPA	High BPA was associated with a lower probability of implantation among women with <400 µg/day intake of folate, but not among women with ≥400 µg/day
Vitamin D			
Fung et al. 2017 [36], USA	n = 132 healthy attempting pregnancy	Serum 25(OH)D, 24h diet recalls every 3 months	Women with vit. D intake below EAR and serum 25(OH)D at risk for inadequacy had a lower pregnancy rate
Jensen et al. 2019 [49], Denmark	n = 16212 infertile	Vitamin D fortification in margarine (mandatory in the nation since 1985)	Exposition to fortified margarine was associated with an increased chance of live birth.
Antioxidants			
Skalnaya et al. 2019 [55], Russia	n = 150 healthy n = 169 pregnant n = 75 miscarriage n = 91 primary infertility	Serum metal levels Iron, copper, manganese	Serum Cu levels in women with miscarriage and infertility were 30 and 35% lower than those in pregnant women. Serum Cu levels were significantly associated both with and reproductive health problems
Li et al. 2019 [37], USA	n = 349 ART	FFQ	There were inverse associations of β-carotene intake from foods and of lutein and zeaxanthin intake with live birth rates. Total consumption of vitamins A, C, and E before infertility treatment was not associated with live birth rates.

25(OH)D—25-hydroxyvitamin D, ART—Assistive Reproductive Technologies, AMH—Anti-Mullerian Hormone, FSH—Follicle-stimulating Hormone, FFQ—Food Frequency Questionnaire, EAR—Estimated Average Requirement, BPA—Bisphenol A, FA—fatty acid, IVF—In Vitro Fertilization, ICSI—Intracytoplasmic Sperm Injection.

Table 2. Quantitative studies concerning bioactive food components and female fertility qualified for the review.

Study	Treatment	Sample	Clinical Pregnancy Rate [%]	Embryo Quality	Fertilisation Rate [%]	Live Birth Rate [%]
Yangying et al. 2018 [48], China	Coenzyme Q10 600mg/day 60 days preceding IVF	Control group n = 93	25	0 (0;1.75)	45	22
		Study group n = 76	32	1 (0;2)	67	32
		poor ovarian response	50	2.3 (0.5;4.0)	51.1	50
Espino et al. 2019 [58], Spain	Melatonin 3mg/day and 6mg/day for 40 days	healthy control n = 10	50	2.0 (0.4;3.6)	47.9	20
		subjected to 2nd IVF:	20	5.1 (2.8;7.4)	67.4	30
		no melatonin n = 10	30	4.6 (2.8;6.3)	63.7	30
Agrawal et al. 2012 [47], UK	Multiple micronutrient supplement or folic acid alone 3–6 months	Micronutrients n = 29	66.7	N/A	N/A	N/A
		Folic Acid n = 27	39.3			
Fatemi et al. [52], Iran	Vitamin E, 400 mg/day and vitamin D3, 50,000 IU/one in two weeks, placebo 8 weeks	Intervention group n = 52	62.1	71.20%	73.3	20
		Placebo n = 53	22.6	67.50%	70.9	7

IVF—In Vitro Fertilization, ICSI—Intracytoplasmic Sperm Injection.

4. Discussion

This systematic review aimed to identify emergent trends in food compounds studies which influence women's fertility. We qualified a total of 29 studies from the past five years among women planning to conceive either naturally or with assisted reproductive technologies.

4.1. Dietary Patterns, Intake of Fruits, Vegetables and Whole Grains

The modern diet and nutrition analysis based on dietary patterns also assessed the nutrition behaviours as a whole, rather than looking at a single nutrient. Dietary patterns are defined as the quantity, variety, or combination of different foods and beverages in a diet and the frequency in which they are habitually consumed. The frequency reflects food compounds consumed in the diet directly. The most common dietary patterns are pro-healthy, Mediterranean, western and dairy-related [61,62]. The results of this systematic review (presented in Table 1) showed that a high intake of fruits and vegetables and adherence to a pro-healthy dietary pattern is associated with a higher average number of oocytes [51] and embryo quality [53]. The Mediterranean dietary pattern has been associated with supporting fertility health in women. Karayannis et al. found that this dietary pattern is only related to the live birth rate in women under the age of 35 [14]. Another study showed that it was related only to higher oocyte number and clinical pregnancy in women over 35 [57]. The Mediterranean diet is characterised by a high intake of extra virgin olive oil, vegetables, fruits, cereals, nuts and legumes, a moderate intake of fish and other meat, dairy products and red wine and low intakes of eggs and sweets [63]. Another dietary pattern used in the studies was a fertility diet dietary pattern characterised by the intake of supplemental folate and B12, low-pesticide residue produce, high intake of whole grains, seafood, dairy and soy foods. This dietary pattern was positively related to the likelihood of live birth [31].

4.2. Fatty Acids and Fish Intake

The current review has shown that there is no conclusive evidence about the impact of polyunsaturated fatty acids, including the intake of omega-3 on human fertility [13]. The results of the review are inconclusive: two studies found an association between omega-3 fatty acids and fertility [40,41], while another study found no impact of these fatty acids on fertility [39]. However, all of the studies analysing fatty acid intake found that the amount of trans fatty acid consumed is negatively related to the live birth ratio [39,41]. These results also support Grieger et al., who found that a high consumption of fast foods (a rich source of trans fatty acids) influences fertility [46].

4.3. Dairy

For many years, the topic of high dairy intake has been controversial and linked with both a positive and negative impact on the health of women [16,64,65]. Nevertheless, to date, most of the studies concerning female reproductive health have been skewed towards a positive association. Moreover, all of the studies in this systematic search, including the period 2015–2019 concerning dairy intake and fertility, have found at least a small positive relationship between these variables [15,43,44]. It should be noted that dairy foods are generally perceived as a pro-healthy dietary attribute. We studied this group of foods previously and found that a more significant effect on dairy consumption by women was the family environment than health-related protective factors [66].

4.4. Caffeine

Decreasing the caffeine intake to moderate during the time of preconception has been recommended to couples who plan pregnancy [13]. A high intake of caffeine, especially black tea [45] and coffee with added sugar and diet soft drinks [54] has been related to a lower live birth rate. However, coffee intake of 1–5 cups daily has been associated with higher chances of a live birth than none [50]. The intake of caffeine and coffee may be associated with more favourable dietary patterns and health behaviours

which could influence fertility [67]. This could be the reason why different types of caffeinated beverages bring contrasting results.

4.5. Soy

The use of nutrients as factor diminishing adverse health effects of environmental pollutants was found in research concerning soy. Soy, as the food product containing phytosterols, could alleviate the effect of endocrine disruptor bisphenol A. This hypothesis is supported by a study concerning women undergoing ART, urinary bisphenol A and soy intake and their influence on live birth rate [32]. Intake of soya, regardless of environmental pollutants, was also related to a higher probability of life birth [33]. High soy intake has also been related to weight loss in women with polycystic ovary syndrome (PCOS), which may improve health and disease results [68]. The results of the above studies show that food ingredients may not always have a direct impact on fertility and their indirect impact is equally important. However, more studies concerning soy intake on fertility and women's health are needed. Many studies suggest that high soy intake may cause interference with ovarian function because of its high phytoestrogen content [69,70]. More studies are needed to determine the appropriate intake of soy of women trying to conceive, since an excessive intake of soy may not be safe.

4.6. Folate

The Center for Disease Control and Prevention (CDC) in the United States, recommends that healthy women with a low risk of birth defects should supplement 400 µg a day of folic acid at least 12 weeks before conception and early pregnancy to avoid neural tube defects [71]. However, it is unknown whether folate intake is related to female fertility. Recent studies have turned to methylenetetrahydrofolate reductase (MTHFR) gene mutations as the cause of recurrent miscarriages [72]. It seems that supplementation of vitamins B6, B12 and supraphysiologic methylfolate could help women with MTHFR gene mutations to conceive [73]. A high intake of folate and B12 was associated with an increased birth rate in women undergoing ART [59]. A high folate-to-homocysteine ratio was related to a lower risk of anovulation in regularly menstruating females [60]. Interesting retrospective studies were also conducted on supplemental folate intake and pollutant exposure among women undergoing ART. The subjects with high pollutant exposure had a lower rate of live birth [35] or implantation ratio [34]; however, folate supplementation positively modified these results in both studies. These results agree with the animal studies mentioned previously [26,27].

4.7. Vitamin D

During the current study, a number of studies were found which analysed the effect of vitamin D [8–11,36,49,74–78]. Nine of them showed a positive, statistically significant association with female fertility [8,9,11,36,49,74,76–78]. However, since only possible interactions with food compounds were searched for, and vitamin D is mostly formed under sun exposure, two of them concerning vitamin D dietary intake were included in the review. Summing up the issues of vitamin D and fertility, it should be emphasised that food products fortified with vitamin D could be advisable [49] for some populations, not only because of the fertility support but also overall health [79].

4.8. Antioxidants

The search also resulted in study findings involved in other single micronutrients. In a Russian study concerning serum metal concentration in the blood of women, it was found that females with infertility and miscarriage had a lower concentration of copper than pregnant women [55]. Moreover, there was no difference between the copper levels of pregnant women and a healthy control group, which supports the hypothesis that copper may play a role in female fertility.

A diet rich in antioxidants, such as the Mediterranean dietary pattern could improve fertility, although the only recent study concerning the intake of antioxidants did not support this hypothesis. Moreover, the intake of foods with a high concentration of β-carotene, lutein and zeaxanthin was

inversely associated with live birth rates [37]. The reasoning of these results may be variable, starting from the accuracy of the food frequency questionnaire used in the study to the dietary pattern which leads to these results. The most important is the fact that supplementing antioxidants as fertility support or for other health conditions could be dangerous and should not be advised to the patients.

4.9. Other Food Compounds

Most of the studies found in the systematic search were qualitative and retrospective, although four prospective randomised trials published between 2015 and 2019 were also included in the review (Table 2). The studies concerned coenzyme Q10 [48], melatonin [58] and multiple nutrient supplementation of vitamin E and D [52] as well as numerous micronutrient or only folate supplement [47]. All of the included study interventions had a positive effect on the pregnancy rate and should be further studied to support fertility treatment nutritionally.

5. Conclusions

In conclusion, it should be noted that reproductive performance is influenced by food and type of nutrition. The findings of the current study suggest that the importance of food production. In particular, the availability and intake of pro-healthy food compounds is a significant factor supporting fertility in females. Women planning pregnancy should especially ensure an intake of fruits and vegetables, folate and vitamin D. A high intake of sweetened beverages and trans-fatty acids appears to decrease the chance of pregnancy and live birth rate. Soy food intake needs to be further analysed because of its endocrine-disruptive properties. Environmental pollution influences fertility around the world, and the appropriate intake of bioactive food compounds could diminish this effect. However, the excessive intake of specific micronutrients, such as antioxidants, may decrease fertility. More randomised prospective studies are needed to analyse the impact of micronutrients on fertility, taking into consideration the patient environment and environmental pollution.

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OŚWIADCZENIE

Jako współautor pracy pt. *Emerging Trends in Research on Food Compounds and Women's Fertility: A Systematic Review. Appl. Sci. 2020, 10, 4518.* oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: *metodologia, pisanie-recenzja i redagowanie, zatwierdzenie ostatecznej wersji manuskryptu*. Mój udział procentowy w przygotowaniu publikacji określam jako 10%.

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Jako współautor pracy pt. *Emerging Trends in Research on Food Compounds and Women's Fertility: A Systematic Review. Appl. Sci. 2020, 10, 4518.* oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: *koncepcję, metodologię, przeprowadzenie badań, zasoby, nadzór, finansowanie, administracja, pisanie-oryginalne opracowanie projektu, zatwierdzenie ostatecznej wersji manuskryptu.* Mój udział procentowy w przygotowaniu publikacji określam jako 30%.

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(podpis oświadczającego)

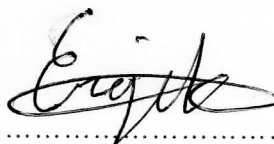
OŚWIADCZENIE

Jako współautor pracy pt. *Emerging Trends in Research on Food Compounds and Women's Fertility: A Systematic Review. Appl. Sci. 2020, 10, 4518.* oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: *metodologia, przeprowadzenie badań, pisanie-oryginalne opracowanie projektu, pisanie-recenzja i redagowanie, zatwierdzenie ostatecznej wersji manuskryptu.* Mój udział procentowy w przygotowaniu publikacji określam jako 5%.

Wkład Aleksandry Bykowskiej-Derdy określam jako 55%,

obejmował on: *koncepcję, metodologię, przeprowadzenie badań, przechowywanie danych, pisanie-oryginalne opracowanie projektu, zatwierdzenie ostatecznej wersji manuskryptu.*

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(podpis oświadczającego)



Diet quality scores in relation to fatness and nutritional knowledge in women with polycystic ovary syndrome: case–control study

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Abstract

Objective: The purpose of the study was to analyse the dietary habits identified by diet quality scores (DQS) in the scope of body fatness (BF) and nutritional knowledge (NK) of polycystic ovary syndrome (PCOS) women.

Design: Case–control study. The DQS were assessed by Dietary Habits, and Nutrition Beliefs Questionnaire (KomPAN, The Committee of Human Nutrition, Polish Academy of Science) included food frequency consumption of thirty-three food items and was formulated by six diet indexes: Pro-Healthy-Diet-Index (pHDI-10), Non-Healthy-Diet-Index (nHDI-14), High-Glycemic-Diet-Index-7 (hGIDI-7), Low-Glycemic-Diet-Index-4 (lGIDI-4), High-Sugar-Diet-Index-4 (hSDI-4) and High-Saturated-Fats-Diet-Index-8 (hSFDI-8). The BF was analysed by air displacement plethysmography (BodPod, Life Measurement Inc.). NK was assessed by using the twenty-five ‘true or false’ statements included in the KomPAN questionnaire.

Setting: Poland, Clinical Hospital, Department of Endocrinology, Metabolism, and Internal Diseases.

Participants: The study group included 122 PCOS women and 116 age- and socio-economic status-matched healthy controls (CON) aged 17–44 years.

Results: Higher BF and lower NK in PCOS women *v.* controls were observed. PCOS women had a lower pHDI-10 and lGIDI-4 than CON. There was no relation between NK and DQS in PCOS women. The higher NK in the CON group was associated with increased intensity of pHDI-10 and lower frequency of hSFDI-8 levels.

Conclusions: Pro-healthy DQS and NK of PCOS women in this study were lower than CON. Professional dietary education might improve dietary behaviours and understanding of the necessity of dietary habits modification in this group. A multi-disciplinary approach is needed in the treatment of PCOS women.

Keywords

PCOS
Diet quality scores
Nutritional knowledge
Body fatness
Food-frequency questionnaire

Polycystic ovary syndrome (PCOS) is a common female endocrinopathy, recognised as a heterogeneous disorder, characterised by hyperandrogenism, ovulatory dysfunction and polycystic ovary ultrasound image⁽¹⁾. The prevalence of PCOS ranges between 8 and 13% around the world and indicates that it has become a major public health issue worldwide⁽²⁾. About 50% of diagnosed women are obese or overweight⁽³⁾. Consequently, PCOS women are at increased risk of insulin resistance and metabolic syndrome⁽⁴⁾.

The choice of treatment is related to the symptoms such as menstruation abnormalities, androgen excess and infertility^(1,5). One of the main goals of PCOS therapy

is to decrease metabolic consequences related to obesity, fatness, insulin resistance and metabolic syndrome. Therefore, it is important to reduce excess of fat mass related to obesity and insulin sensitivity in PCOS women. According to the Androgen Excess Society and the European Society of Endocrinology, PCOS therapy should be based on lifestyle changes, including increased physical activity and dietary modifications concerning the intake of SFA, low Glycaemic Index (GI) foods and weight reduction if necessary^(6,7). Following this, diet quality recommendations and lifestyle modifications for PCOS women should be the prior treatment approach. Despite many studies,

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the optimum and effective diet composition has not yet been identified. A limited number of papers analysing the correlation between diet quality and body composition in PCOS women are available^(8,9). The only confirmed beneficiary strategy for obese PCOS women was concluded by Moran *et al.*⁽¹⁰⁾ and indicated weight loss, without defined diet composition. Other studies suggest instead the role of the particular features of the diet like GI, energy intake reduction, protein and carbohydrates in the management of PCOS^(11–18). Only a few studies analysed the dietary patterns of PCOS women, while their relation to body fatness (BF) had not been studied yet^(19,20). Bearing in mind the fact that diet is the composition of many nutrients, it is increasingly recognised that whole dietary scores are a more important predictor of non-communicable disease risk^(21–23). Moreover, the analysis of overall dietary scores more closely parallels real life, where subjects do not take isolated nutrients but rather as meals consisting of a variety of foods with complex combinations of nutrients which may be interactive or synergistic. The current approach to examine the link between nutrition and diseases recommends moving from single nutrients to dietary patterns, including a group of foods as diet quality scores (DQS). For this reason, the nutritional management of PCOS should be discussed and debated under consideration of overall diet quality and then selected nutrients and their relation to the BF.

Dietary patterns are influenced by social, physiological and economic factors and vary between individuals and populations^(24,25). The status and critical role of nutrition knowledge (NK) have been hypothesised and are still uncertain in public health nutrition. Health abnormalities might be an additional significant factor influencing their dietary choices. As proved in previous studies, nutrition education can cause the change in nutrition behaviours⁽²⁶⁾, body weight and prevalence of obesity^(27,28). To the best of our knowledge, no studies were investigating whether the NK of PCOS women could be related to their dietary behaviours. Considering that the search of mutual relations between DQS, BF and NK will give a possibility to plan, complementary therapy addresses metabolic abnormalities of PCOS women.

The limited amount of literature in this area provides a basis for further research on the recommended composition of the diet in relation to BF and NK of PCOS women. Therefore, based on the presented studies, it is essential to determine the relation of the DQS, NK and BF in PCOS and compare these with a group of healthy women with similar age and socio-economic status.

Materials and methods

Participants

This case–control study included 122 women with PCOS (PCOS) and 116 age and socio-economically matched

healthy controls (CON). Participants were selected and diagnosed in the Department of Endocrinology, Metabolism and Internal Diseases. The patients flow chart is shown in Fig. 1. Women with PCOS were classified according to the Rotterdam criteria⁽²⁹⁾, which are the most common diagnostic criteria for PCOS. Rotterdam criteria recommend PCOS to be diagnosed when at least two of the following three features were present: (1) oligoovulation; (2) hyperandrogenism (elevated androgen levels: testosterone >2.67 nmol/l, free testosterone >11 pmol/l and/or free androgen index >5.5) or hyperandrogenisation (acne and hirsutism) and/or (3) ultrasonographic findings: the presence of at least twelve follicles in each ovary measuring 2–9 mm in diameter, and/or ovarian volume more than 10 ml. Lack of food allergies and intolerances were inclusion criteria. The CON women were a convenient sample of female volunteers recruited through advertising at the university, local workplaces and public spaces. Inclusion criteria for CON were normal ovulating cycles with no signs of hyperandrogenism. Chronic hepatic, renal and rheumatic diseases, overt hypothyroidism, steroid therapy in the last 3 months and pregnancy were exclusion criteria for both PCOS and CON groups. The use of oral contraceptives was also among exclusion criteria for both groups, due to the inability of PCOS diagnosis while using this type of pharmacotherapy. The same day after endocrinologist appointment, all the participants were directed to the Institute of Human Nutrition and Dietetics, Poznan University of Life Sciences, where the body composition was measured and a dietary interview was performed. The study appointments took place in the mornings, between October 2016 and January 2018.

One hundred seventy-five patients were screened towards PCOS diagnosis between 2016 and 2018, from which 134 patients had positive PCOS diagnosis. One hundred forty-six subjects were self-reported as healthy, but after the screening process, six participants were rejected. During the matching process (described in the Statistics part), twelve participants with PCOS and twenty-four healthy participants were rejected due to age and/or socio-economic status. The BMI of the rejected participants was no different than the study group.

The diet quality scores

The DQS were calculated as dietary indexes, collected with a validated questionnaire (the Dietary Habits and Nutrition Beliefs KomPAN Questionnaire) developed by the Committee of Human Nutrition, Polish Academy of Science⁽³⁰⁾. The interview was conducted by a qualified pollster. Closed questions regarding the frequency of consumption of thirty-three food groups were used in the questionnaire. Six food frequency intake categories were used: (1) never, (2) 1–3 times/month, (3) once a week, (4) 2–3 times/week, (5) once a day and (6) a few times during the day. For each food item, the categories of frequency consumption were converted to values

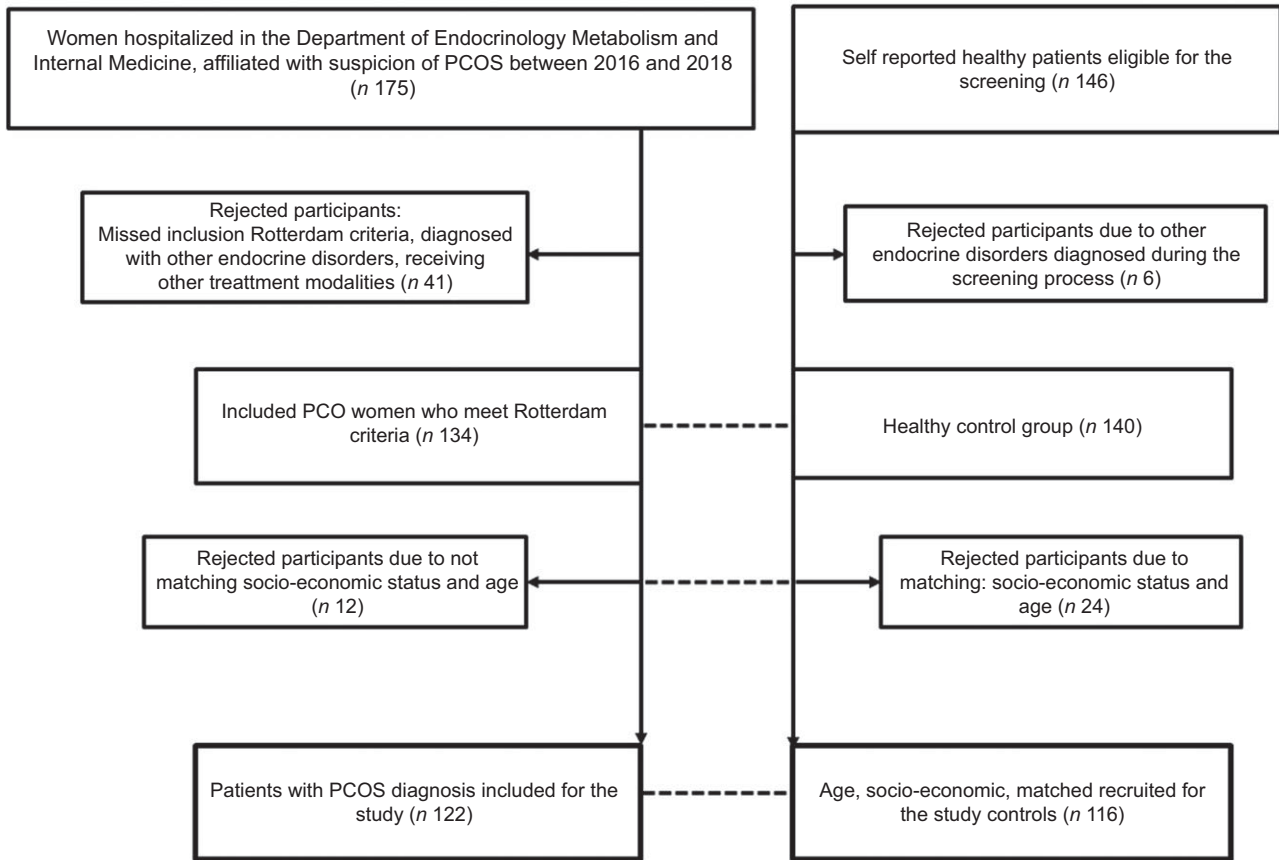


Fig. 1. Study recruitment process

reflecting daily frequency consumption (1) never = 0.00, (2) 1–2 times/month = 0.06, (3) once a week = 0.14, (4) 2–3 times/week = 0.5, (5) once a day = 1 and (6) a few times during the day = 2^(31,32). Conversion rates have been arbitrarily accepted by literature analysis and the authors' own experience⁽³³⁾. The description of food frequency intake was undertaken by using the diet indexes characterising the intensity of food frequency intake of chosen groups of products widely known as healthy, unhealthy, with a high- and low-GI, high content of simple sugars and saturated fats. To evaluate overall diet quality, a pro-Healthy-Diet-Index (pHDI-10) and a non-Healthy-Diet-Index (nHDI-14) scores were established based on previous knowledge and other validated studies⁽³⁴⁾. Due to multiple reports on its effects in PCOS management, high- and low-GI foods as well as foods with high saturated fats and high simple sugar were analysed^(10,11,35). To elucidate dietary intake of high- and low-GI foods, high-sugar, and high saturated fat dietary sources, the four novum DQS were created by the authors based on the previously validated scores (pHDI-10, n-HDI-14) (Table 2). Each index was designed and calculated based on the same conversion formula as previously validated⁽³³⁾:

$$\text{Diet Quality Index} = \frac{100\% * \sum A}{\sum B} [\%]$$

where *A* is the sum of the reported daily intake of all items listed in specific food groups (e.g. low GI, see Table 2), for example, $\Sigma = 0 + 0.14 + 0.06 + 0.5$. *B* is the sum of the maximum possible to report daily intake of the same (low GI) foods, determined for one product as 2 (e.g. $\Sigma = 2 + 2 + 2 + 2$).

All dietary scores were created *a priori* by summing the consumption frequencies (times/d) of the following food items: the pHDI – dairy products, fish, vegetables, fruit; the nHDI – fast food, sweetened soft drinks, energy drinks, and sweets, both already validated⁽³³⁾. For this study, the high-Glycaemic-Diet-Index-7 (hGIDI-7), low-Glycaemic-Diet-Index-4 (LGIDI-4), high-Sugar-Diet-Index-4 (hSDI-4) and the high-saturated-fats-Diet-Index-8 (hSFDI-8) indexes were designed. Groups of food products classified in individual diet indexes are presented in Table 2. The consumption levels of the food groups (indexes) were classified on a percentage scale. Each DQS was expressed in % points and was categorised as follows: low (0–33.32 % points), moderate (33.33–66.65 % points) and high (66.66–100 % points) intensity of consumption of selected food groups. For example, the calculation for low-Glycaemic-Diet-Index-4 (LGIDI-4) was: $\text{LGIDI-4} = 100\% * 0.7/8 = 8.75\%$. There was a low intensity of consumption of low GI foods in the studied group.

Body fatness

The subject's BF was assessed by the air displacement plethysmography method using BodPod (Life Measurement Inc.). During the measurement, all the subjects wore swimming suits and swimming caps; they fasted for 2 h before the analysis⁽³⁶⁾. The measurements were taken in morning hours. The reference values for the body fat (BF) percentage were accepted from the literature⁽³⁷⁾ in the three ranges: normal (below 30%), above normal (30–36%) and high risk (above 36%). The basic anthropometric measurements were also taken: body mass (kg), height (cm), waist and hip circumference (cm).

Nutrition knowledge

The nutrition beliefs and knowledge of the studied groups were determined by using the validated KomPAN questionnaire⁽³³⁾. It included the twenty-five statements and assessments expressed as 'truth', 'false' and 'hard to say'. For each correct answer, the respondent received 1 point, and for an incorrect answer or 'hard to say', 0 point. Points were summed up for each respondent (range 0 to 25 points). The respondents were divided into three nutrition knowledge categories: insufficient (0–8 points), sufficient (9–16 points) and good (17–25 points).

Physical activity

To assess physical activity, the short version of the international physical activity questionnaire was used⁽³⁸⁾.

Statistics

To calculate the sample size, the Sample Size Calculator Clinical Calc (ClinCalc, LLC) was used⁽³⁹⁾. The anticipated means of the pHDI-10 score were set as 27 ± 15 (low score) and 34 (high score). The minimum number of subjects for adequate study power was calculated as 119 for each independent group with the enrolment ratio set at 1, type I error at 0.05 and power 95%.

To achieve comparability between the study groups (PCOS *v.* CON), propensity score 1:1 matching was performed, in which patients in the PCOS group were matched with counterparts in the CON group according to age and socio-economic status. The subjects were matched according to the closest distance with the replacement of the matched control subject⁽⁴⁰⁾. The normality of the distribution data was verified with the Shapiro–Wilk test. The logistic regression was used to determine the OR for DQS and body fat by nutrition knowledge. Differences in nutritional status and frequency intake were calculated using the *t* test of two independent samples. For non-normal distribution data, the Mann–Whitney *U* test was used. Values are presented as mean and median. The 95% CI was set. A *P* value of <0.05 was considered to be statistically significant. The statistical analysis was carried out using Statistica 13.1 software (Dell Inc. 2016).

Results

As depicted in Table 1, the general characteristics show that most of the women participated in the study lived in cities with more than 20 000 residents, declared an average economic situation, had higher education level and lived in 1–4 person households. In the PCOS group, more women smoked cigarettes. As shown in Table 1, over 40% of women with PCOS were overweight or obese and presented a higher BF.

Table 3 shows the significant anthropometric differences between the PCOS and CON groups. The women with PCOS had significantly higher body fat and BMI. The waist:height ratio was significantly higher in comparison with the CON group. Women with PCOS declared less intense physical activity and more sitting time than the control group. Ninety-one percentage of the PCOS group were diagnosed with hyperandrogenism, 76% had oligoovulation, 91% irregular menstruation, 13% hyperlipidaemia and 34% insulin resistance.

As shown in Table 4, both groups presented low intensity of consumption of foods perceived as generally healthy. The PCOS group had a significantly lower frequency intake of pro-healthy foods (pHDI-10) and low GI foods (LGIDI-4) than the CON group. There was a tendency in a higher frequency of high-sugar product (hSFDI-8) intake in the PCOS group than the CON group. PCOS had a lower intake of fruits, vegetables and cottage cheese, what has been shown in detailed components of the indexes included in the online supplementary material, Supplementary Table 6. To ensure that the frequency of eating is not only related to the higher body mass of PCOS women, we stratified the PCOS and CON groups by BMI: 1. BMI < 25 and BMI ≥ 25 (PCOS) and 2. BMI < 30 and BMI ≥ 30 (CON). After performing a Mann–Whitney *U* test in the CON group, the PCOS group and combined, we did not find any statistical differences between the DQS stratified by BMI. The subjects from the PCOS group had lower average (sufficient level) NK compared with the CON group (at a good level) according to the validation protocol⁽³³⁾, as shown in Table 4.

CON women with at least a good level of NK were more than two times likely to have a high intensity of intake of pro-healthy foods (pHDI-10) and had less than a half likely to have a high intensity of intake of saturated fat dietary sources (hSFDI-8) (Table 5). There was also a tendency in controls with at least good knowledge to have a high intensity of consumption of low GI foods (IGIDI-4) and low intensity of high GI foods. These results did not repeat in the PCOS group.

Discussion

Our study revealed the dietary habits identified by DQS in the scope of fatness and NK of PCOS women. To the best of

Table 1. Sample characteristics between women with polycystic ovary syndrome (PCOS) and control group

Variables†	PCOS (n 122)	PCOS (%)	CON (n 116)	CON (%)	P‡
Age (years)					0.48
≤25	63	52	51	44	
26–29	33	27	27	23	
30–35	18	15	23	20	
36–45	8	7	15	13	
BMI (kg/m ²)					0.00*
<18.5 underweight	3	3	10	9	
18.5–24.9 normal	65	53	85	73	
25.0–29.9 overweight	28	23	12	10	
≥30.0 obesity	26	21	10	9	
BF%					0.00*
≤30 normal	36	30	55	48	
30–36 increased	25	20	21	18	
≥36 increased risk	61	50	39	34	
Place of residence					0.69
Village	26	21	26	22	
City < 20 000 residents	9	7	8	7	
City 20 –100 000 residents	27	22	19	16	
City > 100 000 residents	60	49	63	54	
Self-reported economic situation					0.91
“Below average”	3	2	3	3	
“Average”	85	70	81	70	
“Higher than average”	31	25	30	26	
Education					0.21
Basic	5	4	0	0	
Vocational	1	1	1	1	
Middle	41	34	47	40	
Higher	72	59	64	55	
Number of people in the household					0.89
1 or 2	49	40	40	34	
3 or 4	55	45	56	48	
5 and over	18	15	20	17	
Employment					0.10
No, I am on retirement/pension	2	2	3	3	
No, I am on maternity leave, parental leave, unemployed, staying at home	25	20	33	28	
Yes, but a temporary job	23	19	14	12	
Yes, I am permanently employed	70	57	57	49	
Smoking cigarettes					0.01*
Yes	16	13	5	4	
No	106	87	111	96	
Physical activity (MET-minute/week)§					0.49
Insufficient	63	52	58	49	
Sufficient	22	18	27	23	
High	14	11	11	9	
Clinical characteristics					0.00*
Hyperandrogenism	111	91	0	0	
Oligovulation	93	76	0	0	
Irregular cycles	111	91	0	0	
Hyperlipidaemia	16	13	0	0	
Insulin resistance	42	34	0	0	

* $P < 0.05$.

†Variables categorised into classes (as percentage and number of subjects in presented category, e.g. age ≤ 24.9).

‡Results from the χ^2 test.

§Physical activity was categorised according to the manual of a short version of International Physical Activity Questionnaire (IPAQ-SF)⁽³⁸⁾.

our knowledge, this research is the first study to identify using the *a priori* approach, the dietary intake in PCOS women through integrated nutrition quality scores covering groups of food items. Based on the frequency intake of thirty-three food groups, DQS were grouped and categorised according to consumed food products: pro-healthy, non-healthy, low- and high-GI, a high simple sugar, high SFA. PCOS women, in comparison with CON subjects, presented lower intensity of consumption of foods recommended as ‘generally healthy’ (pHDI-10, Pro-Healthy-Diet-Index-10) and foods

characterised by low GI (IGDI-4, Low-Glycemic-Diet-Index-4). We found no relation between DQS, nutrition knowledge and body fat percentage among PCOS women, which was apparent in the healthy control group. Concurrently, we observed a higher body fat and lower nutrition knowledge in the PCOS group.

The first dietary characteristics in PCOS women we present were the low-intensity consumption of foods perceived as healthy. It was found that fruits, vegetables and cottage cheese intake were the main factors involved in

Table 2. Characteristics of dietary indexes

Dietary indexes	Groups of products
pHDI-10 (Pro-Healthy-Diet-Index-10)	(1) Whole-wheat bread; (2) whole-wheat cereals, oatmeal, whole-wheat pasta; (3) milk; (4) fermented milk drinks; (5) cottage cheese; (6) white meat; (7) fish; (8) dishes with legumes; (9) fruits; (10) vegetables
nHDI-14 (Non-Healthy-Diet-Index-14)	(1) White bread; (2) white rice, pasta, fine-ground groats; (3) fast food; (4) fried dishes; (5) butter; (6) lard; (7) cheese; (8) cold meats, smoked sausages, hot-dogs; (9) red meat dishes; (10) sweets; (11) tinned meats; (12) sweetened carbonated and non-carbonated drinks; (13) energy drinks; (14) alcoholic beverages
hGIDI-7 (High-Glycemic-Diet-Index-7)	(1) White bread; (2) white rice, pasta, fine-ground groats; (3) sweets; (4) sweetened carbonated and non-carbonated drinks; (5) juices; (6) sweetened hot drinks; (7) fruits
IGIDI-4 (low-Glycaemic-Diet-Index-4; IGIDI-4 = 100 % × 0.7/8 = 8.75 %. The consumption of low GI foods in diet low intensity.)	(1) Whole-wheat bread; (2) whole-wheat cereals, oatmeal, whole-wheat pasta; (3) dishes with legumes; (4) vegetables
hSDI-4 (High-Sugar-Diet-Index-4)	(1) Sweets; (2) sweetened carbonated and non-carbonated drinks; (3) sweetened hot drinks; (4) juices
hSFDI-8 (High-Saturated-Fats-Diet-Index-8)	(1) butter; (2) lard; (3) red meat dishes; (4) cold meats, smoked sausages, hot-dogs; (5) tinned meat; (6) cheese; (7) fried dishes; (8) fast food

Table 3. Anthropometrics, physical exercise and body composition measurements between polycystic ovary syndrome (PCOS) and control group

	PCOS (n 122)		CON (n 116)		P†
	Mean	SD	Mean	SD	
Age (years)	27	6	26	5	0.39
Body mass (kg)	72.5	17.5	63.8	13.7	0.00*
BMI (kg/m ²)	26.2	6.2	22.8	4.6	0.00*
BF (%)	36.5	9.7	31.1	8.6	0.00*
Waist (cm)	82.7	14.3	75.7	10.7	0.00*
WHtR (-)	0.50	0.08	0.45	0.06	0.00*
High-intensity physical activity‡	1892	9215	6855	21 629	0.03*
Medium-intensity physical activity‡	2168	6988	2995	9119	0.46
Walking‡	2637	7710	2990	7543	0.73
Sitting‡	2205	2863	1535	894	0.02*

WHtR, waist:height ratio.

†Level of significance for the comparison of means between groups: **P* < 0.05.

‡MET-minute/week.

Table 4. Diet indexes and nutritional knowledge in polycystic ovary syndrome (PCOS) and CON women

	PCOS (n 122)					CON (n 116)					P†
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
pHDI-10 (%)	23.5	10.0	23.0	6.0	51.0	26.1	10.0	26.0	6.0	49.0	0.04*
nHDI-14 (%)	13.0	7.2	11.0	0.6	37.8	13.4	8.2	11.1	1.2	38.0	0.94
hGIDI-7 (%)	16.1	11.2	22.0	13	0.0	16.3	11.8	13.0	0.0	87.0	0.82
hSDI-4 (%)	14.9	13.5	11.1	0.0	75.0	13.5	13.9	9.2	0.0	100.0	0.08
hSFDI-8 (%)	11.9	7.6	10.9	0.0	45.0	12.1	7.7	11.1	0.0	32.0	0.97
IGIDI-4 (%)	27.5	13.1	26.3	3.0	57.0	30.5	12.7	28.5	4.5	62.0	0.02*
NK (points)	15.0	4.9	16.0	4.0	23.0	16.7	5.9	18.0	0.0	25.00	0.01*

pHDI-10, Pro-Healthy-Diet-Index-10; nHDI-14, Non-Healthy-Diet-Index-14; hGIDI-7, High-Glycemic-Diet-Index-7; hSDI-4, High-Sugar-Diet-Index-4; hSFDI-8, High-Saturated-Fats-Diet-Index-8; IGIDI-4, Low-Glycemic-Diet-Index-4; NK, nutrition knowledge.

†Level of significance for the comparison of means between groups: **P* < 0.05.

lowering pHDI-10. Other characteristics were the low intensity of consumption of low GI foods, recommended for consumption for PCOS, and included whole-wheat bread, whole-wheat cereals, oatmeal, whole-wheat pasta, dishes with legumes and vegetables. The vegetables were

the most significant group to differentiate PCOS and controls. In spite of above food groups, PCOS women declared a higher intensity (30 % more than control) of consumption of fast food. Our results suggest that PCOS women were prone to a less healthy lifestyle; they were smokers more

**Table 5.** OR (95% CI) for diet quality scores and body fat by nutrition knowledge in polycystic ovary syndrome (PCOS) women and healthy control group

Dietary scores	PCOS					CON				
	%	n	OR	95% CI	P	%	n	OR	95% CI	P
Body fat $\geq 36\%$ †										
Nutrition knowledge \geq good§	16	19	0.92	0.4, 2.0	0.85	9	11	0.58	0.2, 1.5	0.26
pHDI-10 \geq high-intensity‡ (Pro-Healthy-Diet-Index-10)										
Nutrition knowledge \geq good§	8	10	0.84	0.3, 2.0	0.70	27	32	2.25	1.0, 4.9	0.03*
nHDI-14 \geq high-intensity (Non-Healthy-Diet-Index-14)										
Nutrition knowledge \geq good§	8	10	0.64	0.3, 1.5	0.31	16	19	0.49	0.2, 1.0	0.07
IGIDI-4 \geq high-intensity (Low-Glycemic-Diet-Index-4)										
Nutrition knowledge \geq good§	11	13	1.16	0.5, 2.6	0.72	27	31	1.90	0.9, 4.2	0.09
HGIDI-7 \geq high-intensity (High-Glycemic-Diet-Index-7)										
Nutrition knowledge \geq good§	9	11	0.69	0.3, 1.6	0.39	16	19	0.54	0.2, 1.1	0.10
hSDI-4 \geq high-intensity (High-Sugar-Diet-Index-4)										
Nutrition knowledge \geq good§	10	12	0.60	0.3, 1.3	0.22	15	18	0.58	0.3, 1.3	0.17
hSFDI-8 \geq high-intensity (High-Saturated-Fats-Diet-Index-8)										
Nutrition knowledge \geq good§	9	11	0.77	0.3, 1.8	0.54	16	19	0.46	0.2, 1.0	0.05*

Level of significance for the comparison of means between groups: * $P < 0.05$.

†Body fat content categories according to Jeukendrup and Michael⁽³⁷⁾.

‡High intensity of frequency intake refers to upper tertile of each of index.

§Nutrition knowledge referred to as good according to the validated questionnaire manual.

often than CON and engaged in less intense physical activity but were sitting more. Such picture of studied PCOS was supplemented by 20% and 22% lower consumption of fruit and vegetables in this group. This tendency was also observed by Shishehgar *et al.*⁽⁴¹⁾. According to the current nutrition guidelines for the general population, the majority of food groups classified in the healthy and low glycaemic intake index (pHDI-10 and IGIDI-4) should be consumed at least several times a day. Food products classified in the nonhealthy dietary index (nHDI-14) and high GI (hGIDI-7) (white bread, white rice, plain pasta or cereal, fast food, butter, lard, cheese, sausages, red meat, sweets, canned meat, sweetened carbonated and non-carbonated drinks, energy drinks and alcoholic beverages) should be consumed in the smallest possible amounts. Dietary intake profile of our PCOS women was contrary to the recommendation of increasing the consumption of low GI products. According to Androgen Excess Society recommendations, it is necessary to increase the intake of low GI products, including fruit and vegetables⁽⁶⁾. This approach may help to improve the effects of treatment associated with insulin resistance, which is supported by multiple intervention studies^(13,15–17).

In our study, the relation of DQS to BF was sought as well. We hypothesised that the diet quality, along with hormonal abnormalities, like hyperandrogenemia, might support increased BF. The etiopathogenesis of obesity in PCOS has not yet been exactly explained. The hyperandrogenaemia, as was mentioned in other studies, could enhance the visceral obesity of PCOS women^(42,43). Having in mind, the fact of hormonal abnormalities in PCOS; we had a look at possible relations of BF to DQS. We could not find any relationship there. Despite this, it is necessary to underline that the comparison of PCOS and CON groups revealed that nonetheless of matching procedure for age and socio-economic

status, the BF of PCOS women was higher than healthy participants. The study group had a similar body composition to subjects in other studies, further supporting the data that half of PCOS women are overweight or obese⁽⁴⁴⁾.

Considering the lower diet quality in PCOS, it is essential to find the reasons standing behind it. Keeping this in mind, we analysed the nutrition knowledge. It has been shown that knowledge influences dietary behaviours, particularly the intake of fruits and vegetables which, in turn, stimulates dietary patterns and determines BF⁽⁴⁵⁾. Our study reveals that women with PCOS presented lower NK than controls. In contrast, the literature suggests that PCOS women show higher knowledge and motivation to implement preventive health strategies, which is related to the economic situation and education level^(28,46–49). Some authors suggest that PCOS women seem to be interested in broadening their knowledge and practising healthy behaviours which are related to DQS⁽⁵⁰⁾. It is possible that women from our study were not engaged in dietary consultations but used fad diets, internet forums and were guided by advertising in their dietary choices. Additionally, it must be underlined that we have been looking at relations between NK and BF in the studied group. The current results in PCOS did not confirm the expected relationships. Such a relationship was evident in healthy controls, where the intake of prohealthy and saturated fat groups of products was driven by NK. This difference between PCOS and CON might suggest additional factors like hormonal abnormalities influencing BF in PCOS, lower motivation and dietary adherence. Additionally, such differences could be explained by nutrition knowledge or related to psychological state, which has been hypothesised by other authors and was not analysed in our study⁽⁵¹⁾.

Although the research has reached its aims, it may have some limitations. First of all, the retrospective setting of the

study. We are not sure if women already have been changing their nutrition behaviours. This problem is partially solved by the time of the diagnosis. Women in our study were diagnosed for the first time with PCOS. However, the nature of symptoms of this disorder could cause the change in their health behaviours before the study commenced. Due to this reason, and higher body weight, there is a possibility that the women involved in the study could have under-reported their intake, especially concerning unhealthy products and simple sugar sources⁽⁵²⁾.

Second, even though the present study determined the dietary scores of 238 women by the frequency of intake of thirty-three foods, the portion size was not determined. This could have prevented an accurate assessment of the dietary nutrient intake. A lack of recording of portion sizes could explain the absence of statistical differences between the intake of non-healthy, high GI, saturated fats and dietary sugar sources. Furthermore, we did not analyse week and weekend fluctuations in dietary intake, as it was proven in previous studies, where women generally report large fluctuations in the intake of sugar and other nutrients⁽⁵³⁾. Moreover, underestimation may be contributed to the compulsive eating of products generally considered unhealthy, which is not possible to observe with the FFQ⁽⁵⁴⁾.

Third, the study did not consider the seasonality of food consumption. As the authors of previous studies showed, DQS would have been more precise and differentiated if the seasonality of consumption had been considered in the frequency of intake⁽⁵⁵⁾.

Fourth, the tool used to analyse the frequency of intake was validated on healthy subjects. Verification questions concerning frequency consumption were collected, analysed and revealed high repeatability of collected data. Another limitation was the size of the study sample, which restricted the use of statistical methods recommended for dietary pattern evaluation^(56,57).

Finally, considering the role of body fat distribution and cardiometabolic risk in PCOS women, it would be valuable to assess the androidal and gynoidal body fat distribution. In this study, despite the use of the 'gold standard', plethysmography, only total BF was assessed. Additionally, the fact that hormonal disturbances potentially influenced fat distribution should be taken into account.

Conclusions

In conclusion, our results pointed to the role of multidisciplinary therapy including dietary behaviours in PCOS women. We found differences between PCOS women and healthy controls in lower DQS related to generally healthy foods and low GI foods. PCOS women presented lower NK. The professional dietary education and improving the NK of PCOS women could affect the diet quality and increase the presence of hygienic lifestyle factors. The complementary treatment of PCOS, to ensure the optimal improvements in

the disease endpoints, should be implemented after PCOS diagnosis.

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Supplementary material

For supplementary material accompanying this paper visit <https://doi.org/10.1017/S1368980020001755>

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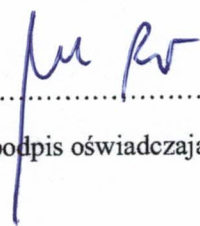
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Article

The Significance of Plant-Based Foods and Intense Physical Activity on the Metabolic Health of Women with PCOS: A Priori Dietary-Lifestyle Patterns Approach

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Featured Application: This study will help develop dietary recommendations for women with PCOS.

Abstract: The study aimed to analyse dietary-lifestyle patterns (DLPs) and their relation with visceral obesity and other metabolic parameters in women with PCOS. A total of 140 women were diagnosed with PCOS. The KomPAN[®] and The ShortIPAQ questionnaires analysed the food frequency intake, health habits, economic situation, and physical activity. The dual-energy-x-ray absorptiometry (DXA) measured the visceral and total adipose tissue. The analysis distinguished three DLPs: western (WDLP), prudent (PDLP) and active (ADLP). The WDLP was characterised by high visceral fat, increased intake of animal foods, sweets and sweetened beverages, white grains, junk and fried foods, and low plant foods. High intakes of plant foods and dairy, high daily meal frequency, and intense exercise characterised PDLP. ADLP was characterised by high visceral fat, intake of plant products, intense exercise, and low intake of junk and fried food. Women with LDL > 135 mg/dL had high adherence to WDLP, and with triglycerides >150 mg/dL had high adherence to WDLP [OR 7.73 (CI95% 1.79; 33.2), $p < 0.05$] and [3.70 (1.03; 13.27); $p < 0.05$]. In conclusion, plant-based foods related to PDLP and intense physical activity offer a significantly higher chance of improving metabolic health in women with PCOS.

Keywords: polycystic ovary syndrome; body composition; densitometry; lipoproteins; androgens



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1. Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disorder characterised by ovarian cysts, clinical or biochemical hyperandrogenism, and oligo-ovulation or anovulation [1]. Parallel to the above criteria, PCOS women have a higher chance for metabolic syndrome, central obesity, and insulin resistance than healthy populations [2]. Primary management of PCOS includes hormonal therapy [1]. Nevertheless, PCOS symptoms may be partially alleviated by incorporating healthy behaviours, including changes in diet composition and weight loss [3]. The different pathways of PCOS diagnosis by Rotterdam criteria cause us to distinguish four PCOS phenotypes: (I) Hyperandrogenism, ano- or oligo-ovulation, cystic ovaries; (II) Hyperandrogenism, ano- or oligo-ovulation; (III) Hyperandrogenism, cystic ovaries; (IV) ano- or oligo-ovulation, cystic ovaries. The evidence shows that different phenotypes are associated with diverse dietary patterns and obesity [4–7].

The low glycemic index (GI) diet is a well-known recommendation for PCOS. It has been published widely that Low GI foods consumption and avoidance of high GI products may influence insulin sensitivity and androgen status [4,8–10]. The relations between dietary carbohydrate composition, low GI and hyperandrogenism are still not fully known

in this group. Moreover, it has been shown that sugar limitations and diet modifications often have unsatisfactory effectiveness in diet therapy [11]. High androgens may be caused by hyperinsulinemia, which increases the local testosterone by inhibiting the synthesis of sex hormone-binding globulin (SHBG) [12]. However, the GI list of foods has many drawbacks, and its indiscriminate use severely limits the diversity of the diet. First, a combination of meals composed of high and low GI foods, such as high protein or fibre, can lower the glucose uptake from the intestines, lowering the peak of insulin [13]. Second, despite the low GI, meat products deliver animal fats, including saturated fatty acids, and their intake above recommendations increases the risk of metabolic syndrome. Third, high GI plant products (such as fruits) enrich the diet with high anti-inflammatory status or prebiotic ingredients. Consumption of anti-inflammatory food and synbiotics also shows some beneficial effects in alleviating symptoms of PCOS [14–18]. It has been studied that following Mediterranean dietary patterns, rich in fruits and vegetables, increase the total dietary antioxidant capacity and decreases inflammatory markers [19,20], as shown in PCOS [21]. Still, researchers should be cautious with this recommendation, given the seasonality of consumption in Central Europe [22,23]. Such arguments show that the discussion on PCOS diet guidelines is still needed and should be developed. Simultaneously, many studies suggest that a hygienic lifestyle with a healthy diet and adequate physical activity improves the PCOS endpoints [24].

Most of the studies mentioned above were performed using a single nutrient or, in the case of observational studies, already established diet quality scores and patterns. Dietary lifestyle patterns (DLP) define the quantities, proportions, variety, or combination of different foods and drinks in diets and behaviours and the frequency with which they are habitually consumed or practised evaluated as a single exposure [19,25]. They can be assessed either a priori or a posteriori. A priori concerns an analysis of already established patterns and quality scores, such as healthy eating index and western or Mediterranean dietary patterns. In turn, the a posteriori is based on the food intake analysis after data collection using factor analysis or principal components analysis [26]. According to the author's knowledge, only two studies in the literature involve a posteriori dietary pattern analysis of women with PCOS [27,28]. Their authors compared PCOS with the control group, not recognising the dietary patterns within the specific group of women with PCOS. Moran et al. [28] concluded that women with PCOS were more likely to follow a Mediterranean dietary pattern than the healthy controls. This dietary pattern is based on an increased intake of plant food sources (such as fruits, vegetable legumes), olive oil and fish but decreased meat intake [28]. Women in this study could improve dietary behaviours even prior to diagnosis due to the existing symptoms. Analysing dietary patterns within this group could point out specific nutrition behaviour problems.

Metabolic disorders are also related to lifestyle patterns, such as the amount of physical activity, sleeping time and sedentary behaviours. Currently, no published literature analysed lifestyle patterns among women with PCOS. However, there are multiple studies on the influence of different intensities and types of physical activity on PCOS disease endpoints, and exercise should be the basis of health recommendations [29].

Simultaneously, women with PCOS have a higher incidence of excess visceral adipose tissue (VAT). Such fat distribution is related to insulin resistance, hyperglycaemia, hypercholesterolemia, and dyslipidemia [30–32]. According to research, VAT is an early marker measurement of metabolic syndrome [33]. A comprehensive analysis of VAT and food frequency intake in young women with PCOS could predict metabolic disorders in the future. According to the author's best knowledge, there is no current research concerning the VAT derived from DXA and a posteriori lifestyle dietary patterns of women with PCOS. Therefore, the study aimed to analyse dietary-lifestyle patterns (DLPs) and their relation with visceral obesity and other metabolic parameters in women with PCOS.

2. Materials and Methods

2.1. Study Participants

A total of 140 patients with PCOS were recruited for the nutrition part of the study from the Department of Endocrinology, Metabolism and Internal Diseases, Poznan University of Medical Sciences (Figure 1). The recruitment process was based on the following inclusion and exclusion criteria; PCOS diagnosis according to Rotterdam criteria, age: 18–40 y.o., BMI < 40, no diagnosis of extreme obesity, heart defect, decompensated thyroid dysfunction, severe acute or chronic renal or liver diseases, Cushing’s disease, congenital adrenal hyperplasia, or eating disorders, no birth control or hormone replacement therapy, ovulation-inducing agents, anti-androgens over the last 2 months prior to the study. Informed and written consent was obtained from all participants. The clinical examination protocol complied with the Declaration of Helsinki for Human and Animal Rights and its later amendments and received ethical approval from the Board of Bioethics of the University of Medical Science (552/16; 986/17).

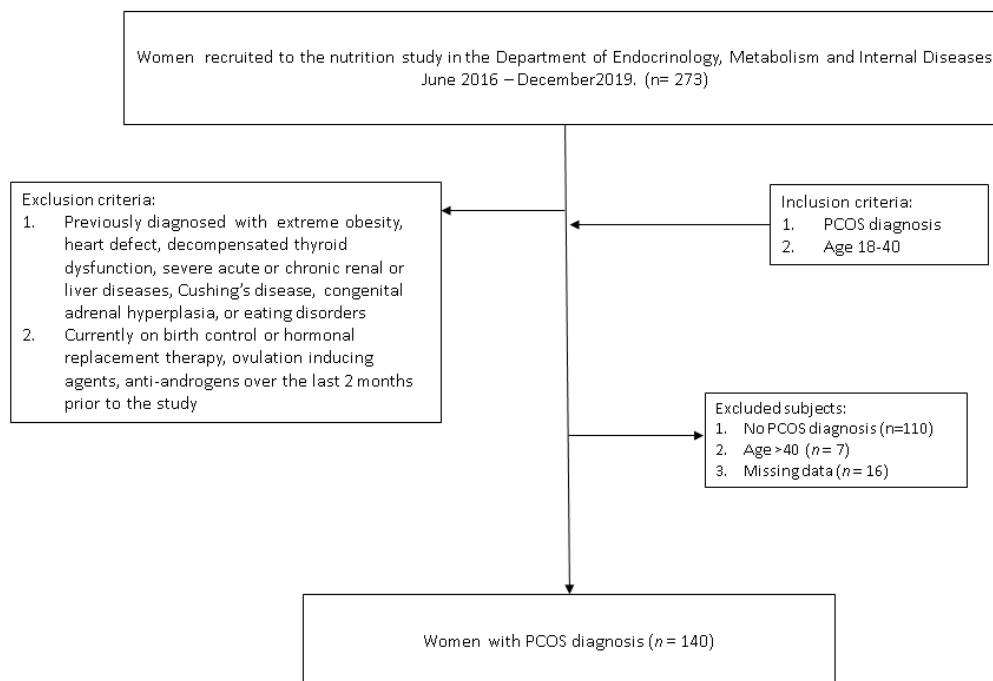


Figure 1. Flowchart of the study.

2.2. Body Composition Parameters

Body composition was measured by the dual-energy x-ray absorptiometry (DXA) method. The Lunar Prodigy™ (GE Healthcare®, Madison, WI, USA, 2013) densitometer was used for evaluation. The quality control was performed according to the user manual on each day of the study visits. VAT was analysed using the software enCORE™ (version 17) and CoreScan™ (GE Healthcare®, Madison, WI, USA). A qualified staff member performed all measures, including weight, height, waist and hip circumference.

2.3. Food Frequency Intake and Lifestyle Habits

Food frequency, lifestyle habits, and socioeconomic status were assessed by validated Dietary Habits and Nutrition Beliefs Questionnaire KomPAN® [34,35]. The food frequency part included twenty-four food groups with six possible answers: (1) never, (2) 1–3 times a month, (3) once a week, (4) 2–3 times a week, (5) once a day, (6) a few times during the day. Those responses were converted into an average frequency of food intake per day [22,34]. The foods were divided into different groups: meats (red meat, white meat, smoked meat, meat conserves), plant foods (vegetables, fruits, legumes), dairy (milk, fermented milk

drinks, cottage cheese, hard cheese), wholegrains (whole bread, wholegrain products such as pasta, rice, groats, oats), white grains (white bread, white pasta, rice) sweets and sweetened beverages (sweets, sweetened beverages). KomPAN[®] also includes questions that verify reliability (crossing questions concerning the same issue). These involve, for example, the typical day number of meals in two parts of the questionnaire. If the two answers differed by two or more meals, the patient was not included in the study since the low reliability of the answers.

2.4. Biochemical Parameters

Blood samples were collected from all patients after an overnight fast. Insulin, follicle-stimulating hormone (FSH), luteinising hormone (LH), and total testosterone (T), androstenedione (A) were analysed using a Cobas 6000 (Roche Diagnostics, GmbH, Mannheim, Germany). Kits available from the manufacturer were used. Total cholesterol (TC), high-density lipoprotein cholesterol (HDL), and triglycerides (TG) were evaluated by the enzymatic colourimetric method. The Friedewald formula calculated low-density lipoprotein cholesterol (LDL). Serum glucose was assessed with the hexokinase method (Roche Diagnostics) and a coefficient of variation (CV) of 3%. The formula (HOMA-IR) calculated the homeostasis model assessment for insulin resistance: $HOMA-IR = (\text{fasting plasma glucose (mg/dL)} \times \text{fasting plasma insulin (mU/L)})/405$. The threshold of $HOMA-IR > 2.5$ was used.

2.5. Statistics

The software Statistica v.13.1 (StatSoft Polska sp. z o.o., Kraków, Poland) was used for the calculations. The study group characteristics involved calculating means, standard deviation, medians and confidence intervals set for 95%. Each variable was checked for normality. The dietary patterns were analysed by Principal Component Analysis (PCA) method, with varimax normalised rotation. A total of twenty-four food frequency intake variables were included in the PCA. The dietary patterns were identified by considering the following criteria: (1) the eigenvalues of the variable correlations >1.0 , (2) the plot of eigenvalues, and (3) the total variance explained [36]. Rotated factor loadings with an absolute value $\geq |0.50|$ were considered specific to the given pattern. For each patient and each pattern, the scores were calculated as a product of factor loading and food frequency consumption. Next, for each dietary pattern, tertile intervals were calculated to measure the adherence to the patterns of each patient.

Logistic regression was used to analyse the associations between dietary patterns and metabolic parameters. The odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated between upper tertiles of dietary patterns and recommended values for metabolic parameters.

3. Results

3.1. Lifestyle-Dietary Patterns and Patient's Characteristics

The patient's characteristics can be seen in Table 1. The study group's mean age was 26 ± 5 years old, and BMI was 25.4 ± 5.2 kg/m². Three lifestyle-dietary patterns have been distinguished among women with PCOS: (1) Western (WDLP), (2) Prudent (PDLP) (3) Active (ADLP). The factor loadings of each dietary pattern are depicted in Figure 2 and Supplementary materials Table S1. The WDLP was characterised by high visceral fat, high-frequency intake of animal foods, sweets and sweetened beverages, white grains, junk and fried foods, and low-frequency intake of plant foods. PDLP was characterised by high-frequency intake of plant foods and dairy, high meal frequency per day, and intense exercise. ADLP was characterised by high visceral fat, high-frequency intake of plant products, intense exercise and low intake of junk and fried food.

Table 1. Patient’s characteristics (*n* = 140).

	Mean	±SD	Median	CI (95%)	
Age (years)	26	5	25	25	27
Height (cm)	165	15	167	163	168
Body mass (kg)	70.8	14.9	68.0	68.3	73.3
BMI (kg/m ²)	25.4	5.2	24.1	24.5	26.3
Waist circumference (cm)	81.5	13.0	79.5	79.3	83.7
Hips circumference (cm)	100.5	11.4	100.0	98.6	102.4
WHR (–)	0.81	0.08	0.80	0.80	0.82
FM (%)	36	8	35	35	37
VAT (g)	467	530	283	378	555
TC (mg/dL)	178	31	176	173	184
HDL (mg/dL)	66	16	63	63	68
LDL (mg/dL)	95	30	93	90	100
TG (mg/dL)	87	58	69	77	97
Fasting glucose (mg/dL)	89	7	88	88	9
Fasting insulin (uU/mL)	11.09	7.15	8.89	9.84	12.34
HOMA-IR (–)	2.52	1.81	1.94	2.20	2.84
FSH (mIU/mL)	6.6	8.00	5.9	5.1	8.00
LH (mIU/mL)	10.4	6.1	8.4	9.3	11.5
LH/FSH (–)	1.8	1.1	1.5	1.6	2.0
T nmol/L	1.9	0.9	1.6	1.7	2.0

Abbreviations: BMI—Body Mass Index; WHR—Waist-to-Hip Ratio; WHtR—Waist-to-Height Ratio; FM—fat mass; VAT—Visceral Fat Tissue; TC—Total cholesterol; HDL—High-density lipoprotein; LDL—Low-density lipoprotein; TG—Triglycerides; HOMA-IR—Homeostatic Model Assessment—Insulin Resistance; FSH—Follicle Stimulating Hormone; LH—luteinising hormone, T—Total testosterone.

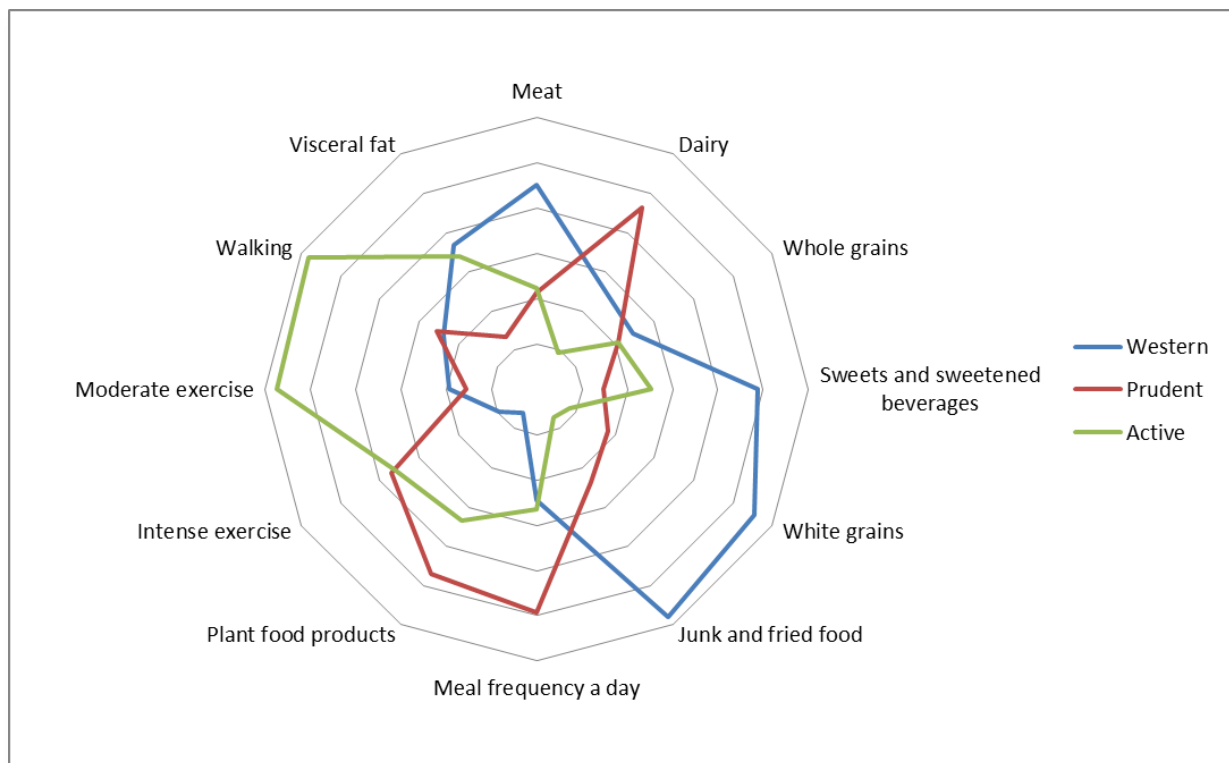


Figure 2. Factor loadings diagram characterising dietary-lifestyle patterns distinguished among women with PCOS.

The mean frequency intakes of different food groups for each adherence can be found in Supplementary Tables S2–S5.

3.2. Metabolic Parameters

Women with PCOS, with high adherence to WDLP, were prone to increase (>135 mg/dL and >150 mg/dL) levels of LDL and triglycerides, respectively (Table 1). The low adherence to WDLP decreased the chance (70%) of BMI over 30 kg/m². They also had a lower chance of WHtR above 0.5 and HDL below 50 mg/dL.

Women with high adherence to PDLP had almost 58% less chance of having a BMI above 25 kg/m² and 54% less chance of having body fat above 35% (Table 2). In turn, middle adherence to prudent DLP was related to a higher chance of BMI over 25 kg/m² and total cholesterol below 200 mg/dL. Low adherence to prudent DLP was associated with over three times higher chance of total cholesterol over 200 mg/dL than the rest of the participants (Table 2).

Table 2. The adherence to the western dietary-lifestyle pattern (DLP) and its relation with different metabolic and endocrine markers.

	High Adherence to WDLP		Middle Adherence WDLP		Low Adherence to WDLP	
	<i>n</i>	OR (CI95%), <i>p</i>	<i>n</i>	OR (CI95%), <i>p</i>	<i>n</i>	OR (CI95%), <i>p</i>
BMI > 30 kg/m ²	12	2.35 (0.94; 5.88), <i>p</i> = 0.06	8	1.13 (0.44; 2.92), <i>p</i> = 0.79	4	0.30 (0.09; 0.97), <i>p</i> = 0.04 *
BMI > 25 kg/m ²	22	1.27 (0.62; 2.63), <i>p</i> = 0.51	22	1.58 (0.76; 3.30), <i>p</i> = 0.21	16	0.49 (0.23; 1.05), <i>p</i> = 0.06
WHR > 0.80	24	1.69 (0.79; 3.60), <i>p</i> = 0.17	21	1.17 (0.55; 2.46), <i>p</i> = 0.68	18	0.51 (0.24; 1.09), <i>p</i> = 0.07
WhtR > 0.5	21	1.37 (0.65; 2.87), <i>p</i> = 0.39	22	1.77 (0.84; 3.72), <i>p</i> = 0.12	14	0.40 (0.19; 0.88), <i>p</i> = 0.02 *
Fat > 35%	24	1.17 (0.56; 2.41), <i>p</i> = 0.66	24	1.47 (0.70; 3.08), <i>p</i> = 0.29	21	0.58 (0.28; 1.51), <i>p</i> = 0.15
T. Chol. > 200 mg/dL	11	1.91 (0.74; 4.92), <i>p</i> = 0.17	9	1.23 (0.48; 3.19), <i>p</i> = 0.66	6	0.40 (0.13; 1.15), <i>p</i> = 0.08
LDL > 135 mg/dL	8	7.73 (1.79; 33.2), <i>p</i> < 0.00 *	1	0.19 (0.20; 1.64), <i>p</i> = 0.13	2	0.32 (0.06; 1.67), <i>p</i> = 0.17
HDL < 50 mg/dL	9	2.24 (0.80; 6.25), <i>p</i> = 0.12	7	1.49 (0.52; 4.20), <i>p</i> = 0.44	2	0.19 (0.04; 0.89), <i>p</i> = 0.03 *
TG > 150 mg/dL	7	3.70 (1.03; 13.27), <i>p</i> = 0.04 *	3	0.71 (0.17; 2.90), <i>p</i> = 0.64	2	0.28 (0.05; 1.44), <i>p</i> = 0.12
HOMA > 2.5	21	1.93 (0.91; 4.07), <i>p</i> = 0.08	16	1.11 (0.52; 2.38), <i>p</i> = 0.77	13	0.44 (0.20; 0.99), <i>p</i> = 0.04 *
Fasting gluc. > 100 mg/dL	5	2.39 (0.62; 9.20), <i>p</i> = 0.19	3	0.95 (0.23; 4.04), <i>p</i> = 0.95	2	0.37 (0.07; 1.95), <i>p</i> = 0.24
Fasting ins. > 10 mU/mL	25	1.53 (0.75; 3.16), <i>p</i> = 0.24	24	1.75 (0.84; 3.66), <i>p</i> = 0.12	16	0.37 (0.17; 0.78), <i>p</i> = 0.01 *
LH > upper tertile	14	1.05 (0.48; 2.31), <i>p</i> = 0.90	16	1.67 (0.76; 3.64), <i>p</i> = 0.19	11	0.56 (0.24; 1.28), <i>p</i> = 0.16
FSH > upper tertile	18	2.30 (1.03; 5.11), <i>p</i> = 0.04 *	9	0.56 (0.24; 1.35), <i>p</i> = 0.19	13	0.72 (0.32; 1.63), <i>p</i> = 0.43
LH/FSH > upper tertile	14	0.98 (0.44; 2.17), <i>p</i> = 0.97	15	1.35 (0.62; 2.96), <i>p</i> = 0.44	13	0.74 (0.34; 1.65), <i>p</i> = 0.47
T > upper tertile	7	0.35 (0.15; 0.83), <i>p</i> = 0.01 *	13	2.01 (0.94; 4.30), <i>p</i> = 0.07	8	1.28 (0.60; 2.71), <i>p</i> = 0.51
A > upper tertile	10	0.37 (0.16; 0.88), <i>p</i> = 0.02 *	21	2.57 (1.21; 5.48), <i>p</i> = 0.01 *	16	0.96 (0.45; 2.05), <i>p</i> = 0.99
DHEA-s > upper tertile	14	0.69 (0.32; 1.51), <i>p</i> = 0.35	18	1.68 (0.79; 3.57), <i>p</i> = 0.17	15	0.86 (0.40; 1.83), <i>p</i> = 0.68
PCOS type 1	24	0.86 (0.42; 1.78), <i>p</i> = 0.69	22	0.90 (0.43; 1.88), <i>p</i> = 0.78	28	1.27 (0.61; 2.61), <i>p</i> = 0.51
PCOS type 2	7	0.79 (0.29; 2.14), <i>p</i> = 0.65	9	1.58 (0.61; 4.04), <i>p</i> = 0.33	8	0.78 (0.29; 2.09), <i>p</i> = 0.62
PCOS type 3	4	0.79 (0.22; 2.78), <i>p</i> = 0.71	4	1.01 (0.29; 3.56), <i>p</i> = 0.97	5	1.23 (0.37; 4.08), <i>p</i> = 0.73
PCOS type 4	12	1.68 (0.70; 4.04), <i>p</i> = 0.24	7	0.75 (0.28; 1.97), <i>p</i> = 0.56	8	0.75 (0.30; 1.89), <i>p</i> = 0.54

Abbreviations: BMI—Body Mass Index, WHR—Waist-to-Hip Ratio, WHtR—Waist-to-Height Ratio, T. Chol.—total cholesterol; HDL—High-density lipoprotein, LDL—Low-density lipoprotein, TG—Triglycerides, HOMA-IR—Homeostatic Model Assessment—Insulin Resistance, Fasting gluc.—fasting glucose, Fasting ins.—fasting insulin, FSH—Follicle Stimulating Hormone, LH—luteinising hormone, T—total testosterone, A—androstenedione; DHEA-s—Dehydroepiandrosterone sulfate. The *p* values below the threshold of statistical significance are marked with the * *p* < 0.05.

High and low adherence to ADLP was not significantly related to any metabolic markers. However, middle adherence was related to body fat above 35% and WHtR above 0.5.

3.3. Endocrine Parameters

Women with high adherence to western DLP had over twice the higher probability of having FSH above the third tertile. High adherence to WDLP was also related to a 65% and 63% lower chance of total T and A, respectively, above the third tertile (Table 2).

Women with high adherence to prudent PDLP were nearly two and a half more likely to have PCOS type 2 (Table 3). In turn, the low adherence to that pattern was related to androstenedione above 245 ng/dL.

High adherence to active DLP was related to PCOS type 2, and low adherence to that pattern was related to androstenedione above 245 ng/dL (Table 4).

Table 3. The adherence to the prudent dietary-lifestyle pattern (PDLP) and it’s relation with different metabolic and endocrine markers.

	High Adherence to PDLP		Middle Adherence to PDLP		Low Adherence to PDLP	
	<i>n</i>	OR (CI95%), <i>p</i>	<i>n</i>	OR (CI95%), <i>p</i>	<i>n</i>	OR (CI95%), <i>p</i>
BMI > 30 kg/m ²	6	0.60 (0.22; 1.65), <i>p</i> = 0.32	8	1.04 (0.40; 2.68), <i>p</i> = 0.93	10	1.52 (0.61; 3.79), <i>p</i> = 0.36
BMI > 25 kg/m ²	14	0.42 (0.20; 0.89), <i>p</i> = 0.02 *	25	2.09 (1.00; 4.34), <i>p</i> = 0.04 *	21	1.11 (0.54; 2.28), <i>p</i> = 0.77
WHR > 0.80	23	1.24 (0.59; 2.58), <i>p</i> = 0.56	19	0.84 (0.40; 1.77), <i>p</i> = 0.64	21	0.95 (0.46; 1.98), <i>p</i> = 0.95
WhtR > 0.5	15	0.54 (0.25; 1.14), <i>p</i> = 0.10	21	1.46 (0.70; 3.05), <i>p</i> = 0.30	21	1.25 (0.60; 2.59), <i>p</i> = 0.53
Fat > 35%	18	0.45 (0.21; 0.94), <i>p</i> = 0.03 *	23	1.11 (0.54; 2.30), <i>p</i> = 0.76	28	1.97 (0.95; 4.10), <i>p</i> = 0.06
T. Chol. > 200 mg/dL	8	0.81 (0.30; 2.16), <i>p</i> = 0.68	4	0.29 (0.09; 0.94), <i>p</i> = 0.04 *	14	3.27 (1.28; 8.39), <i>p</i> = 0.01 *
LDL > 135 mg/dL	3	0.68 (0.16; 2.83), <i>p</i> = 0.59	3	0.77 (0.18; 3.16), <i>p</i> = 0.71	5	1.78 (0.49; 6.43), <i>p</i> = 0.37
HDL < 50 mg/dL	4	0.51 (0.16; 1.69), <i>p</i> = 0.27	5	0.77 (0.25; 2.33), <i>p</i> = 0.64	9	2.21 (0.80; 6.08), <i>p</i> = 0.12
TG > 150 mg/dL	4	0.94 (0.25; 3.47), <i>p</i> = 0.92	2	0.38 (0.08; 1.89), <i>p</i> = 0.23	6	2.22 (0.64; 7.67), <i>p</i> = 0.20
HOMA > 2.5	14	0.59 (0.27; 1.29), <i>p</i> = 0.18	15	0.87 (0.40; 1.85), <i>p</i> = 0.71	21	1.88 (0.90; 3.95), <i>p</i> = 0.09
Fasting gluc. > 100 mg/dL	4	1.30 (0.69; 5.09), <i>p</i> = 0.70	2	0.50 (0.10; 2.52), <i>p</i> = 0.39	4	1.37 (0.35; 5.34), <i>p</i> = 0.64
Fasting ins. > 10 mU/mL	19	0.62 (0.30; 1.28), <i>p</i> = 0.19	23	1.33 (0.65; 2.75), <i>p</i> = 0.42	23	1.20 (0.59; 2.45), <i>p</i> = 0.61
LH > upper tertile	12	0.74 (0.33; 1.66), <i>p</i> = 0.46	15	1.29 (0.59; 2.81), <i>p</i> = 0.51	14	1.03 (0.47; 2.26), <i>p</i> = 0.93
FSH > upper tertile	12	0.69 (0.30; 1.58), <i>p</i> = 0.38	14	1.22 (0.55; 2.72), <i>p</i> = 0.61	14	1.15 (0.52; 2.56), <i>p</i> = 0.71
LH/FSH > upper tertile	15	1.13 (0.52; 2.45), <i>p</i> = 0.75	14	1.05 (0.48; 2.29), <i>p</i> = 0.90	13	0.83 (0.38; 1.84), <i>p</i> = 0.66
T > upper tertile	14	0.68 (0.31; 1.49), <i>p</i> = 0.32	17	1.34 (0.63; 2.86), <i>p</i> = 0.44	16	1.08 (0.51; 2.30), <i>p</i> = 0.84
A > upper tertile	14	0.76 (0.35; 1.63), <i>p</i> = 0.47	16	1.12 (0.53; 2.38), <i>p</i> = 0.76	17	1.17 (0.55; 2.46), <i>p</i> = 0.67
DHEA-s > upper tertile	17	1.17 (0.55; 2.46), <i>p</i> = 0.68	15	0.98 (0.46; 2.08), <i>p</i> = 0.95	15	0.87 (0.41; 1.86), <i>p</i> = 0.72
Pcos type 1	22	0.64 (0.31; 1.32), <i>p</i> = 0.22	25	1.08 (0.52; 2.24), <i>p</i> = 0.82	27	1.44 (0.69; 3.00), <i>p</i> = 0.32
Pcos type 2	13	2.45 (0.98; 6.16), <i>p</i> = 0.05 *	5	0.51 (0.17; 1.50), <i>p</i> = 0.22	6	0.67 (0.24; 1.87), <i>p</i> = 0.45
Pcos type 3	6	1.72 (0.54; 5.53), <i>p</i> = 0.32	3	0.59 (0.15; 2.31), <i>p</i> = 0.45	4	0.89 (0.26; 3.11), <i>p</i> = 0.86
Pcos type 4	7	0.60 (0.23; 1.58), <i>p</i> = 0.30	12	1.88 (0.78; 4.50), <i>p</i> = 0.15	8	0.82 (0.33; 2.09), <i>p</i> = 0.69

Abbreviations: BMI—Body Mass Index, WHR—Waist-to-Hip Ratio, WhtR—Waist-to-Height Ratio, T. Chol.—total cholesterol; HDL—High-density lipoprotein, LDL—Low-density lipoprotein, TG—Triglycerides, HOMA-IR—Homeostatic Model Assessment—Insulin Resistance, Fasting gluc.—fasting glucose, Fasting ins.—fasting insulin, FSH—Follicle Stimulating Hormone, LH—luteinising hormone, T—total testosterone, A—androstenedione; DHEA-s—dehydroepiandrosterone sulfate. The *p* values below the threshold of statistical significance are marked with the * *p* < 0.05.

Table 4. The adherence to the active dietary-lifestyle pattern (ADLP) and it’s relation with different metabolic and endocrine markers.

	High Adherence to ADLP		Middle Adherence to ADLP		Low Adherence to ADLP	
	<i>n</i>	OR (CI95%), <i>p</i>	<i>n</i>	OR (CI95%), <i>p</i>	<i>n</i>	OR (CI95%), <i>p</i>
BMI > 30 kg/m ²	11	1.83 (0.74; 4.53), <i>p</i> = 0.18	9	1.35 (0.53; 3.41), <i>p</i> = 0.52	4	1.09 (0.42; 2.81), <i>p</i> = 0.80
BMI > 25 kg/m ²	23	1.39 (0.68; 2.87), <i>p</i> = 0.36	23	1.67 (0.80; 3.46), <i>p</i> = 0.16	14	0.87 (0.41; 1.81), <i>p</i> = 0.70
WHR > 0.80	24	1.34 (0.64; 2.78), <i>p</i> = 0.43	21	1.22 (0.58; 2.57), <i>p</i> = 0.60	18	0.84 (0.40; 1.78), <i>p</i> = 0.65
WhtR > 0.5	21	1.20 (0.58; 2.48), <i>p</i> = 0.62	24	2.37 (1.12; 5.01), <i>p</i> = 0.02 *	12	0.97 (0.46; 2.03), <i>p</i> = 0.93
Fat > 35%	24	0.97 (0.47; 1.99), <i>p</i> = 0.94	29	2.71 (1.27; 5.77), <i>p</i> = 0.01 *	16	1.60 (0.77; 3.33), <i>p</i> = 0.21
Cholesterol > 200 mg/dL	13	2.35 (0.93; 5.89), <i>p</i> = 0.07	4	0.32 (0.10; 1.06), <i>p</i> = 0.06	9	1.82 (0.72; 4.63), <i>p</i> = 0.20
LDL > 135 mg/dL	6	2.51 (0.70; 9.05), <i>p</i> = 0.15	1	0.20 (0.02; 1.68), <i>p</i> = 0.13	4	1.23 (0.33; 4.63), <i>p</i> = 0.75
HDL < 50 mg/dL	8	1.65 (0.60; 4.58), <i>p</i> = 0.32	7	1.42 (0.50; 4.01), <i>p</i> = 0.50	3	1.88 (0.68; 5.22), <i>p</i> = 0.22
TG > 150 mg/dL	5	1.39 (0.40; 4.84), <i>p</i> = 0.60	5	1.78 (0.50; 6.31), <i>p</i> = 0.36	3	1.60 (0.46; 5.60), <i>p</i> = 0.46
HOMA > 2.5	18	1.03 (0.49; 2.18), <i>p</i> = 0.92	17	1.21 (0.58; 2.48), <i>p</i> = 0.61	15	1.09 (0.53; 2.27), <i>p</i> = 0.80
Fasting gluc. > 100 mg/dL	5	1.28 (0.33; 4.96), <i>p</i> = 0.71	1	0.22 (0.03; 1.92), <i>p</i> = 0.17	4	0.88 (0.21; 3.76), <i>p</i> = 0.81
Fasting ins. > 10 mU/mL	26	1.52 (0.75; 3.12), <i>p</i> = 0.24	21	1.05 (0.51; 2.17), <i>p</i> = 0.88	18	1.10 (0.53; 2.27), <i>p</i> = 0.79
LH > upper tertile	16	1.35 (0.63; 2.92), <i>p</i> = 0.43	11	0.70 (0.31; 1.61), <i>p</i> = 0.40	14	1.00 (0.47; 2.12), <i>p</i> = 0.99
FSH > upper tertile	14	0.93 (0.87; 2.09), <i>p</i> = 0.87	12	0.94 (0.41; 2.12), <i>p</i> = 0.88	14	1.10 (0.49; 2.48), <i>p</i> = 0.80
LH/FSH > upper tertile	16	1.28 (0.59; 2.77), <i>p</i> = 0.52	12	0.79 (0.35; 1.77), <i>p</i> = 0.57	14	0.80 (0.36; 1.80), <i>p</i> = 0.60
T > upper tertile	18	1.20 (0.57; 2.55), <i>p</i> = 0.62	13	0.77 (0.35; 1.69), <i>p</i> = 0.51	16	1.06 (0.49; 2.29), <i>p</i> = 0.87
A > upper tertile	17	1.17 (0.56; 2.47), <i>p</i> = 0.67	14	1.57 (0.47; 5.26), <i>p</i> = 0.46	16	1.01 (0.47; 2.17), <i>p</i> = 0.96
DHEA-s > upper tertile	16	1.02 (0.48; 2.17), <i>p</i> = 0.95	18	1.48 (0.70; 3.13), <i>p</i> = 0.30	13	0.75 (0.34; 1.64), <i>p</i> = 0.47
Pcos type 1	31	2.10 (1.00; 4.40), <i>p</i> = 0.04 *	18	0.46 (0.22; 0.96), <i>p</i> = 0.04 *	25	1.83 (0.85; 3.90), <i>p</i> = 0.11
Pcos type 2	6	0.47 (0.16; 1.39), <i>p</i> = 0.17	13	3.47 (1.37; 8.82), <i>p</i> = 0.00 *	5	0.58 (0.19; 1.69), <i>p</i> = 0.31
Pcos type 3	3	0.55 (0.14; 2.14), <i>p</i> = 0.39	5	1.35 (0.41; 4.44), <i>p</i> = 0.62	5	0.65 (0.17; 2.56), <i>p</i> = 0.54
Pcos type 4	8	0.77 (0.30; 1.94), <i>p</i> = 0.58	8	0.86 (0.34; 2.17), <i>p</i> = 0.75	11	0.75 (0.29; 1.96), <i>p</i> = 0.56

Abbreviations: BMI—Body Mass Index, WHR—Waist-to-Hip Ratio, WhtR—Waist-to-Height Ratio, T. Chol.—total cholesterol; HDL—High-density lipoprotein, LDL—Low-density lipoprotein, TG—Triglycerides, HOMA-IR—Homeostatic Model Assessment—Insulin Resistance, Fasting gluc.—fasting glucose, Fasting ins.—fasting insulin, FSH—Follicle Stimulating Hormone, LH—luteinising hormone, T—total testosterone, A—androstenedione; DHEA-s—dehydroepiandrosterone sulfate. The *p* values below the threshold of statistical significance are marked with the * *p* < 0.05.

4. Discussion

The study met its aim and distinguished three dietary-lifestyle patterns (DLP): western (WDLP), prudent (PDLP) and active (ADLP). The WDLP was characterised by a high-frequency intake of animal foods, sweets and sweetened beverages, white grains, junk and fried foods, and a low-frequency intake of plant foods. This DLP was also characterised by high visceral fat mass. PDLP was characterised by high-frequency intake of plant foods and dairy, high meal frequency per day, and intense exercise. ADLP was characterised by high visceral fat, high-frequency intake of plant products, intense exercise and low intake of junk and fried food.

4.1. The Relation of DLPs with Metabolic and Endocrine Markers

High adherence to WDLP was related to high LDL, triglycerides, and FSH but low total testosterone and androstenedione. Patients with low adherence to the WDLP were at lower risk of being obese and having insulin resistance. This result agrees with other studies showing that western dietary patterns harm metabolic health in different populations [26,37].

In turn, high adherence to PDLP was related to the low chance of overweight and excess fat tissue. At the same time, they were more likely to have PCOS type II. Nevertheless, this result contradicts the previous study, which found that PCOS type II is inversely associated with healthy eating [38]. However, most studies on PCOS phenotypes, nutrition status and dietary intake show that obesity and adherence to western dietary patterns tend to be related to classic PCOS phenotype (type I) [4–6]. This statement agrees with our findings that type I of PCOS was related to ADLP. It is worthwhile to underline that this pattern, although characterised by high physical activity, also had high visceral fat volume and some unhealthy dietary behaviours.

4.2. Plant Products Intake

The distinguished DLPs support the results of other studies controlling the intake of sweets and sweetened beverages, where increasing the vegetable intake was related to a lower incidence of insulin resistance and dyslipidemia [8,12]. This result supports studies showing the importance of the GI of diet for women with PCOS. A low GI diet has been recommended for women with PCOS, especially with increased insulin resistance [39]. Low GI foods are primarily plant-based foods containing complex carbohydrates, such as unprocessed grains, legumes and vegetables. However, there are some drawbacks to following only the list of low GI products [13]. As mentioned earlier, the proper combination of products with high and low GI in one meal will reduce glucose absorption, and restriction in different fruits may influence the antioxidant dietary capacity. In our study, a high intake of fruits did not negatively affect metabolic markers. Moreover, the combination of vegetables and legumes had a positive effect. In turn, meat intake in our study, which has a low GI, negatively affected metabolic markers in women with PCOS.

4.3. Meat Intake

In our study, the intake of meats (white and red meat) has been a significant factor in distinguishing DLPs. High-frequency intake of meat as part of WDLP was related to metabolic disorders in PCOS. Patients with high adherence to WDLP consumed meat products on average over once a day while comparing it to those with low adherence, where meat intake was on average a few times a week (Supplement Table S2). Excessive intake of meat is related to multiple chronic diseases. It has been shown that saturated fatty acid intake, presented in meat, was related to heart rate variability [40]. Some studies suggest that women with PCOS consume more saturated fatty acids than recommended [24]. A high saturated fat intake is present in red meats, but sweets and fried food in WDLP could lower insulin sensitivity. Excess of saturated fatty acids, especially palmitate, influences the increase of white adipose tissue and apoptosis through oxidative or endoplasmic reticulum stress, generation of ceramide and reactive oxygen species, and protein kinase C signalling [41]. Information concerning meat intake is very limited in the dietary manage-

ment of PCOS. Servings of fruits and vegetables are carefully explained, yet there is no recommendation concerning the number of servings and portion sizes of meats. Setting the proper animal product servings in diet therapy is also essential to establish the most optimal diet to alleviate the PCOS symptoms and protect the environment.

4.4. Dairy Intake

One of the alternative protein sources is dairy. The high frequency of dairy consumption in our study was a part of PDLP and has been related to a more desirable metabolic profile in women with PCOS. The literature shows that high-frequency dairy intake is related to a lower risk of obesity and cardiovascular risks [42]. However, dairy intake and its relation to PCOS, fertility and insulin resistance are unclear. Some studies suggest that consuming dairy products was negatively associated with the risk of type 2 diabetes mellitus, insulin resistance and ovulation disorders [43]. The fermented dairy had a significant part in this group. Fermented dairy, such as yoghurt, has been associated with lowering body mass [44], and its probiotic properties improve anti-inflammatory response [45]. Consumption of fermented products could reduce pancreatic lipase activity, decreasing fatty acid absorption [46].

It is essential to mention that dairy restrictions could increase the consumption of phytoestrogens from dairy alternatives such as soy products. Phytoestrogens could be beneficial in PCOS therapy; however, more studies in this field are needed [47,48].

4.5. Meal Frequency

Additionally, women following the PDLP had a high frequency of meals eaten during the day, and women following WDLP had a low frequency of meals per day. These results emphasise the importance of regular meals in diet therapy. The high frequency of meals has been related to lower body fat and a high fat-free mass among the adult population [49].

4.6. Physical Activity

Intensive exercise has been a significant factor in PDLP, and low exercise, in turn, has been a characteristic of WDLP, which supports the importance of physical activity for health. However, the surprise has been the ADLP, which, even though significantly high medium intensity exercise and walking, also had high VAT and was more prone to complete PCOS symptoms [50].

4.7. Limitations

Even though the study reached its aims, it had some limitations. First, the sample size has been limited; however, the smaller sample size allowed us to include more endocrine and metabolic markers analysis. Second, the physical activity was self-reported in our study by an internationally validated questionnaire. Physical activity tracking by online devices could be used in future research to support the results of our study. Third, the food frequency questionnaire was used. Even though the validated questionnaire allowed the calculation of multiple nutrition scores, it could be valuable to see the daily energy intake and the nutritional density in future research. However, the food frequency questionnaire allowed us to analyse long-term nutrition habits, which are not depending on seasonal variability. The KomPAN questionnaire specifically asks about the intake in the past year. A 24-h recall cannot show a typical annual intake [51].

5. Conclusions

Three dietary-lifestyle patterns (DLPs) were distinguished and related to the visceral fat tissue in women with PCOS: Western, prudent, and active. Low adherence to WDLP was additionally related to desirable levels of metabolic markers. High adherence to PDLP was linked to type two PCOS. The PDLP was characterised by increased frequency intake of plant-based food and intense physical activity. In turn, the least desirable WDLP was

characterised by a high intake of meat products and low physical activity. The role of plant-based foods could be underestimated in diet therapy, and it needs further investigation.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/app13042118/s1>, Table S1. Factor loadings of three dietary-lifestyle patterns (DLP): western (WDLP), prudent (PDLP), and active (ADLP). Table S2. Food frequency intake of the study group ($n = 140$) described in means and medians. Table S3. Mean food frequency intake per day for high, medium and low adherence to the western dietary-lifestyle pattern (WDLP). Table S4. Mean daily food frequency intake for high, medium and low adherence to the prudent dietary-lifestyle pattern (PDLP). Table S5. Mean food frequency intake per day for high, medium and low adherence to the active dietary-lifestyle pattern (ADLP).

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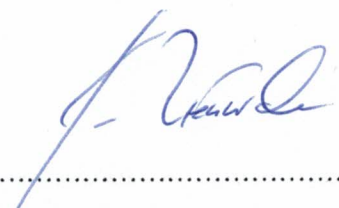
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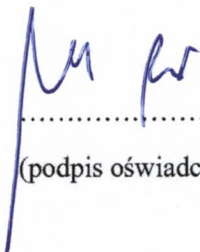
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Article

Intake of Low Glycaemic Index Foods but Not Probiotics Is Associated with Atherosclerosis Risk in Women with Polycystic Ovary Syndrome

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Abstract: Women with polycystic ovary syndrome (PCOS) are at high cardiometabolic risk. The atherogenic index of plasma (AIP) strongly predicts atherosclerosis. Some studies suggest that probiotic intake may lower AIP. This study analysed the relationship between the frequency of dietary intake of low glycaemic index (prebiotic) and probiotic foods and atherosclerosis risk in women with PCOS. **Methods:** A total of 127 women were divided into two groups: AIP over 0.11 (highAIP) and AIP \leq 0.11 (lowAIP). The KomPAN[®] questionnaire was used to measure food frequency intake; pro-healthy, non-healthy, low glycaemic and probiotic dietary indexes were calculated based on daily food consumption. Body composition was measured by air displacement plethysmography (BodPod). AIP was calculated as a logarithm of triglycerides and high-density lipoproteins from plasma. **Results:** The highAIP group was 63% less likely to consume low glycaemic index foods three or more times a day than the lowAIP group. The HighAIP group was also 62% less likely to consume buckwheat, oats, whole-grain pasta or coarse-ground grains at least a few times a week. Pro-healthy foods tended to be less frequently consumed by the highAIP group, when adjusted for BMI and age. **Conclusion:** Women with PCOS at high risk of atherosclerosis consumed less low glycaemic index foods than women with a low risk of atherosclerosis. Intake of high-fibre, low glycaemic index foods could prevent atherosclerosis in women with PCOS; however, the effect of probiotic food intake remains unclear.

Keywords: atherosclerosis; frequency intake; diet quality; BodPod; body composition; AIP



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1. Introduction

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder that affects reproductive-age women, and is characterised by both ovarian cysts and high levels of androgenic hormones [1]. This disorder can be accompanied by insulin sensitivity, diabetes, high blood pressure, hypercholesterolemia, and depression [2]. Additionally, more than 50% of women with PCOS are believed to be overweight or obese, with an increased cardiometabolic risk due to the conditions listed above [3–5].

Research has shown that the vast majority of women with PCOS consume an unbalanced diet deficient in fibre, fatty acid omega 3, calcium, magnesium, zinc, and vitamins (folic acid, vitamin C, and vitamin B12) [6]. In contrast, excesses of sucrose, sodium, total fats, saturated fatty acids, and cholesterol have been noted [6]. With the aim of cardiometabolic prevention, women with PCOS are advised to increase their intake of plant-based foods—including whole grains, fruits, vegetables, legumes, nuts, and less-

processed foods of animal origin [7]. If insulin resistance is present, they should also lower the glycaemic index and saturated fats of food they consume. Our previous research has shown that women with PCOS consume fewer low glycaemic index foods than those in a control group [8]. Additionally, women who restrict sugar (foods with a high glycaemic index) tend to have better diet quality overall than women who do not [9]. Some studies indicate that vitamin B3 supplementation could be valuable, as a deficiency in vitamin B3 contributes to inflammation and thus increases cardiometabolic risk [10,11]. While drawing attention to cardiometabolic risk protection in women with PCOS, it has recently been shown that 8 weeks of CoQ10 supplementation had a beneficial effect on inflammatory and endothelial dysfunction markers in overweight and obese patients with PCOS [12–14]. In addition, vitamin D supplementation increases insulin synthesis, insulin receptor expression, and insulin response to glucose transport [15]. Similarly, herbal supplements seem to be highly effective in combating chronic inflammation (*Curcuma longa*) and improving liver steatosis (*Silybum marianum*, *Nigella sativa*) in PCOS [16,17].

Recently, the relationship between the gut-brain axis and health has been discussed. Multiple studies suggest using probiotics to manage metabolic syndrome; however, results vary [18–20]. *Lactobacillus* and *Bifidobacterium*, found in naturally fermented foods such as yoghurt, could improve the gut microbiota of obese patients and therefore improve metabolic syndrome status [21]. Some studies suggest that probiotic supplementation in both humans and animals lowers plasma's blood lipid and atherogenic index, a strong marker of coronary artery disease [22–24]. Additionally, it has been shown that microbiota is affected by BMI and body composition [25,26]. After weight reduction in obese patients, the total abundance of bacteria increases; specifically, the ratio of *Firmicutes/Bacteroidetes* decreases, and *Lactobacilli* significantly increase [25].

The novel concept of “microgenderome,” the potential interaction between sex hormones and gut microbiota, has also recently emerged in microbiota research [27]. This theory suggests that the composition of the commensal microbiome of males and females becomes different during puberty, and that sex hormone levels have specific effects on microbiota composition. A mouse model found that a decrease in gut microbiota increased testosterone concentration in female mice but decreased it in male mice. Thus, the commensal gut microbiota affected the production of the male sex hormone [27,28]. Taken together, these results and the research on intestinal microbiota problems in women with PCOS indicate that this relationship needs to be investigated; some researchers suggest that the treatment of PCOS should include probiotic supplementation [29]. Additionally, research shows that the intake of polyphenols from whole grains can regulate both microbiota and serum lipid profile [30]. Therefore, considering that women with PCOS have microbiota alterations [28], the intake of prebiotics and high-fibre foods should be emphasised, and recommendations for consumption should be discussed.

Although cardiometabolic risk can be life-threatening in women with PCOS, research on the consumption of synbiotic foods in this population is limited, so studies should be developed with this aim. It is worth noting that the search for markers that estimate cardiometabolic risk in different populations, including women with PCOS, is widely discussed in the literature [3,31]. However, few studies have reported on the properties of dietary probiotics that lead to changes in cardiometabolic markers in women with PCOS. Among several such markers, the atherogenic index of plasma (AIP) is a logarithmic transformation of the ratio of triglycerides and high-density lipoproteins [24]. AIP is inversely related to LDL particle size, and small dense LDL-C is very vulnerable to oxidative damage; therefore, it is more likely to cause atherosclerotic lesions. This marker is considered a good early predictor of cardiovascular disease in women with PCOS and has previously been used in research with this population [3,18,32–34]. Nevertheless, AIP has never been analysed in relation to the intake frequency of antiatherogenic foods.

Despite the apparent benefits of synbiotic foods on health outcomes, their effect on PCOS outcomes remains unclear. Additionally, the frequency of consumption of selected food groups that guaranteed improvement was not identified. Those facts prompted us

to look for associations between atherosclerosis risk and the consumption of synbiotic food groups. With this in mind, we analysed the relationship between the consumption frequency of pro- and prebiotic foods and atherosclerosis risk, as such consumption could have a potential protective effect in supporting the treatment of women with PCOS.

2. Materials and Methods

2.1. Study Participants

A total of 127 women of reproductive age diagnosed with PCOS were recruited from the Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences (Figure 1). Participants were classified according to Rotterdam criteria. Specific inclusion criteria for the study group were as follows: PCOS diagnosis (according to Rotterdam criteria), age 18–40, and BMI 18–35 kg/m². Exclusion criteria for both low and medium-high AIP groups comprised: chronic hepatic, renal or rheumatic diseases; overt hypothyroidism; and pregnancy. Written informed consent was obtained from all participants. The clinical examination protocol complied with the Declaration of Helsinki for Human and Animal Rights and its later amendments and received ethical approval from the Board of Bioethics of the University of Medical Science (552/16; 986/17).

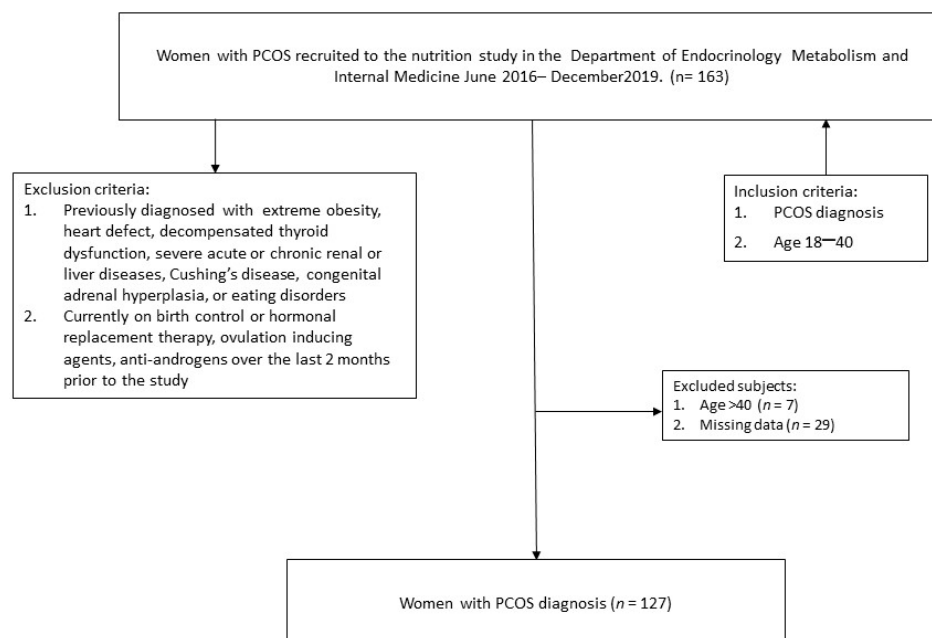


Figure 1. Patient recruitment flowchart.

2.2. Atherogenic Markers

Total cholesterol (TC-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG-C) were evaluated using the enzymatic colourimetric method. The Friedewald formula was used to estimate low-density lipoprotein cholesterol (LDL-C). Serum glucose was assessed with the hexokinase method (Roche Diagnostics) and a coefficient of variation (CV) of 3%. The following formula calculated the homeostasis model assessment for insulin resistance (HOMA-IR): $\text{HOMA-IR} = (\text{fasting plasma glucose (mg/dL)} \times \text{fasting plasma insulin (mU/L)}) / 405$. To determine IR, a threshold of $\text{HOMA-IR} > 2.5$ was used [35]. The atherogenic index of plasma (AIP) was calculated as the logarithm of the total triglycerides to high-density lipoproteins ratio. A ratio of 0.11 and above was considered medium–high risk [36].

2.3. Food Frequency Intake and Diet Quality Indexes

Food frequency intake was assessed using the validated Dietary Habits and Nutrition Beliefs KomPAN[®] Questionnaire, which consists of 25 questions about different food

groups. According to the manual, each answer is rated from 0 (never eaten) to 2 (eaten twice a day or more) [37,38]. For each food item, the frequency consumption categories were converted to values reflecting daily consumption (1) never = 0.00, (2) 1–2 times/month = 0.06, (3) once a week = 0.14, (4) 2–3 times/week = 0.5, (5) once a day = 1 and (6) a few times during the day = 2. These conversions are accepted in the literature and bear out the authors' own experiences [39,40].

The intensity of food frequency intake was characterised using diet indexes for products widely considered healthy, unhealthy, probiotic, and low glycaemic index. To evaluate overall diet quality, pro-Healthy-Diet-Index (pHDI-10), non-Healthy-Diet-Index (nHDI-14), Probiotic diet index (ProDI-4), and low-glycaemic diet index (IGIDI-4) scores were established based on previous knowledge and other validated studies [8,41].

Each index was designed and calculated based on the same conversion formula as previously validated in [8,38]: Groups of food products classified in the individual diet indexes are presented in Table 1.

$$\text{Diet Index (\%)} = \frac{\sum A * 100\%}{\sum B}$$

where *A* was the patient's actual frequency intake per day, and *B* was the patient's maximum possible frequency intake per day. For example, for the probiotic food index:

$$\sum A = 0.06 + 0.14 + 1 + 2 \text{ and } \sum B = 2 + 2 + 2 + 2.$$

Table 1. Probiotic (ProDI-4), low glycaemic (IGIDI-4), pro-healthy (pHDI-10), and non-healthy (nHDI-14) diet quality indexes and their product content.

Food Group	Products Included
proDI-4 ¹	(1) Fermented milk drinks, (2) Pickled vegetables, (3) Fresh cheese-curd products, (4) Cheese
IGIDI-4 ²	(1) Wholemeal bread, (2) Buckwheat, oats, whole-grain pasta or other coarse-ground grains, (3) Legume-based foods, (4) Vegetables
pHDI-10 ³	(1) Wholemeal bread, (2) Buckwheat, oats, whole-wheat pasta, (3) Milk, (4) Fermented milk drinks, (5) Fresh cheese-curd products, (6) White meat, (7) Fish, (8) Legume-based foods, (9) Fruits, (10) Vegetables
nHDI-14 ⁴	(1) White bread, (2) White rice, pasta, fine-ground grains (3) Fast food, (4) Fried dishes, (5) Butter, (6) Lard, (7) Cheese, (8) Cold meats, smoked sausages, hot dogs, (9) Red meat dishes, (10) Sweets, (11) Tinned meats, (12) Sweetened carbonated and non-carbonated drinks, (13) Energy drinks, (14) Alcoholic beverages

¹ Probiotic diet index, ² low glycaemic diet index, ³ Pro-healthy diet index, ⁴ Non-healthy diet index.

For each food group (diet index), consumption level was classified on a percentage scale. Each diet index was expressed in % points and was categorised as follows: low- (0–33.32% points), moderate- (33.33–66.65% points), or high- (66.66–100% points) intensity consumption of selected food groups.

To control for both fat intake and for preferences of whole fat, low fat, and non-fat dairy, as well as for sweetened and non-sweetened dairy, the following questions were added to the analysis:

1. What is the usual fat content of dairy products you consume?
2. Do you consume sweetened milk drinks and desserts for snacks?
3. Do you consume non-sweetened milk drinks and desserts for snacks?

The answers to these questions were analysed in Table 2.

2.4. Body Composition

Patient body composition was assessed using air plethysmography via BodPod (Life Measurement Inc., Concord, CA, USA); measurements were performed according to the validated protocol. Participants came to sessions after overnight fasting. The patients were advised to wear approved clothing, such as bathing suits, compression shorts, and

bras with no wiring or padding, and not to wear any jewellery. Additionally, each patient wore a swim cap to decrease hair volume. The equipment was calibrated every morning before study sessions; each session took place at 21–26 °C with relative humidity between 20–70%. Patients' height, weight, and waist and hip circumferences were also recorded. Measurements (and their respective cut-off points) were performed according to WHO recommendations [42] (Supplementary Table S1)

Table 2. Characteristics of the study sample and their dairy preferences.

Variable	Low AIP (n = 68)		High AIP (n = 59)		p
	Mean ± SD	Median (CI95%)	Mean ± SD	Median (CI95%)	
Age (y)	26 ± 5	25 (4; 6)	26 ± 6	25 (5; 7)	0.74
Body mass (kg)	66.4 ± 11.2	63.6 (11.2; 9.6)	75.3 ± 16.1	72.7 (13.6; 19.7)	0.00 *
BMI (kg/m ²)	23.5 ± 3.3	22.9 (2.9; 4.0)	27.4 ± 5.7	26.8 (4.8; 7.0)	0.00 *
Waist circumference (cm)	77.3 ± 9.9	76.0 (8.4; 11.9)	86.5 ± 14.3	88.0 (12; 18)	0.00 *
WHR (-)	0.79 ± 0.06	0.78 (0.05; 0.07)	0.84 ± 0.10	0.80 (0.09; 0.12)	0.00 *
FM (%)	37.2 ± 22.9	33.0 (19.5; 27.7)	45.8 ± 25.8	41.1 (21.8; 31.6)	0.05
FFM (%)	70.5 ± 16.9	68.2 (14.4; 20.5)	66.9 ± 21.2	60.5 (17.9; 26.1)	0.30
T. Cholesterol (mg/dL)	170.6 ± 29.2	168.5 (25.0; 35.2)	187.4 ± 32.0	185.0 (27.1; 39.2)	0.00 *
HDL (mg/dL)	75 ± 14	73.0 (12.0; 16.9)	55 ± 11	55.0 (9.0; 13.0)	0.00 *
LDL (mg/dL)	84 ± 25	83.0 (21.5; 30.3)	108 ± 30	110.4 (25.7; 37.1)	0.00 *
TG (mg/dL)	55 ± 15	53.0 (12.7; 17.9)	123 ± 67	103 (56; 81)	0.00 *
Fasting glucose (mg/dL)	87 ± 7	88 (6; 9)	91 ± 7	90 (5.6; 8.0)	0.00 *
Fasting insulin (uU/mL)	8.10 ± 3.63	7.35 (3.10; 4.37)	14.59 ± 8.58	12.4 (7.3; 10.5)	0.00 *
HOMA-IR (-)	1.79 ± 0.89	1.58 (0.76; 1.07)	3.37 ± 2.19	2.9 (1.8; 2.7)	0.00 *
AIP ¹ (-)	-0.33 ± 0.29	-0.35 (0.25; 0.36)	0.73 ± 0.55	0.59 (0.47; 0.67)	0.00 *
proDI-4 ² (%)	13.85 ± 8.75	14.12 (7.48; 10.53)	14.84 ± 8.26	14.00 (6.99; 10.10)	0.52
IGIDI-4 ³ (%)	30.47 ± 16.19	27.50 (13.85; 19.48)	25.27 ± 14.29	26.75 (12.09; 17.46)	0.05 *
pHDI-10 ⁴ (%)	27.50 ± 11.04	26.10 (9.44; 13.29)	23.99 ± 10.72	20.3 (9.07; 13.10)	0.07
nHDI-14 ⁵ (%)	13.63 ± 7.83	11.39 (6.70; 9.43)	13.92 ± 8.03	11.86 (6.80; 9.82)	0.83
	n	%	n	%	
Unsweetened milk drinks as a snack	25	20	21	17	0.89
Sweetened milk drinks as a snack	12	9	18	14	0.08
Milk and milk drinks					
Whole fat	27	21	27	21	
Low fat	30	24	27	21	0.68
Non-fat	2	2	1	1	
No dairy	9	7	4	3	

¹ AIP—atherogenic index of plasma; ² proDI-4—probiotic diet index; ³ IGIDI-4—low glycaemic diet index; ⁴ pHDI-10—pro-healthy diet index; ⁵ nHDI-14—non-healthy diet index. *p* values below the statistical significance threshold are marked with * (*p* < 0.05). Non-parametric values were calculated with chi-square tests.

2.5. Statistics

Statistical analysis was performed using Statistica (Stat Soft, Krakow, Poland) software. Differences in patient characteristics between the two groups were calculated using independent samples *t*-tests. For data that was not normally distributed, the Mann-Whitney *U* test was used. Chi-square tests were performed for non-parametric and categorisation data. Logistic regression analysis was used to estimate odds ratios (OR) and 95% confidence intervals (95% CI) of the estimated dietetic intake in relation to the atherogenic index of plasma. Statistical analyses were performed according to other previously published studies [8,41,43].

3. Results

A total of 127 women with PCOS took part in the study (Figure 1). Women were divided into two groups: one of the participants with either a moderate or high risk of atherosclerosis (AIP ≥ 0.11; *n* = 59), and one of those with a low risk of atherosclerosis (AIP < 0.11; *n* = 68). Women with high AIP had significantly higher metabolic markers (body mass, BMI, waist circumference, WHR, total cholesterol, LDL, triglycerides, HOMA, fasting insulin, and glucose). HDL was significantly higher in women with low API, and women with high API tended to have a higher fat percentage than women with low API. Fat-free mass and age were not significantly different between the two groups (Table 2).

In both groups, low-intensity consumption of both pre-and probiotic foods was observed; we noted values below 33%. Nevertheless, in the low AIP group, preDI-4 was significantly lower than in the group with high AIP (30% vs. 25%; $p < 0.05$). There was also no significant difference in consumption of sweetened milk drinks and desserts, unsweetened milk drinks and desserts, and low and whole-fat milk between groups. Additionally, 13% of the women did not consume dairy at all.

The association between food frequency intake and high AIP is shown in Table 3. Women with AIP equal to or above 0.11 were 68% less likely to have IGIDI-4 equal to or above the upper quartile than women with low AIP (Figure 2, Supplementary Table S2). Women with high AIP were also 65% less likely to consume buckwheat, oats, whole-grain pasta or coarse-ground grains at least a few times a week (Table 3).

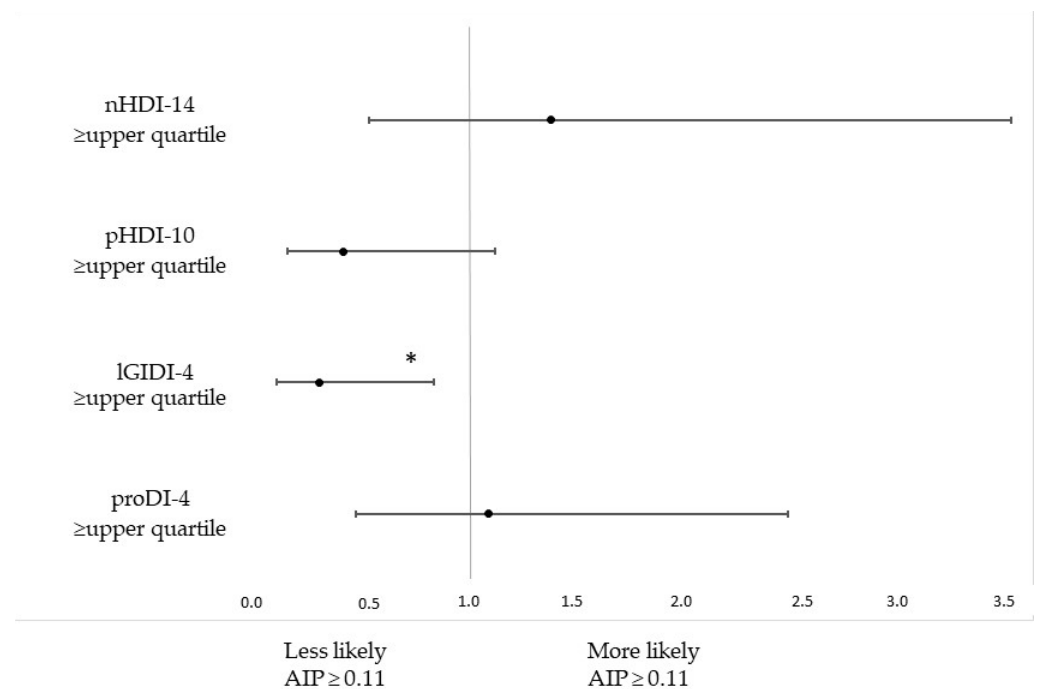
Table 3. Odds ratios (ORs with 95% confidence intervals (95% CI)) of the high atherogenic index of plasma according to the consumption frequency of selected food groups.

Food Groups	Atherogenic Index of Plasma ≥ 0.11		
	Occurrence (%) / n	Crude OR (CI 95%)	OR Adjusted for BMI and Age (CI 95%)
Wholemeal (brown) bread/bread rolls \geq once a day	(13)/16	1.21 (0.54; 2.72); $p = 0.64$	1.18 (0.48; 2.89); $p = 0.71$
Buckwheat, oats, whole-grain pasta or other coarse-ground grains \geq two times a week	(16)/20	0.38 (0.18; 0.79); $p = 0.01$ *	0.35 (0.16; 0.78); $p = 0.01$ *
Pickled vegetables \geq two times a week	(7)/9	1.35 (0.48; 3.80); $p = 0.57$	0.82 (0.24; 2.84); $p = 0.76$
Milk (including flavoured milk, hot chocolate, or latte) \geq once a day	(16)/19	0.64 (0.31; 1.33); $p = 0.23$	0.51 (0.22; 1.18); $p = 0.11$
Fermented milk drinks, e.g., yoghurts, kefir (natural or flavoured) \geq once a day	(8)/10	1.18 (0.45; 3.11); $p = 0.73$	0.96 (0.32; 2.85); $p = 0.94$
Fresh cheese-curd products, e.g., cottage cheese, cream cheese, cheese-based puddings \geq once a day	(2)/2	1.16 (0.16; 8.66); $p = 0.86$	1.03 (0.10; 10.4); $p = 0.98$
White meat, e.g., chicken, turkey, rabbit \geq two times a week	(35)/45	1.25 (0.56; 2.80); $p = 0.59$	1.25 (0.56; 2.80); $p = 0.59$
Fish \geq two times a week	(4)/5	0.61 (0.19; 1.95); $p = 0.40$	0.47 (0.13; 1.78); $p = 0.26$
Legume-based foods, e.g., beans, peas, soybeans, lentils \geq once a week	(16)/19	0.72 (0.35; 1.51); $p = 0.38$	0.60 (0.26; 1.37); $p = 0.22$
\geq two times a week	(6)/7	0.60 (0.21; 1.55); $p = 0.27$	0.50 (0.16; 1.54); $p = 0.22$
Fruits \geq two times a day	(9)/12	0.66 (0.29; 1.52); $p = 0.32$	0.59 (0.23; 1.51); $p = 0.27$
Vegetables \geq two times a day	(17)/22	1.16 (0.56; 2.43); $p = 0.68$	1.21 (0.54; 2.70); $p = 0.64$
White bread and bakery products, e.g., wheat bread, rye bread, wheat-rye bread, toast bread, bread rolls \geq once a day	(14)/18	0.71 (0.34; 1.50); $p = 0.36$	0.98 (0.43; 2.26); $p = 0.97$
White rice, white pasta, fine-ground groats, e.g., semolina, couscous \geq two times a week	(12)/15	0.55 (0.26; 1.19); $p = 0.13$	0.67 (0.29; 1.56); $p = 0.35$
Fast foods, e.g., potato chips/French fries, hamburgers, pizza, hot dogs \geq once a week	(9)/11	0.81 (0.34; 1.95); $p = 0.64$	1.03 (0.40; 2.67); $p = 0.95$
Fried foods (e.g., meat or flour-based foods such as dumplings, pancakes, etc.) \geq two times a week	(20)/26	1.12 (0.52; 2.43); $p = 0.77$	1.12 (0.52; 2.43); $p = 0.77$
Butter as a bread spread or as an addition to your meals/for frying/for baking, etc. \geq once a day	(15)/19	1.06 (0.50; 2.27); $p = 0.87$	0.85 (0.36; 1.98); $p = 0.70$

Table 3. Odds ratios (ORs with 95% confidence intervals (95% CI)) of the high atherogenic index of plasma according to the consumption frequency of selected food groups.

Food Groups	Atherogenic Index of Plasma ≥ 0.11		
	Occurrence (%)/n	Crude OR (CI 95%)	OR Adjusted for BMI and Age (CI 95%)
Lard as a bread spread, or as an addition to your meals/for frying/for baking, etc. \geq once a week	(1)/1	0.28 (0.03; 2.60); $p = 0.26$	0.25 (0.02; 3.09); $p = 0.27$
Cheese (including processed cheese and blue cheese) \geq two times a week	(24)/30	1.10 (0.54; 2.22); $p = 0.80$	1.34 (0.61; 2.94); $p = 0.46$
Cured meat, smoked sausages, hot dogs \geq two times a week	(26)/33	1.35 (0.66; 2.73); $p = 0.41$	1.45 (0.66; 3.17); $p = 0.35$
Red meat, e.g., pork, beef, veal, lamb, game \geq two times a week	(16)/20	1.98 (0.88; 4.43); $p = 0.10$	1.81 (0.75; 4.36); $p = 0.18$
Sweets, e.g., confectionery, biscuits, cakes, chocolate bars, cereal bars, etc. \geq two times a week	(31)/39	1.06 (0.51; 2.23); $p = 0.87$	1.25 (0.55; 2.85); $p = 0.59$
Tinned (jar) meats \geq 1–3 times a month	(9)/12	1.32 (0.53; 3.30); $p = 0.54$	0.94 (0.33; 2.67); $p = 0.91$
Sweetened carbonated or still drinks \geq two times a week	(6)/8	1.18 (0.41; 3.39); $p = 0.76$	0.92 (0.27; 3.08); $p = 0.89$
Energy drinks \geq once a week	(2)/2	0.76 (0.12; 4.80); $p = 0.77$	1.01 (0.14; 7.61); $p = 0.99$
Alcoholic beverages \geq once a week	(10)/13	0.79 (0.34; 1.79); $p = 0.56$	0.79 (0.32; 1.97); $p = 0.61$

p values below the threshold of statistical significance are marked with * ($p < 0.05$).

**Figure 2.** Odds ratios with 95% confidence intervals for upper quartiles of diet quality indexes when the atherogenic index of plasma (AIP) was above or equal to 0.11, adjusted for age and BMI. p values below the statistical significance threshold are marked with * ($p < 0.05$).

4. Discussion

The present study is an original investigation examining the effect of synbiotic food consumption on atherosclerosis risk in women diagnosed with PCOS. Overall, we observed that consuming low glycaemic index foods at least twice a week decreased cardiometabolic risk.

Before discussing prebiotic, probiotic or synbiotic foods, it is essential to clarify that their health-promoting properties are widely confirmed [44–46]. Probiotics are living microorganisms that, when administered adequately, confer a health benefit to the host [47,48]. Prebiotics are non-digestible foods that positively affect the growth and/or activity of certain bacteria in the gastrointestinal tract, thus improving the host's condition [49]. Synbiotics combine probiotics and prebiotics; all can be found in popular food products. Prebiotics are found in wholemeal grains, chicory root, garlic, onions, legumes, or apples; the soluble fibre present in those foods feeds beneficial microbiota in the human large intestine. Additionally, reports have shown that the intake of polyphenols influences the gut-brain axis [50]. Probiotics can be found in fermented foods like yoghurt, kimchi, pickles, or tempeh.

Since eating behaviour is complex and respondents eat foods with similar properties; we designed probiotic and low glycaemic, high-fibre diet indexes. The probiotic index included fermented milk drinks, tinned vegetables, fresh cheese-curd products, and cheese. In comparison, the low glycaemic index consisted of wholemeal bread, buckwheat, oats, whole-grain pasta or other coarse-ground grains, legume-based foods, and vegetables.

Compared with women with PCOS and high AIP, those with low AIP reported higher-intensity consumption of low glycaemic index (prebiotic) foods, like wholemeal bread, buckwheat, oats, whole-grain pasta or other coarse-ground groats, legume-based foods, and vegetables. A high frequency of consumption of products from this particular group (above the top quartile: 38.25%) indicated a significantly lower (68%) cardiometabolic risk. However, the risk changed when we excluded legumes and vegetables from this group. It turned out that they did not have as strong a protective effect as wholemeal bread, buckwheat, oats, whole-grain pasta or other coarse-ground groats. Ultimately, the analysis showed that consuming products from this particular group at least twice a week reduced cardiometabolic risk by 65%.

Given the discussion in the literature concerning carbohydrate intake, these results may be surprising. In recent years, the ketogenic diet has gained popularity because of its low glycaemic index; the ketogenic diet is characterised by very restrictive carbohydrate consumption. Some studies show that this diet positively influences insulin sensitivity and lipoprotein and androgen status in women with PCOS [51–53]. However, these studies did not include control groups, so a broad conclusion is difficult. Other studies show that both a high intake of whole-grain carbohydrates and a low glycaemic index effectively support pharmacological therapy for PCOS [54–57]. In our study, the decisive role in decreasing atherosclerosis risk was played by low glycaemic index products, which are a significant source of carbohydrates with prebiotics, soluble fibre, and antioxidant. The diet's antioxidant capacity is hard to ignore when discussing the beneficial effects of its nutrition; our previous studies have repeatedly highlighted and discussed this [58,59].

The current results have unique significance because of the combination of nutritional intake analysis and atherosclerosis risk. To examine this, we chose markers like body fat composition and anthropometrics (Supplementary Table S1), fasting glucose and insulin, lipid profile, HOMA-IR, and atherogenic index of plasma (AIP). AIP was used to calculate atherosclerosis risk; its use in women with PCOS has been previously demonstrated in the literature [60]. The AIP is based on a positive association with lipoprotein particle size, cholesterol esterification rates, and remnant lipoproteinemia, and it is even recommended as a sole marker of cardiovascular diseases (CVD) [61]. AIP values of -0.3 to 0.1 are associated with a low risk of CVD, values of 0.1 to 0.24 with a medium risk, and values above 0.24 with a high risk [36].

We must emphasise that our results have important implications for managing dietary recommendations for women with PCOS. In our study, we analysed the consumption of all food groups; nevertheless, only low glycaemic index products affected atherosclerosis risk as expressed by the atherogenic index of plasma (AIP). In that group, the consumption of buckwheat, oats, whole-grain pasta or other coarse-ground groats strongly influenced atherosclerosis risk. This outcome supports other studies concluding that the quality of

consumed carbohydrates influences atherosclerosis risk. However, we did not find an adverse relationship between AIP and low-quality carbohydrates (processed grains or white bread). Notably, the groups we found significant included products containing high amounts of soluble fibre. Soluble fibre feeds probiotic bacteria and decreases cholesterol by binding bile salts to the intestinal passage and excreting it with faeces [62,63]. In total, 10 pro-healthy food groups had a tendency to lower AIP.

Although the beneficial effect of probiotics on atherosclerosis has been previously observed in the literature [18,63], our research quantifies this relationship for the first time. Interestingly, we found no correlation between consumption of probiotic foods and AIP; probiotic foods were mainly represented by dairy products. Frequent dairy intake seems to lower the risk of diabetes mellitus; however, it is unclear whether it benefits women with PCOS [64,65]. It is also known that low-fat, unsweetened dairy intake has much better health outcomes than sweetened, full-fat dairy intake; low-fat dairy is recommended to reduce the risk of atherosclerosis [7]. In our study, there was no significant association between the intake of sweetened dairy and the risk of atherosclerosis. A high risk of atherosclerosis was also not significantly associated with whole-fat dairy intake. This result agrees with research showing that including whole-fat dairy in an otherwise healthy dietary pattern is not associated with hypercholesterolemia [66].

Despite reaching its aims, this study may have some limitations. For example, the calculation of both prebiotics and probiotics is limited; specifically, we used the low glycaemic index dietary score to assess prebiotic intake. Although this index includes most prebiotic foods (such as breads, grains, vegetables, and legumes), it does not include single products from different groups (e.g., apples or onions, which are also high-prebiotic foods). However, using a strong atherosclerosis marker, a validated food frequency questionnaire appropriate for the Polish population, and a thorough body composition analysis, this study provides valuable information on maintaining cardiovascular health in women with PCOS. It should be emphasised that the obtained results could be supported by microbiota analysis (currently a missing element), as this could provide a complete picture of microbiota in women with PCOS. Following this analysis, further research should include a high-fibre diet intervention study. Although we have observed the associations between dietary patterns and atherosclerosis risk in women with PCOS, the mechanisms behind it are still unclear.

5. Conclusions

In conclusion, intake of prebiotic foods is inversely associated with a medium or high risk of atherosclerosis in women with PCOS. Such an association has not been found between atherosclerosis risk and probiotic foods. Our data provide further evidence that promoting dietary recommendations to consume good quality carbohydrates and low GI products in a balanced diet should be considered part of a PCOS treatment plan. Future multidisciplinary approaches involving dietary intervention and microbiota analysis should be regarded to characterise changes meant to counteract atherosclerosis risk in women with PCOS. We believe that further research should move in this direction.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/life13030799/s1>, Table S1: Anthropometric measurements characteristics of the study group. Table S2: Odds ratios (ORs with 95% confidence interval (95% CI)) of the high atherogenic index of plasma according to the diet quality indexes.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data supporting the conclusions of this article are included within the article and its additional files. The other datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

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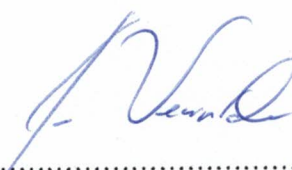
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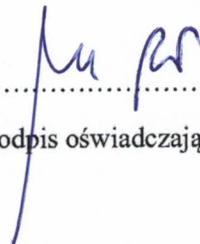
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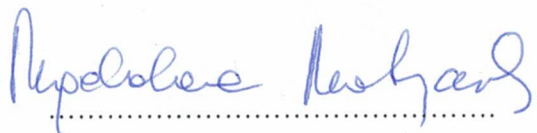
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