Akademia Wychowania Fizycznego im. Bronisława Czecha
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AUTOREFERAT ROZPRAWY DOKTORSKIEJ

# Wpływ treningu fizycznego na skład ciała i stan zdrowia mężczyzn z zespołem metabolicznym

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Rozprawa napisana w Zakładzie Anatomii

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*Serdeczne podziękowania*
*za zaufanie, poświęcony czas*
*oraz nieocenioną pomoc na każdym*
*etapie tworzenia pracy*
*kieruję do mojej Promotor,*
*Pani* ***dr hab. Agnieszki Suder, prof. AWF***

# Spis treści

## Wykaz skrótów

ADIPO – adiponectin – adiponektyna

ADIPO/LEP ratio – stosunek adiponektyny do leptyny

ANDR – android adipose tissue – poziom tkanki tłuszczowej androidalnej

ANOVA – analysis of variance – analiza wariancji

ANZCTR – Australian New Zealand Clinical Trials Registry – Australijski Rejestr Badań Klinicznych w Nowej Zelandii

BF – body fat – poziom tkanki tłuszczowej

BH – body height – wysokość ciała

BM – body mass – masa ciała

BMI – body mass index – wskaźnik masy ciała

CG – control group – grupa kontrolna

COVID-19 – SARS-CoV-2 coronavirus infection – zakażenie koronawirusem SARS-CoV-2

DAG – diacylglycerols – diacyloglicerole

DBP – diastolic blood pressure – ciśnienie rozkurczowe

DEXA – dual-energy x-ray absorptiometry – absorpcjometria promieniowania rentgenowskiego o podwójnej energii

EG1 – experimental group 1 – grupa z interwencją treningiem aerobowym

EG2 – experimental group 2 – grupa z interwencją treningiem aerobowo-oporowym

ELISA – enzyme-linked immunosorbent assay – test immunoenzymatyczny

ES – effect size – wielkość efektu

FFM – fat free mass – beztłuszczowa masa ciała

FM – fat mass – masa tkanki tłuszczowej

FNDC5 – fibronectin domain-containing protein 5 – białko zawierające domenę fibronektyny 5

GL – glucose – glukoza

GYNOID – gynoid adipose tissue – tkanka tłuszczowa gynoidalna

HDL-C – high-density lipoprotein cholesterol – lipoproteina cholesterolu o wysokiej gęstości

HOMA-AD – homeostatic model of insulin resistance – adiponectin – homeostatyczny model oporności na insulinę - adiponektyna

HOMA-TG – homeostatic model for assessing insulin resistance – triglycerides – homeostatyczny model oceny oporności na insulinę - trójglicerydy

HR – heart rate – częstość skurczów serca

HR max – heart rate maximum – maksymalna częstość skurczów serca

ICD-10 – International Statistical Classification of Diseases and Related Health Problems – Międzynarodowa Statystyczna Klasyfikacja Chorób i Problemów Zdrowotnych

IDF – International Diabetes Federation – Międzynarodowa Federacja Diabetologiczna

IL-6 – interleukin-6 – interleukina-6

IL-8 – interleukin-8 – interleukina-8

INS – insulin – insulina

IPAQ – The International Physical Activity Questionnaire – Międzynarodowy Kwestionariusz Aktywności Fizycznej

IR – irisin – iryzyna

IRS – insulin receptor substrate

LDL-C – low-density lipoprotein cholesterol – lipoproteina cholesterolu o niskiej gęstości

LEP – leptin – leptyna

MET – metabolic equivalent of task – metaboliczny równoważnik pracy

MetS – metabolic syndrome – zespół metaboliczny

NEAT – non-exercise thermogenesis – termogeneza niezwiązana z ćwiczeniami fizycznymi

NAFLD – non-alcoholic fatty liver disease – niealkoholowe stłuszczenie wątroby

NW – Nordic Walking – chód nordycki

OMEN – omentin – omentyna

QUICKI – quantitative insulin sensitivity check index – indeks ilościowej oceny wrażliwości na insulinę

RBP4 – Retinol Binding Protein 4 – białko wiążące retinol 4

RT – resistance training – trening oporowy / siłowy

SBP – systolic blood pressure – ciśnienie skurczowe

SERBP1c – sterol-regulatory element binding protein 1c – sterol-regulacyjny białko wiążące element 1c

TC – total cholesterol – cholesterol całkowity

TG – triglyceride – trójglicerydy

$VO_{2max}$ – maximal oxygen uptake – maksymalny minutowy pobór tlenu

WC – waist circumference – obwód talii

WHtR – waist circumference to body height ratio – stosunek obwodu talii do wysokości ciała

1RM – 1 repetitions maximum – jedno powtórzenie maksymalne

## Spis publikacji wchodzących w skład cyklu dysertacyjnego

Przedstawiona rozprawa doktorska została przygotowana w formie cyklu trzech publikacji naukowych powiązanych ze sobą tematycznie. Jestem pierwszym autorem tych prac; brałem istotny udział w projektowaniu, organizacji i przeprowadzeniu badań, a także w tworzeniu wszystkich rozdziałów i przygotowaniu publikacji dysertacyjnych. W Aneksie zamieszczono publikacje wraz z przygotowanymi do nich suplementami oraz oświadczenia o wkładzie pracy poszczególnych autorów, włożonego w przygotowanie publikacji.

Publikacja nr 1

Makiel, K., Suder, A., Targosz, A., Maciejczyk, M., Haim, A. *Effect of exercise interventions on irisin and interleukin-6 concentrations and indicators of carbohydrate metabolism in males with metabolic syndrome.* J Clin Med. 2023, 12, 369, DOI: https://doi.org/10.3390/jcm12010369

- 140 pkt MEiN, 4,964 IF;

Publikacja nr 2

Makiel, K., Suder, A., Targosz, A., Maciejczyk, M., Kozioł-Kozakowska, A., Haim, A. *Impact of two types of exercise interventions on leptin and omentin concentrations and indicators of lipid and carbohydrate metabolism in males with metabolic syndrome.* J Clin Med. 2023, 12, 2822. https://doi.org/10.3390/jcm12082822

- 140 pkt MEiN, 4,964 IF;

Publikacja nr 3

Makiel, K., Suder, A., Targosz, A., Maciejczyk, A., Haim, A. *Exercise-induced alternations of adiponectin, anterleukin-8 and indicators of carbohydrate metabolism in males with metabolic syndrome.* Biomolecules. 2023, 13, 852. https://doi.org/10.3390/biom13050852

- 100 pkt MEiN, 6,064 IF.

Powyższe publikacje wchodzące w skład cyklu uzyskały sumarycznie 380 punktów MEiN oraz 15,992 punktów Impact Factor.

Pozostałe publikacje autorstwa doktoranta nie wchodzące w skład cyklu:

1. Suder, A., Jagielski, P., Piórecka, B., Płonka, M., Makiel, K., Siwek, M., Wronka, I., Janusz, M. *Prevalence and factors associated with thinness in rural polish children.* Int J Environ Res Public Health. 2020, 31, 2368. https://doi.org/ 10.3390/ijerph17072368

2. Makiel, K., Suder, A., Kasza, S., Kubasiak, K. *Body Composition and dietary patterns in professional and amateur bodybuilders.* Anthropol Rev. 2020, 83, 225–238. https://doi.org/10.2478/anre-2020-0016.

Powyższe publikacje nie wchodzące w skład cyklu uzyskały sumarycznie 210 punktów MEiN oraz 3,390 punktów Impact Factor.

# 1. Wstęp

W ostatnich latach wiele uwagi poświęcono zespołowi metabolicznemu (MetS), ze względu na jego związki z rozwojem chorób takich jak otyłość, cukrzyca i choroby układu krążenia (CVD). Patogeneza MetS jest złożona, wieloczynnikowa, a mechanizmy jego rozwoju i przebiegu - nie są w pełni poznane [1]. Zaburzenia metaboliczne stają się zespołem, jeśli u pacjenta potwierdzą się trzy z pięciu kryteriów: otyłość brzuszna, niski poziom cholesterolu HDL, wysoki poziom trójglicerydów, wysoki poziom glukozy, wysokie ciśnienie krwi lub prowadzone leczenie konkretnego zaburzenia [2]. MetS obejmuje wiele systemów biologicznych, powodując wysoką zachorowalność i śmiertelność z powodu powikłań sercowo-naczyniowych oraz metabolicznych [3]. Jednostka ta jest również nazywana zespołem X, zespołem insulinooporności, zespołem cywilizacyjnym oraz polimetabolicznym [4]. Stanowi ona wyzwanie dla zdrowia publicznego, a jej rozpowszechnienie istotnie wzrasta na całym świecie [5, 6]. Skala problemu MetS dotyczy 20-25% dorosłej populacji [7]. Współwystępowanie jego składowych wynika z interakcji genów i czynników środowiskowych takich jak niska aktywność fizyczna oraz spożywanie nadmiernej ilości energii w diecie, przekraczające zapotrzebowanie energetyczne organizmu [8]. MetS prowadzi do wielu konsekwencji zdrowotnych, w tym cukrzycy typu 2, dny moczanowej [9], chorób sercowo-naczyniowych, ostrego zespołu wieńcowego, udaru mózgu, nowotworów złośliwych [10], bezdechu sennego [11], niealkoholowego stłuszczenia wątroby (NAFLD) i nadciśnienia tętniczego [6]. Każda jego składowa może predysponować pacjentów do CVD. Ryzyko konsekwencji zdrowotnych wzrasta, gdy u jednej osoby współwystępuje kilka objawów MetS [12, 13]. Czynnikami związanymi z rozwojem omawianego zespołu nieprawidłowości są insulinooporność i otyłość (szczególnie otyłość centralna) [14, 15]. Nadmiar tkanki tłuszczowej trzewnej wiąże się z wyższym ryzykiem insulinooporności i hiperinsulinemii, wzrostem wolnych kwasów tłuszczowych i ciśnienia tętniczego oraz spadkiem HDL-C, predysponując do zakrzepicy oraz innych incydentów sercowo-naczyniowych [4, 16]. Występowanie silnej korelacji pomiędzy otyłością i składowymi MetS oraz ich potencjalne związki przyczynowo-skutkowe [17] podkreślają rolę znajomości przyczyn, przebiegu, konsekwencji oraz procesu leczenia otyłości. Międzynarodowy kodeks chorób (ICD-10) klasyfikuje otyłość w kategorii „Choroby endokrynologiczne, żywieniowe i metaboliczne" [18]. Ma ona charakter przewlekły ze skłonnością do nawrotów [19]. Otyłość prosta jest wynikiem nierównowagi pomiędzy

poborem energii, a wydatkami energetycznymi, co powoduje dodatni bilans energetyczny, a w perspektywie czasu - nadmierną kumulację tkanki tłuszczowej [20]. Mechanizmy leżące u jego podstaw są liczne, złożone, wieloczynnikowe i w dużej mierze poza świadomą kontrolą, tylko częściowo pokrywające się pomiędzy pacjentami [21]. Cechami klinicznymi otyłości są: rozwój przewlekłego stanu zapalnego w tkance tłuszczowej [22], nieprawidłowy poziom neurohormonów regulujących odczuwanie sytości po spożyciu pokarmów, [23] oraz zwiększone ryzyko zespołu metabolicznego [24] i zaburzeń psychicznych [25]. Ważną rolę w rozwoju oraz przebiegu otyłości odgrywają uwarunkowania genetyczne oraz procesy adaptacyjne organizmu występujące w obszarze opisanych zaburzeń [26, 27]. Jej konsekwencją jest zwiększone ryzyko wystąpienia chorób: od 0,2 do 8% w przypadku zapadalności na wszystkie nowotwory, od 7 do 44% - na choroby sercowo-naczyniowe oraz od 3 do 83% - na cukrzycę typu II. Otyłość prowadzi do wzrostu ryzyka śmierci od 5 do 15% w przypadku zgonów z jakiejkolwiek przyczyny [28, 29]. Sprzyja ona gromadzeniu się trzewnej tkanki tłuszczowej, co wiąże się z występowaniem ogólnoustrojowych stanów zapalnych o małym nasileniu i przyczynia się do rozwoju zaburzeń metabolicznych [22, 30, 31].

Zarówno tkanka tłuszczowa, jak i mięśnie szkieletowe są narządami wydzielania wewnętrznego, które prowadzą swoisty dialog, uwalniając cytokiny, adipokiny i miokiny - hormony, które docierają do swoich receptorów, odgrywając ważną rolę w homeostazie organizmu [32, 33]. Odpowiadają one za regulację procesów energetycznych i metabolicznych organizmu [34, 35]. Tkanka tłuszczowa i mięśnie szkieletowe są kluczowymi regulatorami tolerancji węglowodanów [36, 37]. W populacji osób otyłych zagrożonych zespołem metabolicznym, zaburzona produkcja adipokin może prowadzić do insulinooporności [38]. Zmiany ich poziomu, zwłaszcza wytwarzanych w trzewnej tkance tłuszczowej, mogą odzwierciedlać powikłania ogólnoustrojowe związane z otyłością [39, 40].

Iryzyna (IR) jest miokiną produkowaną głównie w mięśniach szkieletowych pod wpływem wysiłku fizycznego, w mniejszym stopniu przez białą tkankę tłuszczową [41]. U myszy, iryzyna pochodząca z mięśni stanowi ~72% całkowitego poziomu hormonu w krążeniu, a pozostałe 28% pochodzi prawdopodobnie z tkanki tłuszczowej [42]. Głównym działaniem iryzyny jest brązowienie białej tkanki tłuszczowej, zwiększenie wydatków energetycznych organizmu oraz poprawa wrażliwości komórek na działanie insuliny [43]. Iryzyna stymuluje lipolizę oraz zwiększa uwalnianie glukozy i wolnych

kwasów tłuszczowych pod wpływem aktywności fizycznej [44]. Lee i inni [45] pokazali, że zwiększa ona wychwyt glukozy do 30%. Ponadto, iryzyna pozytywnie wpływa na zaburzenia lipidowe spowodowane otyłością i zespołem metabolicznym [46]. W meta-analizie 18 badań zaobserwowano wyższe poziomy iryzyny u osób z nadwagą lub otyłością w stosunku do osób z prawidłową masą ciała, co można tłumaczyć zjawiskiem „iryzynooporności" [47]. Podobny proces obserwuje się wśród osób z MetS [48]. Ćwiczenia fizyczne prowadzą do wzrostu poziomu iryzyny zarówno u osób zdrowych jak i z zespołem metabolicznym. Zastosowanie treningu oporowego prowadzi do większej produkcji iryzyny niż w przypadku treningu o umiarkowanej intensywności lub ćwiczeń interwałowych o wysokiej intensywności. Wzrost iryzyny jest widoczny natychmiast po rozpoczęciu treningu; stabilizacja jej poziomu następuje do godziny po zakończeniu ćwiczeń. Opisane zależności dotyczą zarówno osób z MetS jak i zdrowych [49].

Interleukina-6 (IL-6) jest cytokiną, której podwyższone stężenia wydzielane przez adipocyty i monocyty wiążą się z wstępującym stanem zapalnym i insulinoopornością w otyłości. Wykazano jednak, że IL-6 uwalniana przez mięśnie szkieletowe wykazuje działanie przeciwzapalne i uwrażliwiające na insulinę [50]. Poziom IL-6, iryzyny oraz parametry metabolizmu węglowodanów takie jak HOMA są zależne od poziomu tkanki tłuszczowej, wzrastają zgodnie z poziomem otyłości wśród badanych pacjentów [51]. Największe znaczenie w produkcji IL-6 ma poziom glikogenu, intensywność i czas trwania aktywności fizycznej [52]. Wzrost poziomu IL-6 może być większy po zastosowaniu umiarkowanej intensywności ćwiczeń przez dłuższy czas (np. biegania) angażujących wiele partii mięśniowych niż po izolowanym treningu oporowym [53].

Leptyna (LEP) jest adipokiną, która poprzez swoje receptory w neuronach podwzgórza wpływa na kontrolę spożycia pokarmów i wydatkowanie energii [54, 55]. Ponadto, leptyna odgrywa wiele ról w organizmie, w tym w systemie immunologicznym i układzie oddechowym, wpływa ona także na regulację hormonów płciowych [56, 57, 58, 59]. W otyłości i u pacjentów z MetS występuje zjawisko oporności na leptynę [60, 61]. Stężenie leptyny w surowicy jest proporcjonalne do poziomu otyłości i odzwierciedla stan energetyczny organizmu. Próg BMI, przy którym stężenie leptyny zaczyna się zwiększać, wynosi 24,6 kg/m$^2$ [62]. Oporność na leptynę jest głównym czynnikiem prowadzącym do postępu MetS, a zrozumienie tego mechanizmu wymaga

dalszych badań [17]. Niewłaściwy poziom leptyny może prowadzić do rozwoju cukrzycy typu 2 (T2DM) [63], chorób serca [64] oraz niektórych nowotworów [65, 66].

W przeciwieństwie do większości adipokin, omentyna (OMEN) nie jest wytwarzana w tkance tłuszczowej podskórnej [67]. Syntetyzowana jest ona głównie w tkance tłuszczowej trzewnej [68]. Omentyna występuje w dwóch formach: jako omentyna-1 i omentyna-2 [68]. Omentyna-1 występuje w największej ilości spośród jej izoform w ludzkim organizmie [69, 70]. W populacji ludzi otyłych obserwuje się obniżone stężenia omentyny, a jej spadek prowadzi do zaburzeń metabolicznych, takich jak oporność na insulinę i nietolerancja glukozy. Osoby o prawidłowej masie ciała charakteryzują się znacznie wyższym stężeniem omentyny w surowicy niż osoby z nadwagą. Istnieją również różnice w jej stężeniach w zależności od płci - w przypadku kobiet są one wyższe niż u mężczyzn. Jej poziom może pozwolić na przewidywanie skutków metabolicznych lub chorób współistniejących z otyłością. W porównaniu do innych adipokin, wykazano, że poziom omentyny jest pozytywnie związany z poziomem adiponektyny oraz ujemnie skorelowany z poziomem leptyny [69]. Niskie stężenia w surowicy występują u pacjentów z cukrzycą typu 1 i typu 2 [71, 72]. Główną funkcją omentyny jest prawdopodobnie zwiększanie wrażliwości na insulinę. Efekt ten jest obserwowany zarówno miejscowo, jak i ogólnoustrojowo [68]. Sekrecja omentyny-1 jest stymulowana w odpowiedzi na zastosowanie aktywności fizycznej. Z jej działaniem może być związana także adaptacja fizjologiczna mięśni szkieletowych do aktywności fizycznej [73].

Jednym z przykładów przepływu informacji z tkanki tłuszczowej do mięśni szkieletowych jest produkcja adiponektyny (ADIPO) syntetyzowanej głównie w tkance tłuszczowej, której receptor Adipo1 znajduje się w mięśniach szkieletowych. Dociera ona również do receptora Adipo2 w wątrobie [74]. Adiponektyna jest hormonem obecnym w stosunkowo wysokim stężeniu we krwi, stanowiącym około 0,01% całkowitej ilości białka w surowicy [75]. Odpowiada ona za utlenianie kwasów tłuszczowych w mięśniach szkieletowych oraz hamowanie produkcji glukozy w wątrobie, co poprawia homeostazę energetyczną całego organizmu. Adiponektyna ma funkcję przeciwzapalną; redukuje poziom stanu zapalnego oraz zmniejsza ryzyko chorób układu krążenia [76, 77, 78, 79]. Adiponektyna zwiększa wrażliwość komórek na insulinę poprzez ograniczenie produkcji glukozy w wątrobie oraz wzrost wrażliwości mięśni szkieletowych na działanie insuliny [80]. Niskie jej stężenia zaobserwowano u ludzi z MetS i otyłością brzuszną [81].

Cytokina interleukina-8 (IL-8), odpowiedzialna za zwiększenie migracji prozapalnych makrofagów M1 do tkanki tłuszczowej, działa prozapalnie, antagonistycznie do adiponektyny [ 82 ]. IL-8 jest syntetyzowana między innymi w adipocytach, a jej nadmierna produkcja może prowadzić do insulinooporności, cukrzycy typu 2 i miażdżycy [83, 84, 85]. Obserwowano podwyższone poziomy IL-8 u osób z MetS [86], chociaż istnieją doniesienia wskazujące na odwrotny związek [87]. Stężenie Il-8 wzrasta podczas skurczów mięśni szkieletowych. Jest ona zaangażowana w procesy proliferacji i angiogenezy w mięśniach [88]. Zaobserwowano jej działanie miejscowe w mięśniach szkieletowych w wyniku podjęcia aktywności fizycznej [89]. Istnieją również doniesienia, że ćwiczenia fizyczne nie zwiększają stężenia krążącej IL-8 [90].

Proces leczenia MetS oraz otyłości rozpoczyna się od modyfikacji stylu życia [91]. Kluczowe zmiany to modyfikacja sposobu żywienia [92] oraz zwiększenie aktywności fizycznej (PA). Niewystarczający poziom ruchu i siedzący tryb życia należą do najważniejszych czynników determinujących rozwój MetS [93, 94]. Aktywność fizyczna prowadzi do wielu interakcji endokrynologicznych pomiędzy mięśniami szkieletowymi, tkanką tłuszczową oraz innymi narządami wydzielania wewnętrznego. Efektem wprowadzenia systematycznych treningów są zmiany w poziomach krążących miokin, adipokin oraz cytokin immunologicznych, w efekcie czego dochodzi do redukcji masy ciała, zmniejszenia ogólnoustrojowego stanu zapalnego i insulinooporności oraz innych zaburzeń z obszaru zespołu metabolicznego [95, 96, 97].

Trening aerobowy prowadzi do znacznego wzrostu wydatku energii i stwarza korzystne warunki do redukcji nadmiernej masy tkanki tłuszczowej. Trening oporowy ma natomiast istotne znaczenie w zwiększeniu beztłuszczowej masy ciała, skutkiem czego jest większa insulino-wrażliwość oraz duża efektywność w zachowaniu lub zwiększeniu spoczynkowej przemiany materii [ 98 ]. Wprowadzenie systematycznych treningów oporowych skojarzonych z treningiem wydolnościowym daje szersze perspektywy w zapobieganiu nawrotom otyłości [ 99 ] oraz prowadzi do poprawy wskaźników zespołu metabolicznego [100]. Istniejące dowody wskazują, że aktywność fizyczna, taka jak trening wytrzymałościowy lub oporowy, wpływając na metabolizm tkanki tłuszczowej i mięśni szkieletowych, prowadzi do poprawy stanu zdrowia, nawet bez spadku masy ciała [91, 101, 102].

Lepsze zrozumienie roli, jaką odgrywają leptyna, adiponektyna, omentyna IL-6, IL-8 i iryzyna w MetS, może pomóc w wyborze bardziej precyzyjnych interwencji terapeutycznych poprzez wybór odpowiednich metod treningowych, prowadzących do zmniejszenia stanu zapalnego, wzrostu insulino-wrażliwości, redukcji poziomu tkanki tłuszczowej trzewnej oraz poprawy stanu zdrowia w wielu innych obszarach [103, 104, 105 ]. Wyniki badań nie wskazują na jednoznaczne rezultaty w zmianach i stężeń adipokin, wywołanych pod wpływem zastosowanej formy ćwiczeń u pacjentów z MetS. Autorzy innych prac sugerują, że należy przeprowadzić więcej badań w tym zakresie [104, 106].

# 2. Cel pracy, pytania oraz hipotezy badawcze

## 2.1. Cel pracy

Celem badań była ocena wpływu dwóch typów dwunastotygodniowego treningu fizycznego (trening o charakterze aerobowym *vs* trening o charakterze aerobowo-oporowym) na skład ciała, poziom wskaźników insulinooporności, profil lipidowy oraz stężenie wybranych adipokin u mężczyzn z MetS, w odniesieniu do mężczyzn z MetS nie poddawanych treningowi (grupa kontrolna). Następnie badani ze wszystkich trzech grup zostali poddani czterotygodniowej obserwacji bez zaplanowanej interwencji (follow-up).

## 2.2. Pytania badawcze

Postawiono następujące pytania badawcze:

1. Jak zmienia się skład ciała u mężczyzn z zespołem metabolicznym poddanych dwóm typom dwunastotygodniowego treningu fizycznego?

2. Jak zmienia się poziom wskaźników insulinooporności u mężczyzn z zespołem metabolicznym poddanych dwóm typom dwunastotygodniowego treningu fizycznego?

3. Jak zmienia się poziom wskaźników profilu lipidowego u mężczyzn z zespołem metabolicznym poddanych dwóm typom dwunastotygodniowego treningu fizycznego?

4. Jak zmienia się stężenie wybranych adipokin u mężczyzn z zespołem metabolicznym poddanych dwóm typom dwunastotygodniowego treningu fizycznego?

5. Czy zaobserwowane podczas interwencji zmiany w składzie ciała, poziomie wskaźników insulinooporności, profilu lipidowego oraz stężeniu adipokin utrzymają się po czterech tygodniach obserwacji bez zorganizowanych treningów?

## 2.3. Hipotezy badawcze

1. Zastosowanie treningu fizycznego o charakterze mieszanym, aerobowo-oporowym wpłynie bardziej korzystnie na skład ciała tj. redukcję masy tkanki tłuszczowej, zwiększenie beztłuszczowej masy ciała oraz poprawę dystrybucji tkanki tłuszczowej u mężczyzn z zespołem metabolicznym w porównaniu do treningu o charakterze aerobowym.

2. Trening fizyczny o charakterze aerobowo-oporowym doprowadzi do bardziej wyraźnej redukcji poziomu insulinooporności u mężczyzn z zespołem metabolicznym w porównaniu do treningu aerobowego.

3. Zastosowanie treningu aerobowo-oporowego będzie wiązało się z bardziej korzystną zmianą we wskaźnikach profilu lipidowego u mężczyzn z zespołem metabolicznym niż zastosowanie treningu o charakterze aerobowym.

4. W grupie mężczyzn z zespołem metabolicznym stosujących trening aerobowo-oporowy dojdzie do bardziej korzystnych zmian w poziomie wybranych adipokin w porównaniu do mężczyzn stosujących trening o charakterze aerobowym.

5. W okresie obserwacji zmiany w składzie ciała, poziomie wskaźników insulinooporności, profilu lipidowego oraz stężeniu adipokin ulegną dalszej poprawie, jeśli uczestnicy projektu utrzymają wysoki poziom aktywności fizycznej.

# 3. Materiał i metody badań

## 3.1. Materiał

Badania zaprojektowano jako prospektywne, randomizowane i kontrolowane. Na ich przeprowadzenie uzyskano zgodę Komisji Bioetycznej Okręgowej Izby Lekarskiej w Krakowie (90/KBL/OK/2020 z dnia 05. 06. 20).

Projekt badawczy został zarejestrowany w rejestrze badań klinicznych na platformie ANZCTR (Australian New Zealand Clinical Trials Registry): numer rejestracji ACTRN 12622001394730. 4.

Na przeprowadzenie projektu (18/RID/2020) uzyskano finansowanie w ramach programu Ministra Nauki i Szkolnictwa Wyższego realizowanego pod nazwą ”Regionalna Inicjatywa Doskonałości” w latach 2019-2022, nr 022/RID/2018/19.

Badanie obejmowało 62 mężczyzn w wieku 30−45 lat (średnia wieku 37 ± 7) z podwyższonym obwodem talii (WC) ≥ 94 cm i ze stwierdzonymi dwoma z czterech kryteriów MetS: hipertrójglicerydemia leczona farmakologicznie lub stężenie trójglicerydów >150 mg/dl (1,7 mmol/l); stężenie HDL-C < 40 mg/dl (1,03 mmol/l) - u mężczyzn lub zaburzenia lipidowe leczone farmakologicznie; ciśnienie skurczowe (SBP) ≥ 130 mm Hg lub rozkurczowe (DBP) ≥ 85 mm Hg, lub leczenie wcześniej zdiagnozowanej nadciśnienia tętniczego; poziom GL na czczo w osoczu krwi ≥ 100 mg/dl (5,6 mmol/l) lub leczenie farmakologiczne cukrzycy typu 2 (IDF, Międzynarodowa Federacja Diabetologiczna, 2006 [107]).

Kryteria wykluczenia stanowiły: brak orzeczenia lekarskiego o braku przeciwwskazań do podjęcia treningu zdrowotnego o charakterze aerobowo-oporowym, niechęć do kontynuowania interwencji (ponad 10% opuszczonych sesji treningowych), niestabilna miażdżyca, niewyrównana niewydolność serca, niekontrolowane zaburzenia rytmu serca, ciężkie nadciśnienie płucne (średnie ciśnienie krwi w płucach > 55 mm Hg), objawowa zwężka aorty, ostre zapalenie mięśnia sercowego, wsierdzia lub osierdzia, niekontrolowane ciśnienie krwi (> 180/110 mm Hg), rozwarstwienie aorty, zespół Marfana, niekontrolowana cukrzyca, zaburzenia psychiczne, problemy zdrowotne

(ortopedyczne, neurologiczne) uniemożliwiające ruch, udział w innym rodzaju aktywności fizycznej podczas projektu oraz brak pisemnej zgody na udział w badaniu.

Badani zostali losowo (poprzez losowanie zapieczętowanych kopert) przydzieleni do trzech grup:

- grupa eksperymentalna EG1 mężczyzn z MetS (n = 21), realizujących trening aerobowy (wiek: 34,21 ± 6,06; wskaźnik masy ciała, BMI: 34,57 ± 4,58; obwód talii, WC: 114,7 ± 10,93);

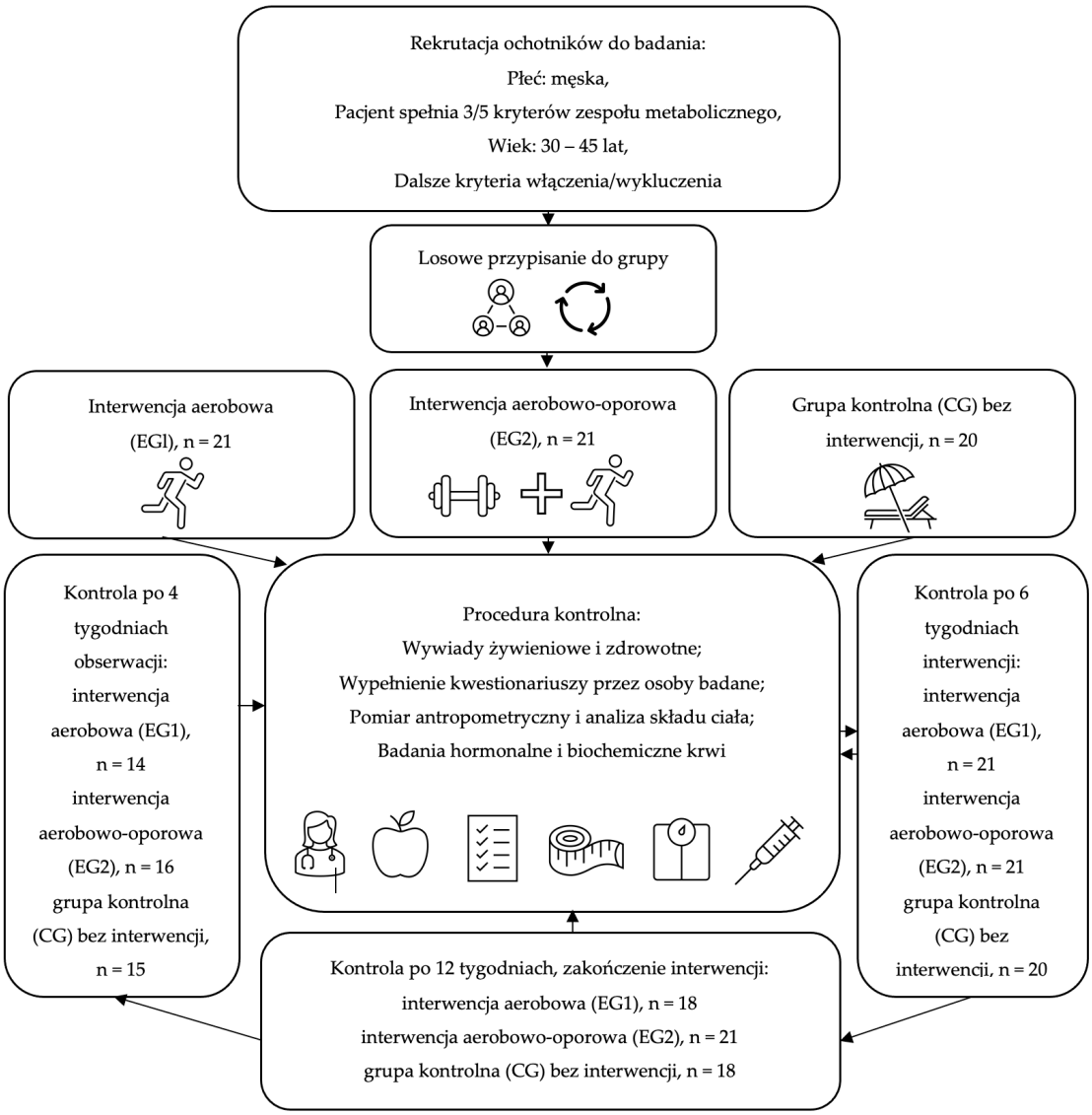
- grupa eksperymentalna EG2 mężczyzn z MetS (n = 21), realizujących trening aerobowo-oporowy (wiek: 37,37 ± 7,08; BMI: 33,14 ± 4,32; WC: 114,8 ± 11,64);

- grupa kontrolna CG mężczyzn z MetS (n = 20), którzy nie realizowali żadnych treningów (wiek: 38,26 ± 7,43; BMI: 33,20 ± 4,31; WC: 115,3 ± 10,54).

Nie wykazano różnic między wiekiem i podstawowymi parametrami antropometrycznymi przed zastosowaniem interwencji.

Poddani badaniom mężczyźni otrzymali szczegółowe informacje na temat procedur i celu badania oraz możliwości rezygnacji z interwencji na każdym etapie. Wystąpiły przypadki pacjentów rezygnujących z treningu oraz wykluczenia uczestników z powodu: ponad 10% pominiętych treningów (3 przypadki), niekontrolowanego spożycia alkoholu (2), nieobecności na sesjach kontrolnych (9) i zakażenia COVID-19 (3). Badani zadeklarowali, że nie będą zmieniać swojej diety, stosować leków ani dodatkowej aktywności fizycznej w czasie wolnym podczas trwania projektu. Wszyscy złożyli pisemną zgodę na udział w projekcie i zaakceptowali wykorzystanie swoich danych oraz wyników badania do celów naukowych.

Ze względu na charakter interwencji, nie stosowano ślepej próby, jednak personel laboratoryjny oraz biostatystyk nie byli świadomi przynależności poszczególnych pacjentów do grup. Przebieg badania przedstawiono na Rycinie 1.




Rycina 1. Przebieg badania

## 3.2. Metody

Zastosowano następujące metody badawcze, które przeprowadzano czterokrotnie: przed rozpoczęciem treningu, podczas projektu (po 6 tygodniach i po 12 tygodniach treningu) oraz 4 tygodnie po zakończeniu sesji treningowych (badanie kontrolne):

### 3.2.1. Pomiary antropometryczne

Bezpośrednio zmierzono wysokość ciała (BH) [cm], masę ciała (BM) [kg] i obwód talii (WC) [cm]. Pomiaru wysokości ciała dokonano bez obuwia, w płaszczyźnie frankfurckiej, w pozycji stojącej z dokładnością do 1 mm, przy użyciu stadiometru (Seca 231 stadiometer, Hamburg, Niemcy). Masa ciała została zmierzona w pozycji stojącej na standaryzowanej wadze medycznej (Beurer PS 240, Budapeszt, Węgry), z dokładnością do 50 g. Obwód talii (WC) zmierzono z dokładnością do 1 mm, przy użyciu taśmy antropometrycznej, między dolnym brzegiem łuku żebrowego, a górnym brzegiem grzebienia biodrowego, w pozycji stojącej. Został on zarejestrowany na końcu delikatnego wydechu. Stosunek obwodu talii do wysokości ciała (WHtR) uzyskano poprzez podzielenie przez siebie wymienionych powyżej parametrów.

### 3.2.2. Skład ciała

Poziom tkanki tłuszczowej (BF) [kg], [%], poziom tkanki tłuszczowej androidalnej (ANDR) [kg], poziom tkanki tłuszczowej gynoidalnej (GYNOID) [kg], [%], beztłuszczowa masa ciała (FFM) [kg], [%] oraz wskaźnik masy ciała (BMI) [kg/m$^2$] zostały ocenione za pomocą podwójnej absorpcjometrii rentgenowskiej (DEXA). Pomiarów dokonano w Centrum Badań Klinicznych - Jagiellońskie Centrum Innowacji, przy użyciu urządzenia Lunar Prodigy Primo PR+352163 (Chicago, IL, USA), zgodnie z instrukcją producenta.

### 3.2.3. Biochemiczne wskaźniki krwi

Próbki krwi pobierano rano, po 12-godzinnym poście i po 24-godzinnej przerwie od treningu, z żyły łokciowej lub promieniowej do probówek (system Vacumed® F.L. Medical, Torreglia, Italy), przez doświadczony personel pielęgniarski. Następnie były one poddane wirowaniu (RCF 1000× g) przez 15 minut w 4 °C (MPW-351R, MPW Med. Instruments, Warsaw, Poland). Osocze było pobierane i przechowywane w temperaturze -80 °C do dalszych badań (BIO Memory 690L, Froilabo, Paryż, Francja).

Stężenie glukozy we krwi na czczo (GL) [mmol/l] zostało oznaczone metodą enzymatyczną, przy użyciu analizatora biochemicznego Cobas c701/702 (Roche Diagnostics International Ltd., Mannheim, Niemcy).

Stężenie insuliny w surowicy (INS) [µIU/ml] zostało oznaczone metodą elektrochemiluminescencyjną (ECLIA), przy użyciu aparatu Cobas e801 (Roche Diagnostics International Ltd., Mannheim, Niemcy). Oznaczenia zostały wykonane zgodnie z instrukcjami producenta, przy użyciu dedykowanych reagentów dla analizatorów GLUC3 i Elecsys Insulin, odpowiednio.

Z kolei poziomy trójglicerydów (TG) [mg/dl], całkowitego cholesterolu (TC) i cholesterolu lipoprotein o dużej gęstości (HDL-C) w surowicy krwi zostały oznaczone przy użyciu spektrofotometrii, z wykorzystaniem specyfikacji analizatora chemicznego klinicznego Architect ci-4100 (Abbott Laboratories). Frakcja cholesterolu nie HDL (nonHDL-C) została określona zgodnie z następującym wzorem:

nonHDL-C [mmol/l − 1] = TC [mmol/l − 1] − HDL-C [mmol/l − 1]

Ocena wrażliwości na insulinę została przeprowadzona z wykorzystaniem homeostatycznego modelu oceny oporności na insulinę - adiponektyna (HOMA-AD) [ 108 ], homeostatycznego modelu oceny oporności na insulinę - trójglicerydy (HOMA-TG) [109] oraz przy użyciu wskaźnika szybkości ilościowej wrażliwości na insulinę (QUICKI) [110], obliczonych na podstawie wzorów:

HOMA-AD = INS (µU/ml) × GL (mmol/l)/ADIPO (µg/ml),

HOMA-TG = INS (µU/ml) × GL (mmol/l)/TG (mg/dl),

QUICKI = 1/ [log INS (µIU/ml) + log GL (mmol/l)].

Stężenie GL, INS i profil lipidowy oznaczono w Laboratorium Medycznym DIAGNOSTYKA w Krakowie.

### 3.2.4. Oznaczenia hormonalne z krwi

Stężenia leptyny, omentyny , iryzyny, IL-6, adiponektyna i IL-8 zostały ocenione za pomocą zestawów ELISA, zgodnie z wytycznymi producenta.

Zestaw do oznaczania ludzkiej leptyny Sandwich ELISA (numer katalogowy EIA-2395) został dostarczony przez DRG Instruments GmbH (Marburg, Niemcy). Zestaw do oznaczania ludzkiej omentyny ELISA (numer katalogowy 201-12-0156) został zakupiony od Shanghai Sunred Biological Technology Co. (Szanghaj, Chiny). Zestaw ELISA do IR (numer katalogowy 201-12-5328) został zakupiony od Shanghai Sunred Biological Technology Co. (Szanghaj, Chiny). Zestaw ELISA do IL-6 (numer katalogowy IL E-3200IL-6) został zakupiony od LDN Labor Diagnostika Nord GmbH & Co.KG (Am Eichenhain, Niemcy). Do pomiaru adiponektyny został wykorzystany zestaw ELISA (numer katalogowy E09) zakupiony od firmy Mediagnost (Reut-Lingen, Niemcy). Zestaw ELISA do oznaczeń IL-8 (numer katalogowy EIA-4700) został zakupiony od firmy DRG Instruments GmbH (Marburg, Niemcy).

Do pomiaru absorbancji przy 450 nm wykorzystano spektrofotometryczny czytnik mikropłytek ELx 808 (BioTek, Winooski, VT, USA). Oznaczenia przeprowadzono w Pracowni Genetyki i Biologii Molekularnej Katedry Fizjologii Collegium Medicum Uniwersytetu Jagiellońskiego w Krakowie.

Wskaźnik stosunku adiponektyny do leptyny (ADIPO/LEP ratio) został obliczony na podstawie wzoru:

ADIPO/LEP ratio = ADIPO (μg/ml) / LEP (μg/ml)

### 3.2.5. Ocena całkowitych wydatków energetycznych oraz wartości energetycznej diety

Do oceny dziennych wydatków energetycznych wykorzystano Międzynarodowy Kwestionariusz Aktywności Fizycznej (IPAQ) [111]. Całkowite wydatki energetyczne (TEE) zostały obliczone jako suma termogenezy niezwiązanej z ćwiczeniami fizycznymi (NEAT) oszacowanej za pomocą kwestionariusza IPAQ i wydatków energetycznych związanych z interwencjami wprowadzonymi w grupach EG1 i EG2.

Aby ocenić wartość energetyczną [kcal/dzień] diety uczestników, pacjenci prowadzili dzienniczki żywieniowe, które były na bieżąco analizowane podczas treningów grupowych. Podczas każdego punktu kontrolnego dietetyk przeprowadził szczegółowy wywiad żywieniowy z ostatnich 3 dni, wykorzystując metodę zapisu żywieniowego.

Dane uzyskane z wywiadu zostały przeanalizowane przy użyciu programu DietaPro (wersja 4.0, Instytut Żywności i Żywienia, Warszawa, Polska), aby ilościowo ocenić nawyki żywieniowe i monitorować zmiany w diecie w trakcie interwencji. Na podstawie uzyskanych wyników wygenerowano raport dotyczący składników odżywczych: białek [g], węglowodanów [g] i tłuszczy [g].

## 3.3. Interwencje treningowe

Interwencje treningowe zostały przeprowadzone w klubie fitness w Krakowie, pod nadzorem trenera personalnego. Sesje treningowe odbywały się o tej samej porze dnia (wieczorem, od 18:00 do 21:00), pod opieką tego samego trenera, w pomieszczeniu z stałą temperaturą (22 stopnie Celsjusza) i wilgotnością powietrza. Przestrzeganie interwencji było monitorowane za pomocą listy obecności na zajęciach, a uczestnicy, którzy opuścili ponad 10% treningów przez 12 tygodni, zostali wyłączeni z analizy.

Indywidualne planowanie i monitorowanie intensywności treningu aerobowego i oporowego oparte było na wytycznych American College of Sports Medicine [112]. Częstość skurczów serca podczas treningu była kontrolowana za pomocą systemu Polar M200 GPS z pulsometrem na nadgarstku. Maksymalne obciążenie jednorazowe (1RM) zostało ustalane przed treningiem oporowym. Obciążenie i liczba powtórzeń były rejestrowane i przeliczane na podstawie kalkulatora 1RM, przy użyciu wzoru Brzyckiego [113, 114].

Celem interwencji było wykonanie 3 treningów aerobowo-oporowych tygodniowo, czyli 3 x 5,5 MET na tydzień lub w przypadku treningu aerobowego: 3 x 6 MET (Compendium of Physical Activities, 2011) [115].

### 3.3.1. Trening aerobowy

Interwencja treningu aerobowego (Rycina S1, Aneks) obejmowała trzy sesje treningowe tygodniowo w klubie fitness, w grupach do pięciu uczestników. Trening rozpoczynał się pięciominutową rozgrzewką na bieżni (Technogym New Excite Run Now 500, Cesena, Włochy), przy 50% maksymalnej pracy serca (HR max). Następnie uczestnicy zwiększali intensywność swojego treningu do 70% HR max poprzez zwiększenie prędkości lub kąta nachylenia bieżni, oporu na rowerach stacjonarnych

(Technogym Artis, Cesena, Włochy) lub zakresu ruchu lub oporu na eliptycznych maszynach treningowych (Precor EFX556i Elipsa, Woodinville, WA, USA). Ćwiczenia aerobowe polegały głównie na szybkim chodzeniu lub truchcie na bieżni. W przypadku pojawienia się bólu ze strony układu mięśniowo-szkieletowego, uczestnicy mieli możliwość zmiany urządzenia. Trening miał charakter ciągły i utrzymywał stały poziom HR, trwał 45 minut. Po treningu aerobowym uczestnicy rozciągali przez 10 minut zaangażowane na treningu grupy mięśniowe.

### 3.3.2. Trening aerobowo-siłowy

Interwencja aerobowo-oporowa (Tabela S1, Aneks) odbywała się trzy razy w tygodniu, w grupach do pięciu uczestników, pod nadzorem trenera personalnego. Jedna sesja ćwiczeń trwała 60 minut. Trening rozpoczynał się pięciominutową, aerobową rozgrzewką na bieżni, na poziomie intensywność 50% HR max.

Trening oporowy obejmował początkowo trzy złożone ćwiczenia, takie jak wiosłowanie jednorącz, przysiady i pompki w odciążeniu, w czterech seriach, ze 120-sekundowymi przerwami między nimi. Ze względu na adaptację treningową uczestników grupy, w drugim tygodniu interwencji zamiast treningu całego ciała wprowadzono trening partii antagonistycznych (push-pull). W dniu treningowym ‘push’ uczestnicy grupy wykonywali ćwiczenia na mięśnie klatki piersiowej, mięśnie naramienne, trójgłowe ramienia oraz mięśnie czworogłowe ud, natomiast w dniu ‘pull’ zostały zastosowane ćwiczenia na mięśnie grzbietu, dwugłowe ramienia, dwugłowe ud oraz mięśnie brzucha. Objętość treningu została natomiast zmieniona na 6 ćwiczeń po 3 serie z 90-sekundowymi przerwami. Po 3 tygodniach interwencji, trening był wykonywany w 9 ćwiczeniach po 3 serie, z przerwami 60-sekundowymi. Obciążenie stopniowo zwiększano od pierwszego tygodnia, od 50% 1RM do 70% 1RM w drugim i pozostałych 10 tygodniach interwencji.

Po ćwiczeniach oporowych nastąpił element treningu aerobowego: uczestnicy trenowali z intensywnością 50% HR max w pierwszym tygodniu i 70% HR max od drugiego tygodnia interwencji na bieżni (Technogym New Excite Run Now 500, Cesena, Włochy), rowerku stacjonarnym (Technogym Artis, Cesena, Włochy) lub x-trainerze (Precor EFX556i Elipsa, Woodinville, WA, USA). Aby uniknąć przeciążenia stawów kończyn dolnych, badani mogli korzystać z tych trzech urządzeń naprzemiennie.

Czas trwania sesji treningu oporowego wynosił odpowiednio 30, 35 i 40 minut, a następnie odpowiednio 20, 15 i 10 minut treningu aerobowego. Sesja treningowa zakończyła się fazą rozciągania (5 min.).

Zmiany w obciążeniach ćwiczeń siłowych w trakcie interwencji i w okresie obserwacji dla grupy EG2 były istotne statystycznie w analizowanym okresie (Tabela S2., Aneks).

## 3.4. Analiza statystyczna

W celu realizacji podjętego problemu badawczego oraz weryfikacji postawionych hipotez zastosowano wybrane metody statystyczne.

Test Shapiro-Wilka został wykorzystany do badania rozkładu analizowanych zmiennych. W przypadku, gdy zmienne wykazywały rozkład inny niż normalny, różnice pomiędzy grupami zostały ocenione za pomocą testu Kruskala-Wallisa. Aby porównać wpływ interwencji na zmiany pomiędzy pomiarami w poszczególnych grupach, w analizowanych zmiennych, zastosowano test Friedmana z porównaniem post hoc (test Wilcoxona-Nemenyi). Wielkość efektu (ES) została oszacowana dla testu Friedmana: W = X2 / N (K - 1), gdzie W to wartość W Kendalla, X2 to wartość statystyki testu Friedmana, N to wielkość próby, a K to liczba pomiarów na jednego uczestnika. Współczynnik W Kendalla używa kryteriów interpretacji Cohena. Dla zmiennych nieparametrycznych obliczono współczynnik korelacji rangowej Spearmana (r).

Dla zmiennych, które wykazywały normalny rozkład, różnice między grupami badanymi i grupą kontrolną oceniano za pomocą jednoczynnikowej analizy wariancji dla grup niezależnych. Do porównania efektów interwencji w analizowanych zmiennych w grupie eksperymentalnej i kontrolnej wykorzystano test ANOVA z powtarzanymi pomiarami z porównaniami post hoc (test Tukeya). Jednorodność wariancji w grupach została sprawdzona za pomocą testu Levene'a.

Wielkość efektu (ES) dla testu ANOVA obliczono, wykorzystując współczynnik eta kwadrat ($\eta^2$), który jest stosunkiem sumy kwadratów (SS) dla efektu do całkowitej sumy kwadratów (SS). Interpretacja współczynnika eta kwadrat opiera się na wytycznych Cohena: 0,1 ≤ 0,3 (niski efekt), 0,3 ≤ 0,5 (umiarkowany efekt) i ≥ 0,5 (duży efekt) [116].

$$\eta^2 = \frac{SS_{effect}}{SS_{total}}$$

W celu określenia zależności liniowej pomiędzy analizowanymi zmiennymi został obliczony współczynnik korelacji Pearsona (r). Interpretacja korelacji Pearsona w zakresie <0 - 1> została dokonana w następujący sposób: $0 \leq r < 0{,}3$ brak lub bardzo słaba korelacja, $0{,}3 \leq r < 0{,}5$ umiarkowana korelacja, $0{,}5 \leq r < 0{,}7$ silna korelacja, $0{,}7 \leq r \leq 1$ bardzo silna korelacja.

Do wyjaśnienia zmienności stężeń iryzyny, IL-6, leptyny oraz adiponektyny, wykorzystano regresję wieloraką, wykorzystując ekonometryczny model regresji liniowej, oszacowano metodą najmniejszych kwadratów. W modelu błędy standardowe reszt i wartości p-value zostały skorygowane, korzystając z odpornych błędów standardowych korygujących heteroskedastyczność.

We wszystkich analizach efekty uznano za istotne, jeśli wartość prawdopodobieństwa p była mniejsza niż przyjęty poziom istotności $\alpha = 0{,}05$ ($p < 0{,}05$). Do wykonania obliczeń wykorzystano pakiet ggplot2 programu RStudio IDE w języku programowania R.

## 4. Najważniejsze wyniki

Dokładny opis uzyskanych podczas analiz wyników przedstawiony jest, także w formie tabel i rycin, w trzech opublikowanych artykułach wchodzących w skład cyklu dysertacyjnego. Poniżej zebrano najważniejsze wyniki.

Zastosowana interwencja w postaci treningu aerobowego w grupie EG1 wiązała się z istotnym wzrostem MET [min/tydzień] oraz wydatkowania energii [kcal/dzień] w każdym tygodniu pomiarów w stosunku do pierwszego tygodnia badań ($p = 0,00$). Całkowite wydatki energetyczne w grupie EG1 wyniosły 823,37 ± 175,76 kcal/dzień po 6 tygodniach oraz 835,18 ± 234,05 kcal/dzień po 12 tygodniach interwencji. Badani z grupy stosującej trening aerobowy, zgodnie z założeniami projektu, nie zmieniali wartości energetycznej diety [kcal/dzień] po 6 ($p = 0,53$) i 12 ($p = 0,22$) tygodniach trwania interwencji.

Zastosowanie treningów aerobowo-oporowych w grupie EG2 również wiązało się ze wzrostem MET [min/tydzień] oraz wydatkowania energii [kcal/dzień] w każdym tygodniu pomiarów w stosunku do pierwszego tygodnia badań ($p = 0,00$). Całkowite wydatki energetyczne w grupie EG2 wyniosły 735,17 ± 119,64 kcal/dzień po 6 tygodniach oraz 797,89 ± 383,25 kcal/dzień po 12 tygodniach interwencji Wraz ze wzrostem wydatków energetycznych w tej grupie badanej doszło do wzrostu energii [kcal/dzień] dostarczanej w diecie ($p = 0,00$).

W okresie obserwacji w grupach EG1 oraz EG2 badani utrzymali wysoki poziom aktywności fizycznej, wynoszący 838,00 ± 350,75 kcal/dzień w grupie EG1 ($p < 0,001$) oraz 749,17 ± 430,71 kcal/dzień w grupie EG2 ($p = 0,03$), utrzymując poziom MET [min/tydzień] oraz wydatkowania energii [kcal/dzień] zbliżony do wydatków energetycznych podczas interwencji.

### 4.1. Zmiany w składzie ciała

Po zastosowaniu interwencji w grupie stosującej trening aerobowy (EG1) potwierdzono redukcję masy ciała ($p < 0,001$) w stosunku do wartości wyjściowych. Spadek masy ciała wyniósł −2,6 kg ($p < 0,001$) już po 6 tygodniach interwencji.

Redukcja poziomu tkanki tłuszczowej (BF), w grupie EG1 została zauważona po 6 ($p < 0,001$) i 12 ($p = 0,01$) tygodniach interwencji w porównaniu z początkowymi pomiarami. Średnia redukcja poziomu tkanki tłuszczowej wyniosła −1,52 kg.

Analizując dystrybucję tkanki tłuszczowej w grupie EG1, potwierdzono spadek gynoidalnej tkanki tłuszczowej po 6 tygodniach interwencji ($p = 0,03$) oraz spadek procentowej zawartości tkanki tłuszczowej trzewnej po 6 ($p = 0,05$) i 12 ($p = 0,03$) tygodniach interwencji. Średni spadek wyniósł −3,4% ($p = 0,04$).

W grupie aerobowo-oporowej (EG2) nie potwierdzono zmian w masie ciała zachodzących pod wpływem interwencji treningowej. Zaobserwowano jednak znaczący wzrost FFM pomiędzy pomiarami ($p < 0,001$), wynoszący 4,07 kg już po 6 tygodniach interwencji ($p < 0,001$) oraz spadek poziomu tkanki tłuszczowej po 6 ($p = 0,02$) i 12 ($p = 0,01$) tygodniach, wynoszący po 12 tygodniach -2,2 kg.

W analizowanej grupie EG2 potwierdzono zmiany zachodzące w obwodzie talii (WC), zarówno pomiędzy pomiarami ($p < 0,001$), jak i w każdym z analizowanych momentów pomiarowych ($p = 0,01$). Zmniejszenie obwodu talii wyniosło średnio 3,8 cm po 12 tygodniach interwencji ($p = 0,01$).

W grupie aerobowo-oporowej również potwierdzono spadek gynoidalnej tkanki tłuszczowej pomiędzy pomiarami ($p < 0,001$). Poziom tkanki tłuszczowej trzewnej również uległ redukcji w grupie EG2, jednak zmiany nie były istotne statystycznie.

## 4.2. Zmiany w poziomie wskaźników insulinooporności i profilu lipidowego

Zastosowanie treningu aerobowego zwiększyło wartość wskaźnika QUICKI pomiędzy pomiarami ($p = 0,02$). W przypadku wskaźnika HOMA-TG, potwierdzono zmiany między pomiarami w grupie EG1 ($p = 0,04$). Podczas interwencji aerobowej zaobserwowano stopniowy spadek poziomu nieHDL-C, był to jednak spadek na granicy istotności statystycznej ($p = 0,05$).

Analizując zmiany wskaźników oporności na insulinę w grupie poddanej treningowi aerobowo-oporowemu (EG2) zaobserwowano, że po początkowym wzroście następował znaczący spadek insulinooporności pomiędzy kolejnymi pomiarami. Potwierdzono zmiany między pomiarami ($p = 0,02$) w wartościach HOMA-AD w grupie EG2.

Zaobserwowano początkowy wzrost po 6 tygodniach ($p = 0,03$), a następnie spadek wartości HOMA-AD w kolejnych pomiarach. W przypadku wskaźnika HOMA-TG, również potwierdzono zmiany między pomiarami ($p = 0,03$), analogiczne jak w przypadku HOMA-AD. W EG2 potwierdzono początkowe zmniejszenie QUICKI po 6 tygodniach interwencji ($p = 0,04$), po czym nastąpił wzrost wartości wskaźnika QUICKI ($p < 0,001$) pomiędzy pomiarami.

## 4.3. Zmiany w stężeniu adipokin

Pod wpływem interwencji aerobowej w grupie EG1 doszło do zmian poziomu miokin oraz adipokin. Stwierdzono zmianę stężenia iryzyny ($p = 0,02$) oraz IL-6 ($p = 0,01$) pomiędzy pomiarami. W przypadku leptyny, po początkowym wzroście ($p = 0,01$), potwierdzono znaczny spadek w 12-tygodniu interwencji ($p = 0,01$). Obserwacje w poziomie omentyny oraz adiponektyny nie potwierdziły istotnych zmian zarówno wewnątrz grup interwencyjnych, jak i pomiędzy grupami. Wystąpiły jednak zmiany w stosunku ADIPO/LEP w grupie EG1 pomiędzy pomiarami ($p < 0,001$) oraz po 6 ($p = 0,01$) i 16 ($p < 0,001$) tygodniach.

Analizując zmiany stężenia cytokiny IL-8 w grupie EG1, odnotowano spadek stężenia IL-8 w pierwszych 6 tygodniach interwencji ($p = 0,04$).

U pacjentów z grupy EG2, podejmujących treningi aerobowo-oporowe nie zaobserwowano zmian w stężeniu iryzyny, potwierdzono jednak spadek IL-6 pomiędzy pomiarami ($p = 0,01$), a średnie stężenia IL-6 były niższe w każdym kolejnym pomiarze, osiągając ponad dwukrotny spadek po 12 tygodniach.

W grupie EG2 zaobserwowano również stopniowy spadek stężenia leptyny w okresie interwencji: po 12 tygodniach stężenie leptyny zmniejszyło się średnio o -2,53 ng/ml ($p = 0,02$). Obserwacje w poziomie hormonu omentyny, IL-8 oraz adiponektyny nie potwierdziły istotnych zmian zarówno wewnątrz grupy interwencyjnej, jak i pomiędzy nimi.

## 4.4. Zmiany w analizowanych parametrach po czterech tygodniach obserwacji

W okresie czterech tygodni obserwacji, w którym badani nie byli poddani zorganizowanym treningom fizycznym, w grupie EG1 utrzymał się obniżony poziom masy ciała ($p = 0,03$) oraz dalszej redukcji uległ zarówno poziom trzewnej ($p = 0,02$), jak i ogólnej tkanki tłuszczowej ($p = 0,02$).

W okresie obserwacji (follow-up) w grupie EG2 zaobserwowano dalszą progresję beztłuszczowej masy ciała (FFM [%]), której wzrost w stosunku do danych wyjściowych wyniósł 5,8% ($p < 0,001$). W tej samej grupie utrzymały się rezultaty dotyczące zmniejszenia obwodu talii w stosunku do wartości wyjściowej ($p = 0,01$). W grupie tej zaobserwowano dalszy spadek gynoidalnej ($p < 0,001$), jak i ogólnej tkanki tłuszczowej ($p < 0,001$).

W okresie obserwacji, po 16 tygodniach projektu, potwierdzono wzrost wartości wskaźnika QUICKI w grupie EG1 ($p = 0,01$) oraz istotny spadek stężenia glukozy we krwi pomiędzy pierwszym, a szesnastym tygodniem trwania projektu ($p = 0,02$).

W okresie czterech tygodni obserwacji (follow-up) potwierdzono istotne zmiany poziomu insuliny ($p = 0,03$) pomiędzy pomiarami w EG2. Największy spadek poziomu insuliny nastąpił między pierwszym a szesnastym tygodniem trwania projektu ($p = 0,03$). Najbardziej znaczące zmiany w HOMA-TG zaobserwowano po 16 tygodniach, w których redukcja wskaźnika insulinooporności wyniosła 40% ($p = 0,04$) w stosunku do pomiaru wyjściowego.

W okresie obserwacji nastąpił wzrost stężenia leptyny w grupie aerobowej ($p < 0,001$) i związana z nim zmiana w proporcji ADIPO/LEP ($p < 0,001$).

Natomiast grupę aerobowo-oporową w okresie follow-up charakteryzował dalszy spadek stężenia IL-6 ($p < 0,001$) o 74% od wartości wyjściowej.

# 5. Dyskusja

Celem projektu była ocena wpływu dwóch różnych interwencji treningowych (trening aerobowy i trening aerobowo-oporowy) trwających dwanaście tygodni oraz czterech tygodni obserwacji - bez zorganizowanych treningów, na skład ciała, poziom iryzyny, interleukiny-6, leptyny, omentyny, adiponektyny, interleukiny-8 oraz wskaźniki zespołu metabolicznego w porównaniu z grupą kontrolną u mężczyzn z zespołem metabolicznym.

Analizując skład ciała osób biorących udział w badaniu, potwierdzono spadek poziomu tkanki tłuszczowej w grupach interwencyjnych oraz tłuszczu trzewnego w grupie stosującej trening aerobowy. Najbardziej korzystne zmiany zaszły w grupie EG2, w której doszło do wzrostu beztłuszczowej masy ciała, a także największego spadku obwodu talii, poziomu tkanki tłuszczowej oraz gynoidalnej tkanki tłuszczowej. Potwierdzono również korzystny wpływ treningu aerobowego i aerobowo-oporowego na wskaźnik oporności insulinowej QUICKI, którego zmiany były istotnie związane z poziomami leptyny. Najwięcej korzystnych zmian we wskaźnikach insulinooporności miało miejsce w grupie EG2, w której znacznej redukcji uległy poziomy zarówno HOMA-AD oraz HOMA-TG, jak i samej insuliny. Wyniki badania potwierdziły istotne zmiany w poziomie iryzyny w grupie stosującej trening aerobowy oraz w poziomie IL-6 w obydwu grupach interwencyjnych. W grupie EG2 zaobserwowano największy spadek poziomu IL-6 w ciągu 16 tygodni. Doszło również do zmian w poziomach leptyny pod wpływem zastosowanych interwencji treningowych. Obserwowano również wahania hormonu w grupie kontrolnej. Największa regresja poziomu leptyny podczas trwania projektu miała miejsce w grupie EG2. W opisanych modelach potwierdzono ścisłą zależność pomiędzy iryzyną, IL-6, a poziomem tkanki tłuszczowej i beztłuszczowej masy ciała, będących źródłem syntezy tych hormonów. Uzyskane wyniki wskazują także na istotną korelację między poziomem leptyny a miejscem jej syntezy, czyli tkanką tłuszczową, w tym tkanką tłuszczową trzewną oraz zmianami zachodzącymi w niej podczas interwencji. Potwierdzono zależność pomiędzy adiponektyną, a gynoidalną tkanką tłuszczową i wskaźnikami insulinooporności.

Najbardziej korzystne zmiany składu ciała zaszły w grupie stosującej połączenie treningu aerobowego z treningiem oporowym. Brak istotnych zmian w poziomie masy ciała był prawdopodobnie wynikiem zmian w proporcji pomiędzy tkanką tłuszczową

a mięśniami szkieletowymi. Podczas trwania interwencji potwierdzono znaczny spadek tkanki tłuszczowej (−6,9% czyli -2,24 kg) i wzrost beztłuszczowej masy ciała (6,0%, już po 6 tygodniach interwencji wzrost o 4,07 kg). W przeglądzie 149 badań dotyczących stosowania treningów fizycznych u pacjentów z nadwagą lub otyłością autorzy podkreślają rolę treningu oporowego w zapobieganiu utraty beztłuszczowej masy ciała. Zastosowanie treningów oporowych prowadzi do mniejszej utraty FFM oraz zauważane są zbliżone efekty w redukcji poziomu tkanki tłuszczowej w stosunku do innych form aktywności fizycznej [117]. W grupie stosującej sam trening aerobowy również zaszły korzystne zmiany w składzie ciała. Doszło do redukcji masy ciała o -2,3 kg, głównie w wyniku utraty poziomu tkanki tłuszczowej -1,81 kg, szczególnie tkanki tłuszczowej trzewnej. W metaanalizie badań [118] autorzy podkreślają bardziej istotną rolę treningu aerobowego lub połączenia treningu aerobowego z oporowym w grupie pacjentów z otyłością w redukcji poziomu trzewnej tkanki tłuszczowej, niż treningów oporowych. Inni badacze również potwierdzili zmiany w składzie ciała osób otyłych podejmujących różne formy interwencji treningiem fizycznym. W badaniu Villareal i inni [99] kobiety oraz mężczyźni wykonywali treningi aerobowe, siłowe lub połączenia obydwu form aktywności fizycznej 3 razy w tygodniu przez okres 26 tygodni. We wszystkich grupach interwencyjnych rezultaty w utracie masy ciała były zbliżone i wyniosły ok. 9 %. Ponadto największy ubytek beztłuszczowej masy ciała został zaobserwowany w grupie stosującej trening aerobowy (-5%), w grupie stosującej sam trening oporowy -2% i grupie stosującej połączenie treningu aerobowego z oporowym również potwierdzono spadek FFM o -3%. Ubytek tkanki tłuszczowej był zbliżony we wszystkich trzech grupach i wyniósł około 17%.

Podczas realizacji projektu potwierdzono istotne zmiany we wskaźnikach metabolizmu węglowodanów w obydwu grupach interwencyjnych. Wyraźne rezultaty w poprawie wrażliwości komórek na działanie insuliny zauważono w grupie stosującej połączenie treningu aerobowo-oporowego po 16 tygodniach trwania projektu. Khan i inni [109] zaproponowali HOMA-TG, jako dobry wskaźnik do diagnozowania MetS, wskazując, że wskaźnik ten może zapewnić wyższą skuteczność diagnostyczną w diagnozowaniu MetS niż HOMA-IR, HOMA2 i QUICKI. Matsuhisa i inni [108] zauważyli, że HOMA-AD wykazał wyższą korelację z poziomem oporności na insulinę niż HOMA-IR. Nasze badania potwierdziły również, że oba wskaźniki były silnie skorelowane ze sobą. Wartości obu wskaźników zmieniały się istotnie po interwencji

aerobowo-oporowej: po 16 tygodniach zmniejszenie HOMA-AD wyniosło 46%, a HOMA-TG uległo spadkowi o 39%. Takie korzystne zmiany w metabolizmie węglowodanów, wynikające z zastosowania połączonego treningu siłowego i aerobowego, mogą otworzyć perspektywy w leczeniu osób z MetS, opornością na insulinę i cukrzycą typu 2.

Procesy, które mogą zachodzić pod wpływem treningów, powinny być dokładnie analizowane, aby właściwie zrozumieć związek między opornością na insulinę, a aktywnością fizyczną u mężczyzn z MetS i otyłością. Mięśnie szkieletowe stanowią główny obszar metabolizmu węglowodanów w organizmie człowieka; ponadto są także głównym obszarem rozwoju oporności na insulinę [119]. Chroniczny dodatni bilans energetyczny organizmu prowadzący do otyłości, prowadzi nie tylko do zaburzeń w poziomach adipokin, ale także do gromadzenia tkanki tłuszczowej w wątrobie i mięśniach szkieletowych, a następnie do nieprawidłowej odpowiedzi metabolicznej, obejmującej głównie oporność na insulinę. Głównym mechanizmem regulującym poziom insuliny jest aktywacja substratu receptora insuliny IRS (insulin receptor substrate), którego funkcjonowanie jest upośledzone przy otyłości [120]. W otyłości, czynniki transkrypcyjne takie jak SERBP1c mogą prowadzić do rozwoju lipotoksyczności w mięśniach szkieletowych poprzez odkładanie trójglicerydów, acylowanych koenzymów A, fosfatydów, diacylogliceroli (DAG) i ceramidów [121]. W naszych badaniach, w grupie EG2 zaobserwowano istotny wzrost FFM w pierwszych 6 tygodniach interwencji, wynoszący 4,1%, a w tym samym okresie obserwowano zmniejszenie poziomu GYNOID. Jednak wskaźniki oporności na insulinę HOMA-AD i HOMA-TG wzrosły o 31,6% i 22,5%. Głównym czynnikiem wpływającym na wzrost oporności na insulinę był wzrost stężenia insuliny w analizowanym okresie. Wzrost stężenia insuliny mógł wynikać z ograniczonej zdolności do reagowania na insulinę w jej receptorze IRS, spowodowanej lipotoksycznością, związaną z odkładaniem trójglicerydów w mięśniach szkieletowych i zaburzeniami sygnalizacji insuliny w tkankach oraz ograniczeniem funkcji transportera glukozy typu 4 (GLUT4) [122, 123]. Insulinooporność mogła być również związana z występowaniem mikrouszkodzeń mięśni, spowodowanych skurczami ekscentrycznymi, których wydłużona faza jest charakterystyczna dla treningu oporowego. Liczne mikrouszkodzenia mięśni wpływają na obniżenie poziomu GLUT4 i ograniczenie resyntezy glikogenu [ 124 ]. Prawdopodobieństwo wystąpienia mikrouszkodzeń mięśniowych było większe w grupie

stosującej trening aerobowo-oporowy, ze względu na początkowe procesy adaptacyjne zachodzące w wyniku zwiększenia objętości i intensywności treningu oporowego.

W grupie stosującej trening aerobowy potwierdzono spadek wskaźnika QUICKI pomiędzy pomiarami oraz - w teście post-hoc - zaobserwowano istotny spadek poziomu glukozy po 16 tygodniach interwencji. Takie zmiany mogą być związane działaniem iryzyny, która wpływa na zwiększenie ekspresji transportera glukozy 4 (GLUT4) w adipocytach [ 125 ]. Stymulacja ludzkich komórek mięśniowych iryzyną istotnie zwiększyła pobieranie glukozy i kwasów tłuszczowych o 30-40 % przez okres 1 godziny [126]. W grupach interwencyjnych potwierdzono ujemną korelację pomiędzy leptyną, a QUICKI oraz istotną statystyczną zmienność pomiędzy adipokiną, a wskaźnikiem metabolizmu węglowodanów w przedstawionym modelu regresji wielorakiej (praca nr 2). Wykazana zależność wskazuje na wysoce prawdopodobny związek przyczynowo skutkowy wpływu leptyny na poziom insulinooporności u pacjentów z zespołem metabolicznym. Szczególnie zauważalne rezultaty w redukcji poziomu leptyny oraz poprawie wskaźników insulinooporności wystąpiły w grupie stosującej trening aerobowo-oporowy. Podobną korelację między leptyną, a QUICKI w przypadku zespołu metabolicznego potwierdzili inni badacze [127].

Wyniki naszego badania wskazują na wzrost poziomu HDL-C o 5,8% w grupie interwencji aerobowej i o 8,3% w grupie interwencji aerobowo-oporowej po 16 tygodniach, jednak opisane zmiany nie osiągnęły wymaganego poziomu istotności. W metaanalizie badań analizujących wpływ aktywności fizycznej na parametry lipidowe potwierdzono, że stosowanie kombinacji treningu oporowego i aerobowego przez 12 tygodni prowadziło do wzrostu HDL-C od 3,5% do 23% [128]. Metaanaliza badań dotyczących profilu lipidowego u osób korzystających z treningu oporowego również wykazała korzystne zmiany w stężeniach nonHDL-C i HDL-C u osób poddanych interwencji [ 129 ]. Pomimo licznych doniesień o korzystnym wpływie ćwiczeń fizycznych na poziom nonHDL-C, nasze badania nie potwierdziły istotnych zmian w opisanym parametrze. Stwierdzono natomiast wzrost stężenia HDL-C i spadek stężenia nonHDL-C w innych badaniach interwencyjnych z wykorzystaniem aktywności fizycznej w leczeniu zespołu metabolicznego [130]. Podjęcie treningu oporowego może prowadzić do 6% zmniejszenia stężenia nonHDL-C i zwiększenia stężenia HDL-C o 1%. W przypadku treningu aerobowego potwierdzono zmniejszenie stężenia nonHDL-C o 2,5% i wzrost o 4% stężenia HDL-C [ 131 ]. Brak zmian w poziomach HDL-C

i nonHDL-C pomimo interwencji, może wynikać z podwyższonej proporcji kwasów tłuszczowych dostarczanych w diecie [132].

Zmiany w poziomie adipokin były zróżnicowane pomiędzy grupami. Najwięcej korzystnych zmian w markerach stanu zapalnego potwierdzono w grupie stosującej połączenie treningu aerobowego i oporowego, gdzie doszło do istotnego spadku leptyny oraz interleukiny-6 pomiędzy pomiarami.

Ważnym aspektem w procesie kontroli poziomu adipokin, jest wybór momentu pobrania krwi do analizy, ze względu na zróżnicowanie w syntezie poszczególnych adipokin oraz ich reakcję na podjęcie treningu fizycznego. Szczególnie wrażliwe na podjęcie treningów fizycznych są iryzyna oraz interleukina-6, ponieważ ich synteza odbywa się zarówno w tkance tłuszczowej, jak i w mięśniach szkieletowych. W niniejszym badaniu pomiary zostały przeprowadzone na czczo, 24-godziny po odbytym treningu lub bez podejmowania aktywności fizycznej w przypadku grupy kontrolnej. W takich warunkach zmiany w poziomach IL-6 oraz iryzyny mogły być wynikiem ich zwiększonej syntezy w tkance tłuszczowej. Stężenia IL-6 oraz iryzyny wzrastają głównie pod wpływem wysiłku fizycznego poprzez aktywacje mięśni szkieletowych, a ich pomiar przeprowadzony w dniu treningu, najlepiej podczas treningu lub tuż po jego zakończeniu, świadczy głównie o syntezie opisanych hormonów w tkance mięśni szkieletowych [133, 134]. Wykazano, że po rozpoczęciu aktywności fizycznej stężenia iryzyny wzrastają zarówno u dorosłych, zdrowych osób, jak i u pacjentów z zespołem metabolicznym [49, 135, 136]. Synteza iryzyny zależy od intensywności wysiłku. Wyższe poziomy są obserwowane po podjęciu wysiłków o wysokiej intensywności [137]. Podobna sytuacja dotyczy IL-6, której poziom wzrasta wykładniczo w odpowiedzi na aktywność fizyczną [133]. Stężenia IL-6 we krwi mogą wzrosnąć nawet 100-krotnie w odpowiedzi na trening [53]. Poziom IL-6 stabilizuje się w ciągu 24 godziny od zakończenia ćwiczeń fizycznych [134].

Istnieją sprzeczne doniesienia dotyczące wyników stężeń iryzyny związanych z interwencjami długotrwałymi (≥ 8 tygodni) aktywnością fizyczną. W metaanalizie badań podejmującej zastosowanie zarówno treningów oporowych, jak i aerobowych w grupach osób z prawidłową masą ciała lub otyłością, autorzy zaobserwowali wzrost stężenia iryzyny, a długoterminowe rezultaty uzyskano u osób wykonujących trening oporowy [138]. Dodatkowo w badaniu przeprowadzonym przez Cosio i inni [139]

potwierdzono zwiększanie stężenia iryzyny u osób wykonujących trening oporowy. W metaanalizie przeprowadzonej przez Qiu i innych [140] autorzy zaobserwowali zmniejszenie stężenia iryzyny w grupach poddawanych interwencji aerobowej. Natomiast w przeglądzie badań dotyczących zdrowych, dorosłych osób nie potwierdzono istotnych zmian w poziomach iryzyny po podjęciu długoterminowych treningów oporowych lub aerobowych [141]. Pozostałe adipokiny, takie jak leptyna oraz adiponektyna wydają się mniej wrażliwe na krótkotrwałe interwencje wysiłkami fizycznymi. Poziom leptyny jest głównie zależny od rytmów dobowych oraz bilansu energetycznego organizmu. Ćwiczenia mogą wpływać na jej stężenie głównie przez zmianę bilansu energetycznego w dłuższej perspektywie czasu [142]. Adiponektyna charakteryzuje się niską amplitudą wahań dobowych, w związku z czym pobrań hormonu należy dokonywać rano na czczo lub po posiłku, aby zapewnić wiarygodny marker insulinooporności u pacjentów z zespołem metabolicznym [143].

W naszym badaniu zaobserwowano stopniowy spadek stężeń IL-6 w grupach stosujących trening fizyczny: w grupie treningowej aerobowo-oporowej wynosił on −74% po 16 tygodniach, a w grupie aerobowej odnotowano spadek o 18%. W grupie kontrolnej natomiast nie zaobserwowano istotnych zmian. Różnica między grupami wskazywała na niższe stężenia IL-6 w grupie wykonującej trening aerobowo-oporowy. Patofizjologia otyłości obejmuje występowanie przewlekłego stanu zapalnego o niskim nasileniu jako wynik, między innymi, nadmiernego wytwarzania IL-6 przez tkankę tłuszczową [144]. W wyniku interwencji treningowej u pacjentów otyłych obserwuje się obniżenie poziomu IL-6, które jest związane z redukcją masy tłuszczowej [145]. Jednak poziomy IL-6 u pacjentów z otyłością i cukrzycą typu 2 są zazwyczaj wyższe niż u osób o prawidłowej masie ciała [146].

W naszym projekcie średni poziom BMI badanych mężczyzn wynosił 33,63 kg/m$^2$, a uczestnicy spełniali co najmniej 3 z 5 kryteriów MetS. Zgodnie z doniesieniami [47, 48] taka grupa pacjentów ma wysokie ryzyko oporności na iryzynę. W badaniu własnym, w grupie EG1 doszło do wzrostu poziomu iryzyny pomiędzy pomiarami, a takie zachowanie hormonu pod wpływem interwencji nie wskazuje na występowanie zjawiska iryzynooporności w badanej grupie. W doniesieniu Polyzos i inni [147], analizującym związek między iryzyną, a chorobami metabolicznymi, w tym otyłością, cukrzycą typu 2 i stłuszczeniem wątroby, zaobserwowano różne wyniki badań. Autorzy opracowania podkreślają, że stężenie iryzyny było wysokie w grupie otyłych osób, podczas gdy

pacjenci z cukrzycą typu 2 i stłuszczeniem wątroby mieli niższe stężenia iryzyny w porównaniu z grupą kontrolną. Werida i inni zaobserwowali natomiast wyższe stężenia iryzyny i IL-6 u otyłych mężczyzn z tendencją do występowania zespołu metabolicznego [51].

W populacji osób otyłych z zespołem metabolicznym, oprócz iryzynooporności, obserwuje się również proces oporności na leptynę, odgrywający kluczową rolę w powikłaniach związanych z przebiegiem otyłości [ 148 ]. Wyniki naszych badań potwierdzają wysokie stężenie leptyny w populacji osób z zespołem metabolicznym i otyłością oraz związek między leptyną, a wskaźnikami insulinooporności. Potencjał terapeutyczny wynikający z zastosowania połączenia treningu oporowego i aerobowego oferuje perspektywy leczenia zespołu metabolicznego i otyłości poprzez wpływ na zmniejszenie poziomu leptyny, poziomu tkanki tłuszczowej będącej źródłem syntezy leptyny [149] oraz związaną z leptyną opornością na insulinę.

Niniejsze badanie potwierdziło zmienność stężenia leptyny między pomiarami we wszystkich grupach, jednak biologiczne zachowanie hormonu różniło się w każdej z analizowanych grup. Po 6 tygodniach interwencji zaobserwowano wzrost stężenia leptyny w grupie aerobowej, jednak wydłużenie czasu interwencji do 12 tygodni wiązało się z tendencją spadkową stężenia leptyny w naszym badaniu. W metaanalizie Yu et al. przedstawiono doniesienia, że ćwiczenia aerobowe mają istotny wpływ na obniżenie poziomu leptyny w surowicy [103]. W badaniu Klempel i inni [150] wykazano, że nawet niewielka utrata masy ciała (4-5%) może mieć korzystny wpływ na stężenie leptyny. W przypadku utraty masy ciała o 2,4% również zaobserwowano spadek stężenia leptyny w surowicy [151]. W naszym badaniu, pomimo początkowej utraty masy ciała, stężenie leptyny wzrosło w grupie EG1 po 6 tygodniach interwencji. Wzrost stężenia leptyny, pomimo stosowania treningu aerobowego, może być wynikiem innych czynników niezależnych od naszej kontroli. Badanie zostało przeprowadzone w okresie pandemii COVID-19, a zwiększone poziomy lęku związane z trwającym okresem izolacji [152], zmniejszenie długości snu [153] oraz podwyższone poziomy stresu [154] są czynnikami związanymi z fluktuacją hormonów [155].

Ze względu na spadki stężenia leptyny w grupie EG2 pomiędzy pomiarami oraz różnice wskazujące na istotnie niże wartości leptyny w EG2 w stosunku do pozostałych grup, nasze wyniki wskazują na bardziej korzystny efekt treningu aerobowo-oporowego,

w porównaniu do samego treningu aerobowego lub braku aktywności fizycznej, na poziom leptyny. Korzystne zmiany w grupie stosującej połączenie treningu aerobowego z oporowym mogą wiązać się z redukcją stanu zapalnego mającego również odzwierciedlenie w spadku IL-6 pomiędzy pomiarami. Inne wyniki uzyskali autorzy w badaniu osób z zespołem metabolicznym, w którym przez okres 12 tygodni stosowano trening Nordic Walking (NW) na poziomie 65-75% HR max lub trening siłowy. Badacze nie potwierdzili zmiany stężenia leptyny u osób stosujących trening siłowy, ale potwierdzili spadek stężenia leptyny o 27% w grupie stosującej trening NW [151]. Przebieg zmian w przedstawionych grupach mógł wynikać z większej redukcji poziomu tkanki tłuszczowej w grupie NW oraz z braku zmian w beztłuszczowej masie ciała obydwu grupach. Inne badania wykazały, że stężenie leptyny zmniejszyło się o 21% podczas 3-miesięcznego programu dynamicznego treningu siłowego [155] i o 14% podczas 6-miesięcznego programu łączącego dietę z umiarkowaną aktywnością fizyczną [156]. W badaniu własnym potwierdzono wzrost stężenia leptyny w grupie kontrolnej, co może wiązać się z rozwojem oporności na leptynę u pacjentów z zespołem metabolicznym, którzy nie podejmują aktywności fizycznej.

Wyniki naszych badań wskazują na rosnącą tendencję średnich stężeń omentyny (OMEN) w kolejnych tygodniach interwencji aerobowej, jednak zmiany wartości omentyny nie osiągnęły istotności statystycznej. W badaniu de Souza Batista i inni [69] autorzy podkreślają wpływ treningów fizycznych na wzrost stężeń omentyny. Wzrost stężenia omentyny w krążeniu również zaobserwowano u osób, które podejmowały 12-tygodniowy trening aerobowy. U badanych osób poziom tkanki tłuszczowej w organizmie uległ istotnej redukcji [157]. Możliwym powodem braku istotnego wzrostu stężenia omentyny w grupach interwencyjnych w naszym projekcie może być niewystarczająca redukcja trzewnej tkanki tłuszczowej, będącej głównym miejscem syntezy hormonu. Utrata masy ciała jest uważana za kluczowy czynnik w interwencji mającej na celu zmniejszenie poziomu cytokin prozapalnych i zwiększenie poziomu cytokin przeciwzapalnych [158,159]. Efekt obniżenia stężenia omentyny uzyskano między innymi w badaniu z interwencją dietetyczną, w którym przez 4 miesiące stosowano niskokaloryczną dietę (deficyt 500–1000 kcal dziennie). W wyniku interwencji uzyskano redukcję masy ciała o 13,8%. Badacze potwierdzili spadek stężenia leptyny o 60,6% i istotny wzrost stężenia omentyny o 22,1% [160]. Osiągnięcie większej

utraty masy ciała u osób z zespołem metabolicznym może prowadzić do klinicznie korzystnych zmian w stężeniach omentyny.

Podobne niejednoznaczne zależności wykazano w przypadku innych adipokin. Wśród pacjentów, którzy utracili 4-5% masy ciała, pomimo istotnego spadku leptyny, nie potwierdzono istotnych zmian w stężeniach IL-6, RBP4 oraz adiponektyny [150]. W pięciu badaniach klinicznych oceniających wpływ redukcji masy ciała o 10% na stężenie i ekspresję adiponektyny w osoczu nie zaobserwowano istotnych zmian w jej poziomie [159, 161, 162, 163, 164]. W badaniu własnym również nie potwierdzono istotnych zmian w poziomie adiponektyny. W metaanalizie badań dotyczących osób z insulinoopornością lub cukrzycą, u których występowała nadwaga lub otyłość, jak również zespół metaboliczny, zaobserwowano, że aktywność fizyczna zwiększa stężenie adiponektyny. Treningi fizyczne o charakterze aerobowym przynosiły korzystne rezultaty, podczas gdy inne formy aktywności fizycznej nie wpłynęły istotnie na poziom adiponektyny [165]. Podobne wyniki przedstawiono we wcześniejszych metaanalizach [103, 166]. Balducci i inni [101] wykazali natomiast, że ćwiczenia aerobowe, ale także połączenie treningu aerobowego z oporowym, przynoszą korzystne zmiany w stężeniu adiponektyny (wzrost o 36% i 38%) oraz w redukcji poziomu oporności na insulinę u pacjentów z zespołem metabolicznym, pomimo braku zmian w masie ciała i poziomie tkanki tłuszczowej. Nasze wyniki pokazały, że stosunek ADIPO/LEP zmniejszył się po 6 tygodniach interwencji aerobowej. Ta zależność wynikała z istotnego wzrostu poziomu leptyny oraz braku istotnych zmian w poziomie adiponektyny w analizowanym okresie. Leptyna może reagować na zmiany zachodzące w populacji osób z zespołem metabolicznym szybciej niż adiponektyna [150].

W naszym badaniu zaobserwowano istotny spadek, o 35% stężenia IL-8 po pierwszych 6 tygodniach interwencji w grupie stosującej trening aerobowy. Obniżone stężenie IL-8 w stosunku do początkowego stężenia obserwowano aż do końca projektu badawczego w grupie z treningiem aerobowym. Wyniki przedstawione w metaanalizie pokazują, że aktywność fizyczna u osób z zespołem metabolicznym prowadzi do obniżenia stężenia IL-8 [167]. Występują jednak badania, które nie potwierdziły zmian w stężeniu IL-8. W grupie 489 osób z zespołem metabolicznym, mężczyzn i kobiet powyżej 55 roku życia, którzy wykonywali umiarkowane lub intensywne ćwiczenia o minimalnym czasie 150 minut tygodniowo, nie zaobserwowano istotnych zmian stężenia IL-8 podczas rocznej obserwacji [168]. W badaniu własnym, w grupie nie

podejmującej aktywności fizycznej doszło do stopniowego wzrost stężenia IL-8 między pomiarami, a poziom cytokiny był o 45% wyższy w grupie kontrolnej w porównaniu do grupy z interwencją aerobową. Według pracy Bruun i inni [169] u pacjentów z otyłością dochodzi do nadmiernej syntezy IL-8 w tkance tłuszczowej, prowadząc do wzrostu poziomu stanu zapalnego w organizmie. Nie podjęcie leczenia otyłości i zaburzeń metabolicznych prowadzi do dalszego nasilenia stanu zapalnego w organizmie i licznych powikłań zdrowotnych [170].

Przedstawiony projekt badawczy nie jest wolny od pewnych ograniczeń. Prezentowane wyniki ukazują zmiany stężeń wybranych adipokin oraz parametrów biochemicznych pod wpływem interwencji w formie aktywności fizycznej. Osoby biorące udział w badaniu mogły być jednak narażone na inne czynniki, takie jak zwiększone poziomy stresu czy zmniejszona długość snu, które mogą wpłynąć na poziom prezentowanych parametrów. Monitorowanie aktywności fizycznej odbywało się za pomocą urządzeń kontrolujących częstość skurczów serca, jednak bardziej precyzyjny nadzór można było uzyskać poprzez pomiar $VO_2$ max [171]. Pomimo początkowych założeń dotyczących utrzymywania bieżącej diety i stałej kontroli diety uczestników badania, ilość dostarczanej energii w pożywieniu wzrosła. Opisując ich jadłospis, nie dokonano szczegółowej analizy kwasów tłuszczowych oraz indeksu glikemicznego, które mogły wpłynąć na profil lipidowy i wskaźniki insulinooporności badanych uczestników.

W podsumowaniu, jako wniosek aplikacyjny warto podkreślić, że w badaniach analizujących zmiany poziomu adipocytokin w grupie pacjentów z otyłością i zespołem metabolicznym ważne jest utrzymanie umiarkowanego lub znacząco ujemnego bilansu energetycznego podczas trwania interwencji treningiem fizycznym. Uzyskanie oczekiwanego ujemnego bilansu energetycznego można otrzymać w wyniku zwiększenia wydatków energetycznych; bezpieczną dla tej grupy pacjentów formą byłaby aktywność fizyczna spontaniczna. Aktywność fizyczna spontaniczna mogłaby zostać zwiększona poprzez wprowadzenie większej liczby kroków w ciągu dnia (np. dłuższy spacer do pracy, chodzenie podczas prowadzonych rozmów telefonicznych), wprowadzenie aktywnie spędzonego czasu w weekend (wycieczki rowerowe, aktywny wypoczynek w górach, gry i zabawy z rodziną i przyjaciółmi, wyjście na basen). Każda z proponowanych aktywności powinna być wprowadzana stopniowo, o niskiej intensywności oraz umiarkowanym czasie trwania. Doprowadzenie do zwiększenia

wydatków energetycznych poprzez zwiększenie intensywności sesji treningowych w tej grupie pacjentów mogłoby zwiększyć prawdopodobieństwo wystąpienia przeciążeń aparatu ruchu. Inną możliwością osiągnięcia oczekiwanego ujemnego bilansu energetycznego byłoby utrzymanie ubogo energetycznej diety.

W badaniach mających na celu ocenę wpływu beztłuszczowej masy ciała na stan zdrowia pacjentów z otyłością i zespołem metabolicznym warto byłoby wykorzystać zastosowaną w badaniu własnym procedurę treningu aerobowo-oporowego, dzięki której uzyskując ujemny bilans energetyczny, prowadzący do redukcji tkanki tłuszczowej, doszło także do znacznego rozwoju beztłuszczowej masy ciała już po 6 tygodniach interwencji.

## 6. Wnioski

1. Zastosowanie treningów aerobowych przez okres 12 tygodni w populacji pacjentów z zespołem metabolicznym związane było z redukcją masy ciała, tkanki tłuszczowej, a także trzewnej tkanki tłuszczowej. Połączenie treningu aerobowego z oporowym doprowadziło natomiast do zwiększenia beztłuszczowej masy ciała oraz redukcji poziomu tkanki tłuszczowej, gynoidalnej tkanki tłuszczowej i obwodu talii. Treningu aerobowy w połączniu z oporowym wpłynął korzystniej na skład ciała mężczyzn z zespołem metabolicznym niż zastosowanie samego treningu aerobowego.

2. Trening fizyczny o charakterze aerobowym związany był z korzystnymi zmianami w poziomie insulinooporności wyrażonych we wskaźnikach QUICKI oraz HOMA-TG. Zastosowanie interwencji łączącej trening aerobowy z oporowym doprowadziło do spadku insulinooporności, opisanej zarówno przez wskaźnik QUICKI, jak i HOMA-AD oraz HOMA-TG. Połączenie treningów aerobowych z oporowymi związane było z wyraźnymi korzyściami w poprawie wrażliwości na insulinę u mężczyzn z zespołem metabolicznym.

3. Nie potwierdzono istotnych zmian we wskaźnikach profilu lipidowego podczas stosowania treningów fizycznych w okresie 12 tygodni u badanych mężczyzn. Na podstawie uzyskanych wyników nie ma podstaw do wyodrębnienia bardziej korzystnej formy treningu fizycznego prowadzącego do poprawy parametrów profilu lipidowego u mężczyzn z zespołem metabolicznym.

4. Zastosowanie treningów aerobowych wywołało zmiany w poziomie wybranych adipocytokin we krwi mężczyzn z zespołem metabolicznym (zwiększenie stężenia iryzyny oraz obniżenie stężenia IL-8 po 6 tygodniach interwencji, a także obniżenie stężenia IL-6 i leptyny po 12 tygodniach interwencji). W grupie stosującej trening aerobowy w połączeniu z oporowym przez 12 tygodni potwierdzono obniżenie stężenia IL-6 oraz leptyny na każdym etapie interwencji, wyraźnie wskazując na działanie przeciwzapalne.

5. W okresie obserwacji, w którym nie prowadzono zorganizowanych treningów, w obu grupach interwencyjnych efekt redukcji tkanki tłuszczowej oraz jej trzewnej kumulacji został podtrzymany. W obu grupach potwierdzono także dalsze korzystne zmiany we wskaźnikach insulinooporności. W grupie aerobowo-oporowej

zaobserwowano dalsze obniżenie stężenia IL-6, wskazując na redukcję stanu zapalnego. Poddani badaniom mężczyźni poprzez podejmowanie systematycznych treningów fizycznych w okresie obserwacji, utrzymali korzystne rezultaty.

# 7. Piśmiennictwo


1 Meshkani, R.; Adeli, K. Hepatic insulin resistance, metabolic syndrome and cardiovascular disease. *Clin Biochem.* **2009,** 42, 1331–1346.

2 Tan, M.C.; Ng, O.C.; Wong, T.W.; Joseph, A.; Yoke, M.C.; Hejar, A.R. Prevalence of metabolic syndrome in type 2 diabetic patients: A comparative study using WHO, NCEP ATP III, IDF and Harmonized definitions. *Health.* **2013**, 05, 1689–1696.

3 Ford, E.S.; Giles, W.H.; Dietz, W.H. Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. *JAMA*. **2002,** 287, 356-359.

4 Bruce, K.D.; Byrne, C.D. The metabolic syndrome: common origins of a multifactorial discussion. *Postgrad Med J*. **2009,** 85, 614–621.

5 Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA.* **2001,** 285, 2486–2497.

6 Pyorala, M.; Miettinen, H.; Halonen, P.; Laakso, M.; Pyorala, K. Insulin resistance syndrome predicts the risk of coronary heart disease and stroke in healthy middle-aged men: the 22-year follow-up results of the Helsinki Policemen Study. *Arterioscler Thromb Vasc Biol.* **2000,** 20, 538–544.

7 Moreira, G.C.; Cipullo, J.P.; Ciorlia, L.A.S.; Cesarino, C.B.; Vilela-Martinet, J.F. Prevalence of metabolic syndrome: Association with risk factors and ardiovascular complications in an urban population. *PLoS One*. **2014**, 9, 105056.

8 Matsuzawa, Y.; Funahashi, T.; Nakamura, T. The concept of metabolic syndrome: contribution of visceral fat accumulation and its molecular mechanism. *J Atheroscler Thromb.* **2011,** 18, 629-639.

9 Thottam, G.E.; Krasnokutsky, S.; Pillinger, M.H. Gout and metabolic syndrome: A tangled web. *Curr Rheumatol Rep.* **2017**, 19, 60.

10 Uzunlulu, M.; Telci Caklili, O.; Oguz, A. Association between metabolic syndrome and cancer. *Ann Nutr Metab*. **2016**, 68, 173–179.

11 Kostoglou-Athanassiou, I.; Athanassiou, P. Metabolic syndrome and sleep apnea. *Hippokratia.* **2008,** 2, 81-86.

12 Attarzadeh Hosseini, S.R.; Mohammad Rahimi, G.R.; Ghaemi, J. Compare waist circumference, waist-to-hip ratio and waist-to-stature ratio in predicting overweight/obese male students. *Razi Journal of Medical Sciences*. **2017**, 24, 67–76.

13 Sang, H.; Yao, S.; Zhang, L.; Li, X.; Yang, N.; Zhao, J.; Zhao, L.; Si, Y.; Zhang, Y.; Lv, X. Walk-run training improves the antiinflammation properties of high-density lipoprotein in patients with metabolic syndrome. *The Journal of Clinical Endocrinology & Metabolism*. **2015**, 100, 870–879.

14 Furukawa, S.; Fujita, T.; Shimabukuro, M.; Iwaki, M.; Yamada, Y.; Nakajima, Y.; Nakayama, O.; Makishima, M.; Matsuda, M.; Shimomura I. Increased oxidative stress in obesity and its impact on metabolic syndrome. *J Clin Invest.* **2004**, 114, 1752-1761.

15 Fulop, T.; Tessier, D.; Carpentier, A. The metabolic syndrome. *Pathol Biol (Paris).* **2006,** 54, 375–386.

16 Grundy, S.M.; Brewer Jr, H.B.; Cleeman, J.I.; Smith Jr, S.C.; Lenfant, C. Definition of metabolic syndrome: Report of the National Heart, Lung and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation*. **2004,** 109, 433-438.

17 Unger, R.H.; Scherer, P.E. Gluttony, sloth and the metabolic syndrome: a roadmap to lipotoxicity . *Trends Endocrinol Metab.* **2010**, 21, 345-352.

18 World Health Organization: International statistical classification of diseases and related health problems. **2016**, 1, 10.

19 Fothergill, E.; Guo, J.; Howard, L.; Kerns, J.C.; Knuth, N.D.; Brychta, R.; Chen, K.Y.; Skarulis, M.C.; Walter, M.; Walter, P.J.; Hall, K.D. Persistent metabolic adaptation 6 years after 'The Biggest Loser' competition. *Obesity (Silver Spring).* **2016**, 24, 1612–1619.

20 Schwartz, M.W.; Seeley, R.J.; Zeltser, L.M.; Drewnowski, A.; Ravussin, E.; Redman, L.M.; Leibel, R.L. Obesity Pathogenesis: An Endocrine Society Scientific Statement. *Endocr Rev.* **2017**, 38, 267-296.

21 Hebebrand, J.; Holm, J.C.; Woodward, E.; Baker, J.L.; Blaak, E.; Durrer Schutz, D.; Farpour-Lambert, N.J.; Frühbeck, G.; Halford, J.G.C.; Lissner, L.; Micic, D.; Mullerova, D.; Roman, G.; Schindler, K.; Toplak, H.; Visscher, T.L.S.; Yumuk, V. A Proposal of the European Association for the Study of Obesity to Improve the ICD-11 Diagnostic Criteria for Obesity Based on the Three Dimensions Etiology, Degree of Adiposity and Health Risk. *Obes Facts.* **2017**, 10, 284-307.

22 Ouchi, N.; Parker, J.L.; Lugus, J.J.; Walsh, K. Adipokines in inflammation and metabolic disease. *Nat Rev Immunol.* **2011**, 11, 85-97.

23 Hopkins, M.; Blundell, J.E. Energy balance, body composition, sedentariness and appetite regulation: pathways to obesity. *Clin Sci.* **2016**, 130, 1615–1628.

24 Hutley, L.; Prins, J.B. Fat as an endocrine organ: relationship to the metabolic syndrome. *Am J Med Sci.* **2005**, 330, 280–289.

25 Vaidya, V. Psychosocial aspects of obesity. *Adv Psychosom Med.* **2006**, 27, 73-85.

26 MacLean, P.S.; Blundell, J.E.; Mennella, J.A.; Batterham, R.L. Biological control of appetite: A daunting complexity. *Obesity (Silver Spring).* **2017**, 25, 8-16.

27 Muller, M.J.; Bosy-Westphal, A. Adaptive thermogenesis with weight loss in humans. *Obesity (Silver Spring).* **2013**, 21, 218–228.

28 Flegal, K.M.; Panagiotou, O.A.; Graubard, B.I. Estimating population attributable fractions to quantify the health burden of obesity. *Ann Epidemiol.* **2015**, 25, 201–207.

29 Lee, I.M.; Manson, J.E.; Hennekens, C.H.; Paffenbarger, R.S. Jr. Body weight and mortality. A 27-year follow-up of middle-aged men. *JAMA*. **1993**, 270, 2823-2828.

30 Donath, M.Y.; Shoelson, S.E. Type 2 diabetes as an inflammatory disease. *Nat. Rev. Immunol.* **2011**, 11, 98-107.

31 Moore, K.J.; Tabas, I. Macrophages in the pathogenesis of atherosclerosis. *Cell*. **2011**, 145, 341-355.

32 Nicholson, T.; Church, C.; Baker, D.J.; Jones, S.W. The role of adipokines in skeletal muscle inflammation and insulin sensitivity. *J. Inflamm (Lond).* **2018**, 15, 9.

33 Rome, S. Muscle and Adipose Tissue Communicate with Extracellular Vesicles. *Int. J. Mol. Sci.* **2022**, 23, 7052.

34 Coelho-Junior, H.J.; Picca, A.; Calvani, R.; Uchida, M.C.; Marzetti, E. If my muscle could talk: myokines as a biomarker of frailty. *Exp. Gerontol.* **2019**, 127, 110715.

35 Nelke, C.; Dziewas, R.; Minnerup, J.; Meuth, S.G.; Ruck, T. Skeletal muscleas potential central link between sarcopenia and immune senescence. *eBioMedicine*. **2019**, 49, 381–388.

36 Tsao, T.S.; Burcelin, R.; Katz, E.B.; Huang, L.; Charron, M.J. Enhanced insulin action due to targeted GLUT4 overexpression exclusively in muscle. *Diabetes.* **1996**, 45, 28–36.

37 Tsao, T.S.; Li, J.; Chang, K.S.; Stenbit, A.E.; Galuska, D.; Anderson, J.E.; Zierath, J.R.; McCarter, R.J.; Charron, M.J. Metabolic adaptations in skeletal muscle overexpressing GLUT4: effects on muscle and physical activity. *FASEB J.* **2001**, 15, 958–969.

38 Blüher, M. Vaspin in obesity and diabetes: pathophysiological and clinical significance. *Endocrine.* **2012**, 41, 176-182.

39 Fève, B.; Bastard, C.; Fellahi S.; Bastard, J.P.; Capeau, J. New adipokines. *Annales d'endocrinologie* **2016**, 77, 49-56.

40 Sahin-Efe, A.; Katsikeris, F.; Mantzoros, C.S. Advances in adipokines. *Metab Clin Exp*. **2012**, 61, 1659-1665.

41 Yu, Q.; Kou, W.; Xu, X.; Zhou, S.; Luan, P.; Li, H.; Zhuang, J.; Wang, J.; Zhao, Y.; Xu, Y.; Peng, W. FNDC5/Irisin inhibits pathological cardiac hypertrophy. *Clin. Sci. (Lond.)* **2019**, 133, 611–627.

42 Roca-Rivada, A.; Castelao, C.; Senin, L.L.; Landrove, M.O.; Baltar, J.; Belén Crujeiras, A.; Seoane, L.M.; Casanueva, F.F.; Pardo, M. FNDC5/irisin is not only a myokine but also an adipokine. *PLoS One.* **2013**, 8, 60563.

43 Boström, P.; Wu, J.; Jedrychowski, M.P.; Korde, A.; Ye, L.; Lo, J.C.; Rasbach, K.A.; Boström, E.A.; Choi, J.H.; Long, J.Z.; Kajimura, S.; Zingaretti, M.C.; Vind, B.F.; Tu, H.; Cinti, S.; Højlund, K.; Gygi, S.P.; Spiegelmanet, B.M. A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. *Nature.* **2012,** 481, 463-468.

44 Xin, C.; Liu, J.; Zhang, J.; Zhu, D.; Wang, H.; Xiong, L.; Lee, Y.; Ye, J.; Lian, K.; Xu, C.; Zhang, L.; Wang, Q.; Liu, Y.; Tao, L. Irisin improves fatty acid oxidation and glucose utilization in type 2 diabetes by regulating the AMPK signaling pathway. *Int. J. Obes. (Lond.)* **2016,** 40, 443–451.

45 Lee, H.J.; Lee, J.O.; Kim, N.; Kim, J.K.; Kim, H.I.; Lee, Y.W.; Kim, S.J.; Choi, J.I.; Oh, Y.; Kim, J.H.; Suyeon-Hwang, N.; Park, S.H.; Kim, H.S. Irisin, a Novel Myokine, Regulates Glucose Uptake in Skeletal Muscle Cells via AMPK. *Mol Endocrinol.* **2015**, 29, 873-881.

46 Chen, N.; Li, Q.; Liu, J.; Jia, S. Irisin, an exercise-induced myokine as a metabolic regulator: an updated narrative review. *Diabetes Metab Res Rev.* **2016**, 32, 51-59

47 Park, K.H.; Zaichenko, L.; Brinkoetter, M.; Thakkar, B.; Sahin-Efe, A.; Joung, K.E.; Tsoukas M.A.; Geladari, E.V.; Huh, J.Y.; Dincer, F.; Davis, C.R.; Crowell, J.A.; Mantzoros, C.S. Circulating irisin in relation to insulin resistance and the metabolic syndrome. *J Clin Endocrinol Metab.* **2013**, 98, 4899-4907.

48 Jia, J.; Yu, F.; Wei, W.P.; Yang, P.; Zhang, R.; Sheng, Y.; Shi, Y.Q. Relationship between circulating irisin levels and over-weight/obesity: A meta-analysis. *World J Clin Cases.* **2019**, 7, 1444-1455.

49 Huh, J.Y.; Siopi, A.; Mougios, V.; Park, K.H.; Mantzoros, C.S. Irisin in response to exercise in humans with and without metabolic syndrome. *J Clin Endocrinol Metab*. **2015**, 100, 453-457.

50 Pal, M.; Febbraio, M.A.; Whitham, M. From cytokine to myokine: The emerging role of interleukin-6 in metabolic regulation. *Immunol. Cell Biol.* **2014**, 92, 331–339.

51 Werida, R.H.; El-Gharbawy, N.M.; Mostafa, T.M. Circulating IL-6, clusterin and irisin in obese subjects with differentgrades of obesity: association with insulin resistance and sexual dimorphism. *Arch Endocrinol Metab.* **2021**, 65, 126-136.

52 Nash, D.; Hughes, M.G.; Butcher, L.; Aicheler, R.; Smith, P.; Cullen, T.; Webb, R. IL-6 signaling in acute exercise and chronic training: Potential consequences for health and athletic performance. *Scand J Med Sci Sports.* **2022**, 00, 1-16.

53 Fischer, C.P. Interleukin-6 in acute exercise and training: What is the biological relevance? *Exerc Immunol Rev.* **2006**, 12, 6-33.

54 Chan, J.L.; Heist, K.; DePaoli, A.M.; Veldhuis, J.D.; Mantzoros, C.S. The role of falling leptin levels in the neuroendocrine and metabolic adaptation to short-term starvation in healthy men. *J Clin Invest.* **2003**, 111, 1409-1421.

55 Coppari, R.; Ramadori, G.; Elmquist, J.K. The role of transcriptional regulators in central control of appetite and body weight. *Nat Clin Pract Endocrinol Metab.* **2009**, 5, 160-166.

56 Malli, F.; Papaioannou, A.I.; Gourgoulianis, K.I.; Daniil, Z. The role of leptin in the respiratory system: an overview. *Respir Res.* **2010**, 11, 152.

57 Veniant, M.M.; LeBel, C.P. Leptin: from animals to humans. *Curr Pharm Des.* **2003**, 9, 811-818.

58 Wabitsch, M.; Ballauff, A.; Holl, R.; Blum, W.F.; Heinze, E.; Remschmidt, H.; Hebebrand, J. Serum leptin, gonadotropin, and testosterone concentrations in male patients with anorexia nervosa during weight gain. *J Clin Endocrinol Metab*. **2001**, 7, 2982-2988.

59 Suder, A.; Płonka, M.; Jagielski, P.; Piórecka, B.; Głodzik, J. Physiological and environmental factors associated with central fat distribution in pubertal girls. *Journal of Physiology and Pharmacology*. **2015**, 66, 463-470.

60 Bremer, A.A.; Devaraj, S.; Afify, A.; Jialal, I. Adipose tissue dysregulation in patients with metabolic syndrome. *J. Clin. Endocrinol. Metab.* **2011**, 96, 1782–E1788.

61 Martin, S.S.; Qasim, A.; Reilly, M.P. Leptin resistance: a possible interface of inflammation and metabolism in obesity-related cardiovascular disease. *J Am Coll Cardiol.* **2008**, 52, 1201-1210.

62 Owecki, M.; Nikisch, E.; Miczke, A.; Pupek-Musialik, D.; Sowinski, J. Leptin, soluble leptin receptors, free leptin index, and their relationship with insulin resistance and BMI: High normal BMI is the threshold for serum leptin increase in humans. *Horm. Metab. Res.* **2010**, 42, 585-589.

63 Tabak, A.G.; Brunner, E.J.; Miller, M.A.; Karanam, S.; McTernan, P.G.; Cappuccio, F.P.; Witte, D.R. Low serum adiponectin predicts 10-year risk of type 2diabetes and HbA1c independently of obesity, lipids, and inflammation: Whitehall II study. *Horm Metab Res*. **2009**, 41, 626–629.

64 Mattu, H.S.; Randeva, H.S. Role of adipokines in cardiovascular disease. *J Endocrinol.* **2013**, 216, 17–36.

65 Liao, L.M.; Schwartz, K.; Pollak, M.; Graubard, B.I.; Li, Z.; Ruterbusch, J.; Rothman, N.; Davis, F.; Wacholder, S.; Colt, J.; Chow, W.H.; Purdue, M.P. Serum Leptin and Adiponectin Levels and Risk of Renal Cell Carcinoma. *Obesity.* **2013**, 21, 1478–1485.

66 Arditi, J.D.; Venihaki, M.; Karalis, K.P.; Chrousos, G.P. Antiproliferative effect of adiponectin on MCF7 breast cancer cells: a potential hormonal link between obesity and cancer. *Horm Metab Res.* **2007**, 39, 9–13.

67 Fu, M.; Gong, D.W.; Damcott, C.; Sabra, M.; Yang, R.; Pollin, T. Systematic analysis of omentin 1 and omentin 2 on 1q23 as candidate genes for type 2 diabetes in the old order amish. *Diabetes*. **2004**, 53, 59.

68 Yang, R.Z.; Lee, M.J.; Hu, H.; Pray, J.; Wu, H.B.; Hansen, B.C.; Shuldiner, A.R.; Fried, S.K.; McLenithan, J.C.; Gong, D.W. Identification of omentin as a novel depot-specific adipokine in human adipose tissue: Possible role in modulating insulin action. *Am. J. Physiol. Metab.* **2006**, 290, 1253-1261.

69 de Souza Batista, C.M.; Yang, R.Z.; Lee, M.J.; Glynn, N.M.; Yu, D.Z.; Pray, J.; Ndubuizu, K.; Patil, S.; Schwartz, A.; Kligman, M,; Fried, S.K.; Gong, D.W.; Shuldiner, A.R.; Pollin, T.I.; McLenithanet, J.C. Omentin plasma levels and gene expression are decreased in obesity. *Diabetes.* **2007**, 56, 1655–1661.

70 Li, Z.G.; Zhao, D.; Xia, C.J.; Wang, T.N.; Liu, Y.P.; Zhang, Y.; Wang, B.J. Decreased synovial fluid omentin-1 concentrations reflect symptomatic severity in patients with knee osteoarthritis. *Scand. J. Clin. Lab. Investig*. **2012**, 72, 623-628.

71 Tan, B.K.; Pua, S.; Syed, F.; Lewandowski, K.C.; O'Hare, J.P.; Randeva, H.S. Decreased plasma omentin-1 levels in Type 1 diabetes mellitus. *Diabet. Med.* **2008**, 25, 1254–1255.

72 Yan, P.; Liu, D.; Long, M.; Ren, Y.; Pang, J.; Li, R. Changes of Serum Omentin Levels and Relationship between Omentin and Adiponectin Concentrations in Type 2 Diabetes Mellitus. *Exp. Clin. Endocrinol. Diabetes.* **2011,** 119, 257–263.

73 Wilms, B.; Ernst, B.; Gerig, R.; Schultes, B. Plasma omentin-1 levels are related to exercise performance in obese women and increase upon aerobic endurance training. *Exp Clin Endocrinol Diabetes.* **2015**, 123, 187-192.

74 Yamauchi, T.; Kamon, J.; Ito, Y.; Tsuchida, A.; Yokomizo, T.; Kita, S.; Sugiyama, T.; Miyagishi, M.; Hara, K.; Tsunoda, M.; Murakami, K.; Ohteki, T.; Uchida, S.; Takekawa, S.; Waki, H.; Tsuno, N.H.; Shibata, Y.; Terauchi, Y.; Froguel, P.; Tobe, K.; Koyasu, S.; Taira, K.; Kitamura, T.; Shimizu, T.; Nagai, R.; Kadowaki, T. Cloning of adiponectin receptors that mediate antidiabetic metabolic effects. *Nature*. **2003**, 423, 762-769.

75 Wiecek, A.; Adamczak, M.; Chudek, J. Adiponectin – an adipokine with unique metabolic properties. *Nephrol. Dial. Transplant.* **2007**, 22, 981–988.

76 Ouchi, N.; Kihara, S.; Arita, Y.; Maeda, K.; Kuriyama, H.; Okamoto, Y.; Hotta, K.; Nishida, M.; Takahashi, M.; Nakamura, T.; Yamashita, S.; Funahashi, T.; Matsuzawaet Y. Novel modulator for endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. *Circulation.* **1999**, 100, 2473–2476.

77 Ouchi N, Kihara S, Arita Y, Matsuyamaet, A.; Okamoto, Y.; Ishigami, M.; Kuriyama, H.; Kishida, K.; Nishizawa, H.; Hotta, K.; Muraguchi, M.; Ohmoto, Y.;Yamashita, S.; Funahashi, T.; Matsuzawa, Y. Adipocyte-derived plasma protein, adiponectin, suppresses lipid accumulation and class A scavenger receptor expression in human monocytederived macrophages. *Circulation*. **2001**, 103, 1057–1063.

78 Arita, Y.; Kihara, S.; Ouchi, N.; Maeda, K.; Kuriyama, H.; Okamoto, Y.; Kumada, M.; Hotta, K.; Nishida, M.; Takahashi, M.; Nakamura, T.; Shimomura, I.; Muraguchi, M.; Ohmoto, Y.; Funahashi, T.; Matsuzawa, Y.Adipocyte-derived plasma protein adiponectin acts as a platelet-derived growth factor- BB-binding protein and regulates growth factor-induced common postreceptor signal in vascular smooth muscle cell. *Circulation.* **2002**, 105, 2893–2898.

79 Fang, H.; Judd, R.L. Adiponectin Regulation and Function. *Society. Compr Physiol.* **2018**, 8, 1031-1063.

80 Yamauchi, T.; Kamon, J.; Waki, H.; Terauchi, Y.; Kubota, N.; Hara, K.; Mori, Y.; Ide, T.; Murakami, K.; Tsuboyama-Kasaoka, N.; Ezaki, O.; Akanuma, Y.; Gavrilova, O.; Vinson, C.; Reitman, M.L.; Kagechika, H.; Shudo, K.; Yoda, M.; Nakano, Y.; Tobe, K.; Nagai, R.; Kimura, S.; Tomita, M.; Froguel, P.; Kadowaki, T.The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. *Nat Med.* **2001**, 7, 941–946.

81 Supriya, R.; Tam, B.T.; Yu, A.P.; Lee, P.H.; Lai, C.W.; Cheng, K.K. Yau, S.Y.; Chan, L.W.; Yung, B.Y.; Sheridan, S.; Siu, P.M. Adipokines demonstrate the interacting influence of central obesity with other cardiometabolic risk factors of metabolic syndrome in Hong Kong Chinese adults. *PLoS One.* **2018**, 13, 8.

82 Meniailo, M.E.; Malashchenko, V.V.; Shmarov, V.A.; Gazatova, N.D.; Melashchenko, O.B.; Goncharov, A.G.; Seledtsova, G.V.; Seledtsov, V.I. Interleukin-8 favors pro-inflammatory activity of human monocytes/macrophages. *Int Immunopharmacol.* **2018**, 56, 217-221.

83 Bruun, J.M.; Pedersen, S.B.; Richelsen, B. Interleukin-8 production in human adipose tissue. Inhibitory effects of anti-diabetic compounds, the thiazolidinedione ciglitazone and the biguanide metformin. *Horm Metab Res.* **2000**, 32, 537–541.

84 Fain, J.N. Release of inflammatory mediators by human adipose tissue is enhanced in obesity and primarily by the nonfat cells: a review. *Mediators Inflamm.* **2010**, 2010, 513948.

85 Bruun, J.M.; Pedersen, S.B.; Richelsen, B. Regulation of interleukin 8 production and gene expression in human adipose tissue in vitro. *J Clin Endocrinol Metab.* **2001**, 86, 1267–1273.

86 Marques, P.; Collado, A.; Martinez-Hervás, S.; Domingo, E.; Benito, E.; Piqueras, L.; Real, J.T.; Ascaso, J.F.; Sanz, M.J. Systemic Inflammation in Metabolic Syndrome: Increased Platelet and Leukocyte Activation, and Key Role of CX3CL1/CX3CR1 and CCL2/CCR2 Axes in Arterial Platelet-Proinflammatory Monocyte Adhesion. *J Clin Med*. **2019**, 8, 708.

87 Mirhafez, S.R.; Tajfard, M.; Zarifian, A.; Movahedi, A.; Amiri, N.; Ghazizadeh, H.; Avan, A.; Ferns, G.A. Ghayour-Mobarhan M. Association between the serum concentrations of 12 cytokines and growth factors and metabolic syndrome in patients undergoing angiography. *Growth Factors.* **2019**, 37, 238-246.

88 Morrison, J.; Larsen, B.; Cox, A.J.; Minahan, C. The Post-Exercise Inflam-matory response to repeated-Sprint running in hypoxia. *J Sports SciMed* **2018**, 17, 533-538.

89 Frydelund-Larsen, L.; Penkowa, M.; Akerstrom, T.; Zankari, A.; Nielsen, S.; Pedersen, B.K. Exercise induces interleukin-8 receptor (CXCR2) expression in human skeletal muscle. *Experimental Physiology* **2007**, 92, 233-240.

90 Moldoveanu, A.I.; Shephard, R.J.; Shek, P.N. The cytokine response to physical activity and training. *Sports Med.* **2001,** 31, 115-44.

91 Suder, A. Body fatness and its social and lifestyle determinants in young working males from Cracow, Poland. *Journal of Biosocial Science.* **2009**, 41, 139-154.

92 Steckhan, N.; Hohmann, C.D.; Kessler, C.; Dobos, G.; Michalsen, A.; Cramer, H. Effects of different dietary approaches on inflammatory markers in patients with metabolic syndrome: A systematic review and meta-analysis. *Nutrition.* **2016,** 32, 338-348.

93 He, D.; Xi, B.; Xue, J.; Huai, P.; Zhang, M.; Liet, J. Association between leisure time physical activity and metabolic syndrome: A meta-analysis of prospective cohort studies. *Endocrine*. **2014**, 46, 231–240.

94 Edwardson, C.L.; Gorely, T.; Davies, M.J.; Gray, L.J.; Khunti, K.; Wilmot, E.G.; Yates, T.; Biddle, S.J.H. Association of sedentary behaviour with metabolic syndrome: A metaanalysis. *PLoS One* **2012**, 7, 34916.

95 Gonzalez-Gil, A.M.; Elizondo-Montemayor, L. The Role of Exercise in the Interplay between Myokines, Hepatokines, Osteokines, Adipokines, and Modulation of Inflammation for Energy Substrate Redistribution and Fat Mass Loss: A Review. *Nutrients.* **2020**, 12, 1899.

96 Turcotte, L.P.; Fisher, J.S. Skeletal muscle insulin resistance: Roles of fatty acid metabolism and exercise. *Phys. Ther.* **2008**, 88, 1279-1296.

97 Gleeson, M.; Bishop, N.C.; Stensel, D.J.; Lindley, M.R.; Mastana, S.S.; Nimmo, M.A. The anti-inflammatory effects of exercise: Mechanisms and implications for the prevention and treatment of disease. *Nat. Rev. Immunol.* **2011**, 11, 607-615.

98 Vincent, H.K.; Raiser, S.N.; Vincent, K.R. The aging musculoskeletal system and obesity-related considerations with exercise. *Ageing Research Reviews.* **2012**, 11, 361-373.

99 Villareal, D.; Aguirre, L.; Gurney, A.; Waters, D.; Sinacore, D.; Colombo, E.; Armamento-Villareal, R.; Qualls, C. Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults. *N Engl J of Med.* **2017**, 376, 1943-1955.

100 Jurca, R.; Lamonte, M.J.; Barlow, C.E.; Kampert, J.B.; Church, T.S.; Blair, S.N. Association of muscular strength with incidence of metabolic syndrome in men. Med and Sci in Sports and Exerc. **2005**, 37, 1849–1855.

101 Balducci, S.; Zanuso, S.; Nicolucci, A.; Fernando, F.; Cavallo, S.; Cardelli, P.; Fallucca, S.; Alessi, E.; Letizia, C.; Jimenez, A.; Fallucca, F.; Pugliese, G. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. *Nutr Metab Cardiovasc Dis.* **2010**, 20, 608-617.

102 Suder, A. Socioeconomic and lifestyle determinants of body fat distribution in young working males from Cracow, Poland. *American Journal of Human Biology,* **2008**, 20, 100-109.

103 Yu, N.; Ruan, Y.; Gao, X.; Sun, J. Systematic Review and Meta-Analysis of Randomized, Controlled Trials on the Effect of Exercise on Serum Leptin and Adiponectin in Overweight and Obese Individuals. *Horm. Metab. Res.* **2017**, 49, 164-173.

104 Golbidi, S.; Laher, I. Exercise induced adipokine changes and the metabolic syndrome. *J. Diabetes Res.* **2014,** 2014, 726861.

105 Das, D.K.; Graham, Z.A.; Cardozo, C.P. Myokines in skeletal muscle physiology and metabolism: Recent advances and future perspectives. *Acta Physiol. (Oxf.)* **2020,** 228, 13367.

106 Parameshwar, A.; Maiya, G.A.; Kamath, S.U.; Shastry, B.A.; Ravishankar. Lifestyle Modification with Physical Activity Promotion on Leptin Resistance and Quality of Life in Metabolic Syndrome - A Systematic Review with Meta-Analysis. *Curr Diabetes Rev.* **2021**, 17, 345-355.

107 Alberti, K.G.; Zimmet, P.; Shaw, J. Metabolic syndrome—A new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabet. Med.* **2006**, 23, 469-480.

108 Matsuhisa, M.; Yamasaki, Y.; Emoto, M.; Shimabukuro, M.; Ueda, S.; Funahashi, T.; Matsuzawa, Y. A novel index of insulin resistance determined from the homeostasis model assessment index and adiponectin levels in Japanese subjects. *Diabetes Res. Clin. Pract*. **2007**, 77, 151-154.

109 Khan, S.H.; Khan, A.N.; Chaudhry, N.; Anwar, R.; Fazal, N.; Tariq, M. Comparison of various steady state surrogate insulin resistance indices in diagnosing metabolic syndrome. *Diabetol Metab Syndr.* **2019**, 14, 11-44.

110 Katz, A.; Nambi ,S.S.; Mather, K.; Baron, A.D.; Follmann, D.A.; Sullivan, G.; Quon, M.J. Quantitative insulin sensitivity check index: A simple, accurate method for assessing insulin sensitivity in humans. *J. Clin. Endocrinol. Metab.* **2000**, 85, 2402-2410.

111 Craig, C.L.; Marshall, A.J.; Sjöström, M.; Bauman, A.E.; Booth, M.L.; Ainsworth, B.E.; Pratt, M.; Ekelund, U.; Yngve, A.; Sallis, J.F.; Pekka, O.J.A. International Physical Activity Questionnaire: 12-country reliability and validity. *Med. and Sci. in Sports and Exerci*. **2003**, 35, 1381-1395.

112 Garber, C.E.; Blissmer, B.; Deschenes, M.R.; Franklin, B.A.; Lamonte, M.J.; Lee, I.M.; Nieman, D.C.; Swain, D.P. American College of Sports Medicine. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med. Sci. Sports. Exerc.* **2011**, 43, 1334-1359.

113 Brzycki, M. Strength Testing—Predicting a One-Rep Max from Reps-to-Fatigue. *J. Phys. Educ. Recreat. Dance.* 1993, 64, 88-90.

114 Grgic, J.; Lazinica, B.; Schoenfeld, B.J.; Pedisic, Z. Test-Retest Reliability of the One-Repetition Maximum (1RM) Strength Assessment: a Systematic Review. *Sports Med. Open*. **2020**, 6, 31.

115 Ainsworth, B.E.; Haskell, W.L.; Herrmann, S.D.; Meckes, N.; Bassett, D.R.Jr.; Tudor-Locke, C.; Greer, J.L.; Vezina, J.; Whitt-Glover, M.C.; Leon, A.S. Compendium of Physical Activities: A second update of codes and MET values. *Med. Sci. Sports Exerc.* **2011**, 43, 1575–1581.

116 Fritz, C.O.; Morris, P.E.; Richler, J.J. Effect size estimates: Current use, calculations, and interpretation. *J. Exp. Psychol. Gen.* **2012**, 141, 2-18.

117 Bellicha, A.; van Baak, M.A.; Battista, F.; Beaulieu, K.; Blundell, J.E.; Busetto, L.; Carraça, E.V.; Dicker, D.; Encantado, J.; Ermolao, A.; Farpour-Lambert, N.; Pramono, A.; Woodward, E.; Oppert, J.M. Effect of exercise training on weight loss, body composition changes, and weight maintenance in adults with overweight or obesity: An overview of 12 systematic reviews and 149 studies. *Obes Rev.* **2021**, 4, 13256.

118 Vissers, D.; Hens, W.; Taeymans, J.; Baeyens, J.P.; Poortmans, J.; Van Gaal, L. The effect of exercise on visceral adipose tissue in overweight adults: a systematic review and meta-analysis. *PLoS One.* **2013**, 8, 56415.

119 Zierath, J.R.; Krook, A.; Wallberg-Henriksson, H. Insulin action and insulin resistance in human skeletal muscle. *Diabetologia* **2000**, 43, 821–835.

120 Achari, A.E.; Jain, S.K. Adiponectin, a Therapeutic Target for Obesity, Diabetes, and Endothelial Dysfunction. *Int. J. Mol. Sci.* **2017**, 18, 1321.

121 Sethi, J.K.; Vidal-Puig, A.J. Thematic review series: Adipocyte biology. Adipose tissue function and plasticity orchestrate nutritional adaptation. *J. Lipid Res.* **2007**, 48, 1253-1262.

122 Paz, K.; Hemi, R.; LeRoith, D.; Karasik, A.; Elhanany, E.; Kanety, H.; Zick, Y. A molecular basis for insulin resistance. Elevated serine/threonine phosphorylation of IRS-1 and IRS-2 inhibits their binding to the juxtamembrane region of the insulin receptor and impairs their ability to undergo insulin-induced tyrosine phosphorylation. *J. Biol. Chem.* **1997**, 272, 29911-29918.

123 Shulman, G.I. Cellular mechanisms of insulin resistance. *J. Clin. Investig.* **2000**, 106, 171-176.

124 Clarkson, P.M. Eccentric exercise and muscle damage. *Int. J. Sport. Med.* **1997**, 4, 314-317.

125 Huh, J.Y.; Dincer, F.; Mesfum, E.; Mantzoros, C.S. Irisin stimulates muscle growth-related genes and regulates adipocyte differentiation and metabolism in humans. *Int. J. Obes.* **2014**, 38, 1538-1544.

126 Huh, J.Y.; Mougios, V.; Kabasakalis, A.; Fatouros, I.; Siopi, A.; Douroudos, I.; Filippaios, A.; Panagiotou, G.; Park, K.H.; Mantzoros, C.S. Exercise-induced irisin secretion is independent of age or fitness level and increased irisin may directly modulate muscle metabolism through AMPK activation. *J. Clin. Endocrinol. Metab.* **2014**, 99, 2154-2161.

127 Gannagé-Yared, M.H.; Khalife, S.; Semaan, M.; Fares, F.; Jambart, S.; Halaby, G. Serum adiponectin and leptin levels in relation to the metabolic syndrome, androgenic profile and somatotropic axis in healthy non-diabetic elderly men. *Eur. J. Endocrinol.* **2006**, 155, 167-176.

128 Tambalis, K.; Panagiotakos, D.B.; Kavouras, S.A.; Sidossis, L.S. Responses of blood lipids to aerobic, resistance, and combined aerobic with resistance exercise training: A systematic review of current evidence. *Angiology* **2009**, 60, 614-632.

129 Kelley, G.A.; Kelley, K.S. Impact of progressive resistance training on lipids and lipoproteins in adults: A meta-analysis of randomized controlled trials. *Prev. Med.* **2009**, 48, 9-19.

130 Zając-Gawlak, I.; Pelclová, J.; Groffik, D.; Přidalová, M.; Nawrat-Szołtysik, A.; Kroemeke, A.; Gába, A.; Sadowska-Krępa, E. Does physical activity lower the risk for metabolic syndrome: A longitudinal study of physically active older women. *BMC Geriatr.* **2021**, 21, 11.

131 Gordon, B.; Chen, S.; Durstine, J.L. The effects of exercise training on the traditional lipid profile and beyond. *Curr. Sports Med. Rep.* **2014**, 13, 253-259.

132 Mensink, R.P.; Zock, P.L.; Kester, A.D.; Katan, M.B. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: A meta-analysis of 60 controlled trials. *Am. J. Clin. Nutr.* **2003**, 77, 1146-1155.

133 Steensberg, A.; van Hall, G.; Osada, T.; Sacchetti, M.; Saltin, B.; Klarlund Pedersen, B. Production of interleukin-6 in contracting human skeletal muscles can account for the exercise-induced increase in plasma interleukin-6. *J. Physiol*. **2000**, 529, 237-242.

134 Więcek, M.; Szymura, J.; Maciejczyk, M.; Kantorowicz, M.; Szygula, Z. Acute Anaerobic Exercise Affects the Secretion of Asprosin, Irisin, and Other Cytokines- A Comparison Between Sexes. *Front. Physiol.* **2018**, 9, 1782.

135 Kraemer, R.; Shockett, P.; Webb, N.; Shah, U.; Castracane, V.A. Transient Elevated Irisin Blood Concentration in Response to Prolonged, Moderate Aerobic Exercise in Young Men and Women. *Horm. Metab. Res.* **2013**, 46, 150–154.

136 Löffler, D.; Müller, U.; Scheuermann, K.; Friebe, D.; Gesing, J.; Bielitz, J.; Erbs, S.; Landgraf, K.; Wagner, I.V.; Kiess, W.; et al. Serum Irisin Levels Are Regulated by Acute Strenuous Exercise. *J. Clin. Endocrinol. Metab.* **2015**, 100, 1289-1299.

137 Daskalopoulou, S.S.; Cooke, A.B.; Gomez, Y.H.; Mutter, A.F.; Filippaios, A.; Mesfum, E.T.; Mantzoros, C.S. Plasma irisin levels progressively increase in response to increasing exercise workloads in young, healthy, active subjects. *Eur. J. Endocrinol.* **2014**, 171, 343-352.

138 Kazeminasab, F.; Sadeghi, E.; Afshari-Safavi, A. Comparative Impact of Various Exercises on Circulating Irisin in Healthy Subjects: A Systematic Review and Network Meta-Analysis. *Oxidative Med. Cell. Longev.* **2022**, 22, 8235809.

139 Cosio, P.L.; Crespo-Posadas, M.; Velarde-Sotres, Á.; Pelaez, M. Effect of Chronic Resistance Training on Circulating Irisin: Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Int. J. Environ. Res. Public Health.* **2021**, 18, 2476.

140 Qiu, S.; Cai, X.; Sun, Z.; Schumann, U.; Zügel, M.; Steinacker, J.M. Chronic Exercise Training and Circulating Irisin in Adults: A Meta-Analysis. *Sports Med.* **2015**, 45, 1577-1588.

141 Rodrigues, A.C.; Ferreira, E.F.; Carneiro-Júnior, M.A.; Natalia, A.J.; Bressanc, J. Effects of exercise on the circulating concentrations of irisin in healthy adult individuals: A review. *Sci. Sports* **2016**, 31, 251-260.

142 Kraemer, R.R.; Chu, H.; Castracane, V.D. Leptin and exercise. *Exp Biol Med.* **2002**, 227, 701-708.

143 Shand, B.; Elder, P.; Scott, R.; Frampton, C.; Willis, J. Biovariability of plasma adiponectin. *Clin Chem Lab Med.* **2006**, 44, 1264-1268.

144 Hotamisligil, G.S. Inflammation and metabolic disorders. *Nature* **2006**, 444, 860-867.

145 Scheja, L.; Heeren, J. The endocrine function of adipose tissues in health and cardiometabolic disease. *Nat. Rev. Endocrinol.* **2019**, 15, 507-524.

146 Raschke, S.; Eckel, J. Adipo-myokines: Two sides of the same coin-mediators of inflammation and mediators of exercise. *Mediat. Inflamm.* **2013**, 2013, 320724.

147 Polyzos, S.A.; Anastasilakis, A.D.; Efstathiadou, Z.A.; Makras, P.; Perakakis, N.; Kountouras, J.; Mantzoros, C.S. Irisin in metabolic diseases. *Endocrine* **2018**, 59, 260-274.

148 Izquierdo, A.G.; Crujeiras, A.B.; Casanueva, F.F.; Carreira, M.C. Leptin, Obesity, and Leptin Resistance: Where Are We 25 Years Later? *Nutrients* **2019**, 8, 2704.

149 Obradovic, M.; Sudar-Milovanovic, E.; Soskic, S.; Essack, M.; Arya, S.; Stewart, A.J.; Gojobori, T.; Isenovic, E.R. Leptin and Obesity: Role and Clinical Implication. *Front. Endocrinol.* **2021**, 12, 585887.

150 Klempel, M.C.; Varady, K.A. Reliability of leptin, but not adiponectin, as a biomarker for diet-induced weight loss in humans. *Nutr. Rev.* **2011**, 69, 145-154.

151 Venojärvi, M.; Wasenius, N.; Manderoos, S.; Heinonen, O.J.; Hernelahti, M.; Lindholm, H.; Surakka, J.; Lindström, J.; Aunola, S.; Atalay, M.; et al. Nordic walking decreased circulating chemerin and leptin concentrations in middle-aged men with impaired glucose regulation. *Ann. Med.* **2013**, 45, 162-170.

152 Cénat, J.M.; Blais-Rochette, C.; Kokou-Kpolou, C.K.; Noorishad, P.G.; Mukunzi, J.N.; McIntee, S.E.; Dalexis, R.D.; Goulet, M.A.; Labelle, P.R. Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: A systematic review and meta-analysis. *Psychiatry Res.* **2021**, 295, 113599.

153 Lin, J.; Jiang, Y.; Wang, G.; Meng, M.; Zhu, Q.; Mei, H.; Liu, S.; Jiang, F. Associations of short sleep duration with appetite-regulating hormones and adipokines: A systematic review and meta-analysis. *Obes. Rev*. **2020**, 21, 13051.

154 Bouillon-Minois, J.B.; Trousselard, M.; Thivel, D.; Benson, A.C.; Schmidt, J.; Moustafa, F.; Bouvier, D.; Dutheil, F. Leptin as a Biomarker of Stress: A Systematic Review and Meta-Analysis. *Nutrients* **2021**, 13, 3350.

155 Klimcakova, E.; Polak, J.; Moro, C.; Hejnova, J.; Majercik, M.; Viguerie, N.; Berlan, M.; Langin, D.; Stich, V. Dynamic strength training improves insulin sensitivity without altering plasma levels and gene expression of adipokines in subcutaneous adipose tissue in obese men. *J. Clin. Endocrinol. Metab.* **2006**, 91, 5107-5112.

156 Monzillo, L.U.; Hamdy, O.; Horton, E.S.; Ledbury, S.; Mullooly, C.; Jarema, C.; Porter, S.; Ovalle, K.; Moussa, A.; Mantzoros, C.S. Effect of lifestyle modification on adipokine levels in obese subjects with insulin resistance. *Obes. Res.* **2003**, 11, 1048-1054.

157 Saremi, A.; Asghari, M.; Ghorbani, A. Effects of aerobic training on serum omentin-1 and cardiometabolic risk factors in overweight and obese men. *J. Sports Sci.* **2010**, 28, 993–998.

158 Puglisi, M.J.; Fernandez, M.L. Modulation of C-reactive protein, tumor necrosis factor-alpha, and adiponectin by diet, exercise, and weight loss. *J. Nutr.* **2008**, 138, 2293-2296.

159 Belza, A.; Toubro, S.; Stender, S.; Astrup, A. Effect of diet-induced energy deficit and body fat reduction on high-sensitive CRP and other inflammatory markers in obese subjects. *Int. J. Obes.* **2009**, 33, 456-464.

160 Moreno-Navarrete, J.M.; Catalán, V.; Ortega, F.; Gómez-Ambrosi, J.; Ricart, W.; Frühbeck, G.; Fernández-Real, J.M. Circulating omentin concentration increases after weight loss. *Nutr. Metab.* **2010**, 7, 27.

161 Esposito, K.; Pontillo, A.; Di Palo, C.; Giugliano, G.; Masella, M.; Marfella, R.; Giugliano, D. Effect ofweight loss and lifestyle changes on vascular inflammatory markers in obese women: A randomized trial. *JAMA* **2003**, 289, 1799-1804.

162 Chan, D.C.; Watts, G.F.; Ng, T.W.; Yamashita, S.; Barrett, P.H. Effect of weight loss on markers of triglyceride-rich lipoprotein metabolism in the metabolic syndrome. *Eur. J. Clin. Investig*. **2008**, 38, 743-751.

163 Larrouy, D.; Barbe, P.; Valle, C.; Déjean, S.; Pelloux, V.; Thalamas, C.; Bastard, J.P.; Le Bouil, A.; Diquet, B.; Clément, K.; Langin, D.; Viguerie, N. Gene expression profiling of human skeletal muscle in response to stabilized weight loss. *Am. J. Clin. Nutr.* **2008**, 88, 125-132.

164 Claessens, M.; van Baak, M.A.; Monsheimer, S.; Saris, W.H. The effect of a low-fat, high-protein or high-carbohydrate ad libitum diet on weight loss maintenance and metabolic risk factors. Int. *J. Obes.* **2009**, 33, 296-304.

165 Becic, T.; Studenik, C.; Hoffmann, G. Exercise Increases Adiponectin and Reduces Leptin Levels in Prediabetic and Diabetic Individuals: Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Med. Sci.* **2018**, 30, 97.

166 Hayashino, Y.; Jackson, J.L.; Hirata, T.; Fukumori, N.; Nakamura, F.; Fukuhara, S.; Tsujii, S.; Ishii, H. Effects of exercise on C-reactive protein, inflammatory cytokine and adipokine in patients with type 2 diabetes: A meta-analysis of randomized controlled trials. *Metabolism* **2014**, 63, 431-440.

167 Alizaei Yousefabadi, H.; Niyazi, A.; Alaee, S.; Fathi, M.; Mohammad Rahimi, G.R. Anti-Inflammatory Effects of Exercise on Metabolic Syndrome Patients: A Systematic Review and Meta-Analysis. *Biol. Res. Nurs.* **2021**, 23, 280-292.

168 Fuentes, G.C.; Castañer, O.; Warnberg, J.; Subirana, I.; Buil-Cosiales, P.; Salas-Salvadó, J.; Corella, D.; Serra-Majem, L.; Romaguera, D.; Estruch, R.; Martínez J.A., Pintó, X.; Vázquez, C.; Vidal, J.; Tur, J.A.; Arós, F.; Bullo, M.; Fitó, M.; Schröder, H. Prospective association of physical activity and inflammatory biomarkers in older adults from the PREDIMED-Plus study with overweight or obesity and metabolic syndrome. *Clin. Nutr.* **2020**, 39, 3092-3098.

169 Bruun, J.M.; Lihn, A.S.; Madan, A.K.; Pedersen, S.B.; Schiott, K.M.; Fain, J.N.; Richelsen, B. Higher production of IL-8 in visceral vs. subcutaneous adipose tissue. Implication of nonadipose cells in adipose tissue. *Am. J. Physiol. Endocrinol. Metab.* **2004**, 286, 8-13.

170 Yang, M.; Liu, S.; Zhang, C. The Related Metabolic Diseases and Treatments of Obesity. *Healthcare* **2022**, 10, 1616.

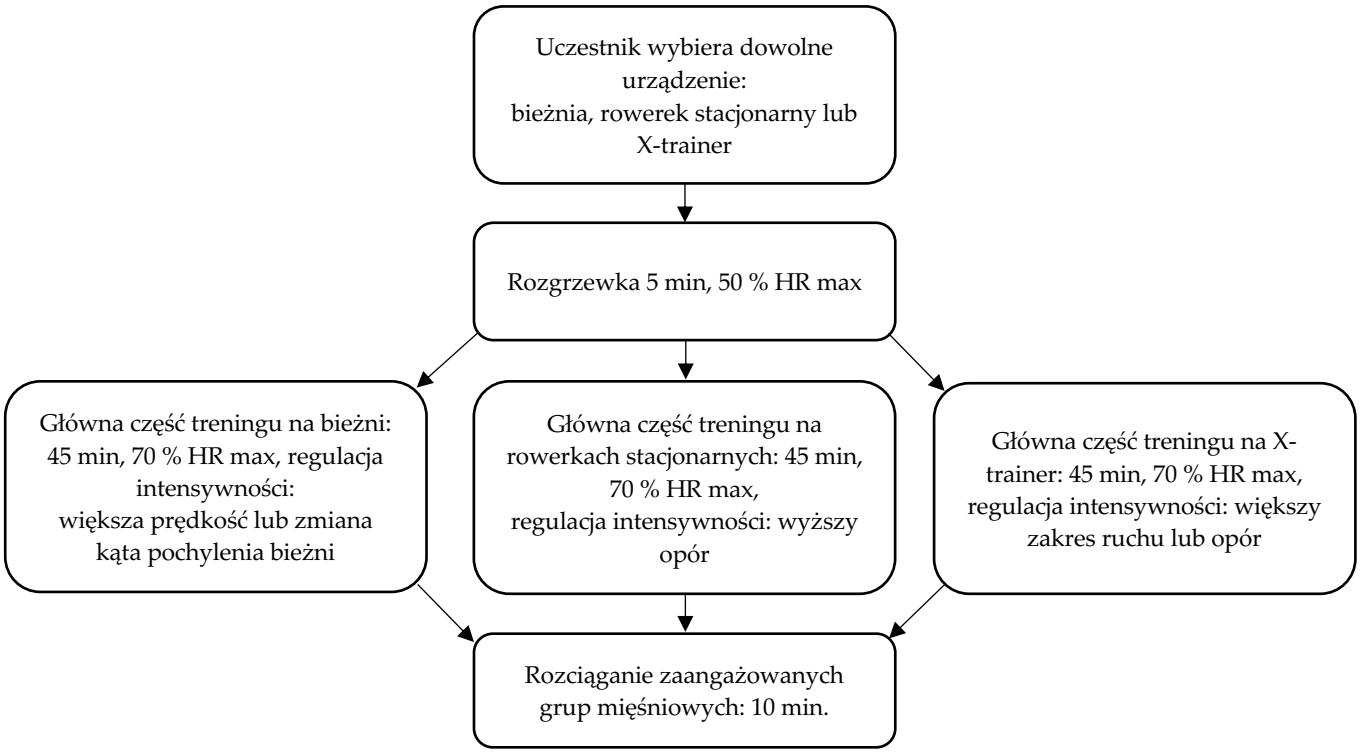
171 Smirmaul B.P., Bertucci D.R., Teixeira I.P. Is the VO2max that we measure really maximal? *Front. Physiol.* **2013**, 5, 4-203.

**Tabela S1. Kompleksowa strategia łączenia programu treningu aerobowego i oporowego przeznaczona dla grupy wykonującej ćwiczenia aerobowo-oporowe (EG2).**

| | **Treningi 1-3** | **Treningi 4-6** | **Treningi 6<** |
|---|---|---|---|
| Rodzaj treningu | Trening całego ciała | Trening partii antagonistycznych | Trening partii antagonistycznych |
| Objętość treningu oporowego [liczba ćwiczeń x liczba serii x liczba powtórzeń] | 3 x 4 x 15 | 6 x 3 x 12 | 9 x 3 x 12 |
| Intensywność treningu oporowego [% 1 RM] | 50 | 70 | 70 |
| Przerwa pomiędzy seriami [min] | 2 | 1.5 | 1 |
| Czas treningu oporowego [min] | 30 | 35 | 40 |
| Czas treningu aerobowego [min] | 20 | 15 | 10 |
| Intensywność treningu aerobowego [% HR max] | 50 | 70 | 70 |
| Ćwiczenia specjalistyczne | Wiosłowanie sztangielką jednorącz,<br>Pompki w odciążeniu (maszyna Smitha),<br>Przysiady w odciążeniu (trzymając się za sztangę)<br>Podpór przodem (plank) | Wyciskanie sztangielek stojąc<br>Wyciskanie sztangi leżąc<br>Ściąganie drążka do klatki piersiowej<br>Prostowanie biodra w pozycji leżącej<br>Wiosłowanie sztangielkami | Martwy ciąg ze sztangielkami<br>Prostowanie przedramion z linkami<br>Uginanie przedramion ze sztangielkami stojąc |

HR max – maksymalna częstość skurczów serca , 1RM – maksimum jednego powtórzenia.

**Rycina S1. Kompleksowa strategia programu aerobowego przeznaczona dla grupy wykonującej treningi aerobowe (EG1).**




HR max – maksymalna częstość skurczów serca.

**Tabela S2. Progresja obciążeń w wybranych ćwiczeniach oporowych podczas interwencji oraz follow up w grupie interwencyjnej EG2.**

| Moment obserwacji | Wyciskanie sztangi leżąc | Ściąganie drążka do klatki piersiowej | Przysiad front z kettlami | Suma obciążeń z 3 ćwiczeń | p-value |
|---|---|---|---|---|---|
| Po 6 tyg. | 15,32 % | 11,76 % | 16,77 % | 15,50 % | 0.00* |
| Po 12 tyg. | 23,84 % | 23,02 % | 25,41 % | 24,35 % | 0.00* |
| Po 16 tyg. | 26,92 % | 25,70 % | 26,30 % | 26,50 % | 0.00* |

p-value – test ANOVA

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# Effect of Exercise Interventions on Irisin and Interleukin-6 Concentrations and Indicators of Carbohydrate Metabolism in Males with Metabolic Syndrome

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**Abstract:** Irisin (IR) is a biomarker that is associated with metabolic syndrome (MetS). However, the available evidence on the association of IR, physical activity, and MetS status are contradictory. Therefore, the present study aimed to investigate the effect of exercise intervention on IR and interleukin-6 (IL-6) levels and indicators of carbohydrate metabolism in males with MetS. The study included 62 males with MetS (age 36.6 ± 6.9 years, BMI 33.6 ± 4.4 kg/m$^2$) randomly assigned to: examined group 1 (EG1, n = 21) with aerobic exercise intervention, examined group 2 (EG2, n = 21) with combined aerobic and resistance exercise intervention, both for 12 weeks, and the control group (CG, n = 20) without intervention. Anthropometric measurements, body composition (body fat [BF], fat free mass [FFM]) as well as a biochemical blood analysis (irisin [IR], interleukin-6 [IL-6], insulin [INS] and glucose [GL]) were performed at baseline, 6 and 12 weeks of intervention, and 4 weeks after ending the intervention (follow-up). Intergroup and intragroup comparisons were performed. In EG1, an increase in IR level was observed as well as decreases in IL-6, BF, and GL levels in relation to the initial measurement. In EG2, decreases in IL-6, BF, and INS levels were observed as well as an increase in FFM level. In CG, no changes were found. Aerobic-resistance exercise led to a greater reduction in the concentrations of IL-6 and INS and more favorable changes in body composition (BF and FFM) than the use of aerobic training alone in males with MetS.

**Keywords:** irisin; interlekin-6; exercise; metabolic syndrome; obesity; physical activity



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## 1. Introduction

Metabolic syndrome (MetS) is characterized by the occurrence of a few mutually connected disorders of metabolic character, including insulin resistance, atherogenic dyslipidemia, visceral obesity, and hypertension. MetS is also linked with chronic inflammation of low intensity. Untreated MetS is related to increased risk of developing diabetes and cardiovascular diseases (CVD) [1].

The pathophysiology of MetS comprises several complex mechanisms that have not been fully explained. MetS can be caused by genetic and epigenetic determinants [2]. The development of MetS is enhanced by a lifestyle combining a low level of physical activity with a high dietary intake of energy that exceeds the needs of the organism [3–5].

It has been demonstrated that myokines such as irisin (IR) and interleukin 6 (IL-6) are released through skeletal muscles during physical activity. They induce positive physiological and metabolic effects not only in skeletal muscle but also in distant tissues,

such as white adipose tissue, the liver, bones, immune system cells, and the central nervous system, thus decreasing inflammation, improving the sensitivity of cells to insulin, and correcting energy expenditure [6–8].

IR is a myokine produced mainly in skeletal muscle during physical effort, and, to a lesser extent, by white adipose tissue [9]. In mice, IR originating from muscle accounts for ~72% of the total level of the hormone in circulation, and the remaining 28% probably originates in adipose tissue [10]. The main effect of IR is the browning of white adipose tissue, an increase of energy expenditure of the body, improvement of cell sensitivity to INS, and body mass reduction [11]. IR stimulates lipolysis and increases the release of GL and free fatty acids during physical activity [12]. Higher concentrations of IR are observed in obese patients [13]. Moreover, IR positively affects lipid disorders that result from obesity and MetS [14]. In a meta-analysis of 18 studies, higher concentrations of IR were registered in overweight or obese people in relation to people with proper body weight, which can be explained by the phenomenon of 'IR resistance' [15]. A similar process has been observed in patients with MetS [16]. The application of resistance training leads to a higher production of IR than moderate intensity training or interval exercises of high intensity. The increase in IR production is detectable immediately after the beginning of training and its stabilization takes place up to one hour after the exercise is finished. The presented dependencies relate both to people with MetS and healthy individuals [17].

IL-6 is a cytokine of which increased concentrations secreted by adipocytes and monocytes are thought to be responsible for inflammation and INS resistance in obesity. However, it was demonstrated that IL-6 released by skeletal muscle features an anti-inflammation effect and increases sensitivity to INS [18]. The concentrations of IL-6 and IR and parameters of carbohydrate metabolism, such as HOMA, were dependent on the level of adipose tissue and increased with the degree of obesity in examined patients [19]. The production of IL-6 is related to the level of glycogen and the intensity and duration of physical activity [20]. The increase in IL-6 level can be higher after moderate intensive exercises with long duration (i.e., running), which engage many muscle parties, than after isolated resistance training [21].

Physical activity leads to many endocrine interactions between skeletal muscles, adipose tissue, and other organs of internal secretion. The introduction of regular physical activity results in changes in the concentrations of circulating myokines, adipokines, and immunological cytokines and the subsequent reduction of body mass, a decrease in the inflammatory condition, INS resistance, and other disorders associated with MetS [22–24]. Aerobic training leads to a significant increase in energy expenditure and creates advantageous conditions to decrease excessive adipose tissue mass, whereas resistance training is of significant importance to increasing fat free body mass, which results in higher INS sensitivity and efficiency in maintaining and increasing the resting metabolic rate [25]. The introduction of regular resistance exercises combined with endurance exercises prevents the recurrence of obesity [25] and improves indices of MetS [26].

The significant role of physical training in improving health conditions can result in a decrease of IR and IL-6 concentrations in people with MetS. The applied training may cause a decrease in the visceral fat level and improvement of MetS parameters. Knowledge of the differences and benefits of applied training may allow males with MetS to choose the most favorable form of intervention to improve their health. The aim of this research was to assess the effects of twelve weeks of two different exercise interventions (training of an aerobic character vs. combined aerobic-resistance training) and four weeks of follow-up on the concentrations of IR and IL-6 in males with MetS. We hypothesized that combined aerobic-resistance exercise intervention would positively affect the secretion of adipocytokines while having anti-inflammatory effects in males with MetS.

## 2. Materials and Methods

### 2.1. Materials

The study design was a prospective, randomized, and controlled trial to investigate the effects of two types of twelve-week exercise intervention (training of an aerobic character vs. combined aerobic-resistance training) on body composition, levels of selected adipokines, and indices of metabolic syndrome (MetS) in males with MetS in relation to males with MetS who did not participate in training (control group, CG). The examined participants from all three groups were then observed for a four-week follow-up period (without scheduled training).

Due to the character of the intervention, a blind trial was not applied; however, the lab personnel, biostatistician, and analysis team were not aware of the group assignments. The studies were registered in the clinical trials registry on the ANZCTR platform (Australian New Zealand Clinical Trials Registry): ACTRN registration number 12622001394730. The course of the study is presented in Figure 1.

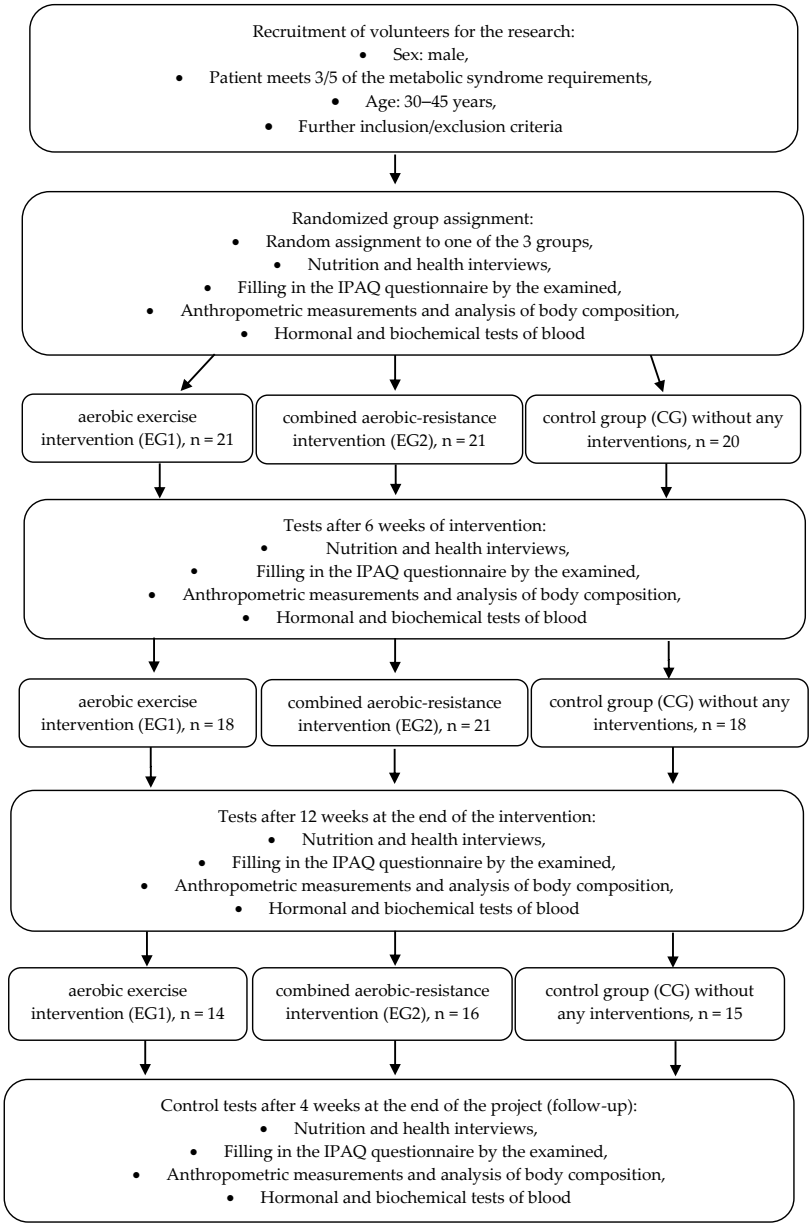


**Figure 1.** The course of the study.

The study included 62 Caucasian males aged 30–45 (mean age 37 ± 7) years with waist circumferences ≥ 94 cm (visceral obesity is a prerequisite for the diagnosis of MetS) and with two out of four criteria of MetS: concentration of triglycerides > 150 mg/dL (1.7 mmol/L) or hypertriglyceridemia under treatment; concentration of HDL C < 40 mg/dL (1.03 mmol/L) or this lipid disorder under treatment; systolic blood pressure (SBP) ≥ 130 mm Hg or diastolic (DBP) ≥ 85 mm Hg, or treatment of formerly diagnosed hypertension; fasting level of GL in blood plasma ≥ 100 mg/dL (5.6 mmol/L) or pharmacological treatment of diabetes type 2 (IDF, International Diabetes Federation, 2006 [27]). The participants were assigned randomly into 3 groups; qualification was based on simple randomization following sealed opaque envelopes:

1. Experimental group 1 (EG1) of males with MetS (n = 21) performing aerobic exercise intervention;
2. Experimental group 2 (EG2) of males with MetS (n = 21) performing combined aerobic-resistance exercise intervention;
3. Control group (CG) of males with MetS (n = 20) not undertaking any physical activity.

The study inclusion criteria were: male aged 30–45 years, medical statement on lack of contraindications to take up health training of aerobic-resistance character, written consent for voluntary participation in the research project, waist circumference ≥ 94 cm, and two criteria out of the following: concentration of triglycerides > 150 mg/dL (1.7 mmol/L) or treated hypertriglyceridemia; concentration of HDL C < 40 mg/dL (1.03 mmol/L) or treatment of the lipid disorder; blood pressure systolic (SBP) ≥ 130 mm Hg or diastolic (DBP) ≥ 85 mm Hg, or treatment of formerly diagnosed hypertension; GL level in plasma on empty stomach ≥ 100 mg/dL (5.6 mmol/) or pharmacological treatment of type 2 diabetes (T2DM). In EG1, the presence of chronic diseases was confirmed, such as: hypertriglyceridemia (8 people), arterial hypertension (12), hypercholesterolemia (4), T2DM (5), chronic sinusitis (1), gout (2), and psoriasis (2). Chronic diseases were confirmed in EG2: hypertriglyceridemia (13), arterial hypertension (15), hypercholesterolemia (9), T2DM (2), and gout (1). In CG, the following chronic diseases were confirmed: hypertriglyceridemia (13), arterial hypertension (15), hypercholesterolemia (5), T2DM (4), and chronic sinusitis (1).

The exclusion criteria were: no medical statement on lack of contraindications to take up health training of aerobic-resistance character, unwillingness to continue intervention (more than 10% of training sessions missed), unstable ischaemia, decompensated heart failure, uncontrolled heart rhythm disorder, severe pulmonary hypertension (mean blood pressure in lungs > 55 mm Hg), symptomatic aortic stenosis, acute myocarditis, endocarditis or pericarditis, uncontrolled blood pressure (>180/110 mm Hg), aortic dissection, Marfan syndrome, uncontrolled diabetes, mental disorders, health problems (orthopedic, neurologic) preventing movement, participation in another form of physical activity during the project, and lack of written consent to take part in the examination.

The volunteers were informed about the procedures and purpose of the research in detail and about the possibility of resigning from participation at any stage. During the period of intervention, there were resignations from the study. The reasons for excluding a participant from the project included: absenteeism at more than 10% (6), excessive alcohol consumption (2), absence during control visits (3), and occurrence of COVID-19 symptoms (3). The number of participants required to show statistical significance was based on previously published studies in this field. An error probability ($\alpha$) of 0.05, power ($1 - \beta$) of 0.80, and an average effect size (d) of 0.8 were used to calculate the sample size. All the examined participants were asked not to alter their nutritional habits, taken medicines, or level of physical activity during the observation. All volunteers provided written consent for participation in the study, as well as for the use of their personal data and research results for scientific purposes. The research project obtained the approval of the Ethics Committee of the Regional Medical Chamber in Krakow (90/KBL/OK/2020).

### 2.2. Methods

For all participants, he following assessments were performed 4 times: before the intervention, in the middle after 6 weeks of intervention, after 12 weeks of intervention, and 4 weeks after ending the intervention (follow-up period):

#### 2.2.1. Anthropometry

For the purpose of this study, body height (BH) [cm], body mass (BM) [kg], and waist circumference (WC) [cm] were used. BH was measured to the nearest 1 mm, in a standing position without shoes, with the head in the Frankfurt plane, using a stadiometer (Seca 231 stadiometer, Hamburg, Germany). BM was obtained in the standing position using a standardized medical scale (Beurer PS 240, Budapest, Hungary), with an accuracy of 50 g. WC was measured to the nearest 1 mm using an anthropometric tape between the lower edge of the costal arch and the upper edge of the iliac crest, with the participant in standing position, and recorded at the end of a gentle expiration.

#### 2.2.2. Body Composition

Dual-Energy X-ray Absorptiometry (DEXA] was applied to assess body composition: percentage of body fat (BF) [%], fat free mass (FFM) [kg], and body mass index (BMI) [kg/m$^2$].

Assessment of body composition was carried out using the Lunar Prodigy Primo PR+352163 (Chicago, IL, USA) device according to the manufacturer's guidelines.

#### 2.2.3. Hormonal Blood Indices

Fasting blood samples were collected in the morning after a 24-h break from training, from the basilic, cephalic, or median cubital vein into test tubes (Vacumed® system, F.L. Medical, Torreglia, Italy) by the experienced nursing team. The collected blood was centrifuged (RCF 1000× *g*) immediately after collection for 15 min at 4 °C (MPW-351R, MPW Med. Instruments, Warsaw, Poland), and the serum was collected and stored at −80 °C until further study (BIO Memory 690L, Froilabo, Paris, France).

The concentrations of IR and IL-6 were measured using commercially available ELISA kits according to the manufacturer's protocol. The human IR ELISA Kit (catalogue number 201-12-5328) was purchased from Shanghai Sunred Biological Technology Co. (Shanghai, China). The IL-6 ELISA kit (catalogue number IL E-3200IL-6) was purchased from LDN Labor Diagnostika Nord GmbH & Co.KG (Am Eichenhain, Germany). An ELx 808 spectrophotometric microplate reader (BioTek, Winooski, VT, USA) was used to determine the optical density at 450 nm. Marking was performed at the Laboratory of Genetics and Molecular Biology, Department of Physiology, Jagiellonian University Medical College, Kraków, Poland.

#### 2.2.4. Biochemical Blood Indices

The concentration of GL [mmol/L] in the blood plasma was performed via the enzymatic method using the Cobas c701/702 biochemical analyzer (Roche Diagnostics International Ltd., Mannheim, Germany). The serum insulin [μIU/mL] concentration was determined by electrochemiluminescence (ECLIA) using the Cobas e801 apparatus (Roche Diagnostics International Ltd., Mannheim, Germany). The determinations were performed according to manufacturer's guidelines with the use of reagents dedicated to the GLUC3 and Elecsys Insulin analyzers, respectively.

#### 2.2.5. Evaluation of Energy Expenditure and Energy Value of Diet

The International Physical Activity Questionnaire (IPAQ) was conducted to assess daily energy expenditures [28]. The total energy expenditure [kcal/week) was calculated based on the sum of non-exercise activity thermogenesis (NEAT) assessed based on the IPAQ questionnaire and energy expenditures connected with intervention in groups EG1 and EG2.

A qualified dietician carried out a 24-h nutrition interview using a nutrition record to quantitatively assess nutrition habits and monitor alterations in the diet during training. The results were introduced into the DietaPro program version 4.0 (Institute of Food and Nutrition, Warsaw, Poland). The energy value of the diet was assessed as kcal/week.

### *2.3. Exercise Interventions*

The exercise interventions took place at a fitness club in Cracow under supervision of a personal coach. All of the training was carried out at the same time of day (evening, 6–9 pm) by the same personal coach, in a room with the same temperature (22 degrees Celsius) and humidity. A session attendance checklist was used to monitor adherence to the intervention. Examined participants who attended less than 90% of the training sessions for 12 weeks were eliminated from the observation and statistics.

Planning and monitoring of the intensity of the aerobic training as well as the amount of load in the resistance training was set individually based on the guidelines of the American College of Sports Medicine [29]. Heart rate (HR) during training was monitored using the Polar M200 GPS Running Watch with Wrist-Based Heart Monitor (Kempele, Finland). Before the resistance training, the One Repetition Maximum (1 RM) was determined. The examined participants underwent the 1 RM test before the examination, and after 6, 12, and 16 weeks. The personal coach carried out the warm-up on the treadmill (Technogym New Excite Run Now 500, Cesena, Italy) for 5 min at 60% HR. Next, the participant started resistance training. The last repetition of a series occurred when the participant could not continue to exercise maintaining the proper technique. The obtained load and number of repetitions were converted into 1 RM based on the 1 RM calculator [30].

The aim of the intervention was to realize 3 training sessions per week, which were converted into 3 × 6 MET of energy expenditure for a week interchangeable with running, and 3 × 5.5 MET for resistance training (Compendium of Physical Activities, 2011) [31].

#### 2.3.1. Aerobic Training

The course of the aerobic intervention: training sessions took place 3 times per week in groups of max 5 participants, starting with a 5-min warm-up (treadmill walk, Technogym New Excite Run Now 500, Cesena, Italy), reaching 50% maximal heart rate (HR max). After the warm-up, the participants increased intensity to 70% HR max, based on increasing velocity or angle for a tread-mill, resistance for upright bikes (Technogym Artis, Cesena, Italy), and range of movement or resistance for an x-trainer (Precor EFX556i Elipsa, Woodinville, WA, USA). Aerobic exercises were performed mainly on a treadmill (fast walk or jog). When the examined participant reported muscle pain, they could use a different training device (upright bike or x-trainer) to reduce discomfort and lower the chance for injury. The training was of a continuous character with a steady HR. The duration of the aerobic training was 45 min. After the training, the participants stretched the engaged muscle groups for 10 min.

#### 2.3.2. Combined Aerobic-Resistance Training

The course of the aerobic-resistance intervention (Table S1, Supplement): the training with elements of aerobic-resistance exercises took place 3 times per week in groups of max 5 participants. The training started with a 5-min aerobic warm-up: walking on a treadmill (Technogym New Excite Run Now 500, Cesena, Italy) to reach an intensity of 50% HR max. Initially, the training comprised 3 complex exercises involving the whole body (FBW—full body workout), such as squats, push-ups with adjustable height of arm prop, bent isolated one-arm dumbbell row, 4 series with 120-s breaks between them. In the second week of intervention, following adaptation of the body to the training, the training changed to 3 series of 6 exercises, with 90-s breaks between them. From the third week of intervention, the training included 3 series of 9 exercises, with 60-s breaks between them. At first, the load was set at 50% of one repetition maximum (1 RM), then it was raised to 70% 1 RM after 4 weeks of training. After the resistance exercises, the participants were

trained on the treadmill (Technogym New Excite Run Now 500, Cesena, Italy), upright bike (Technogym Artis, Cesena, Italy), or x-trainer (Precor EFX556i Elipsa, Woodinville, DC, USA) at an intensity of 50% HR max in the first week and 70% HR max from the second week of intervention. The duration of the resistance training sessions was 30, 35, and 40 min, respectively, followed by 20, 15, and 10 min for aerobic training, respectively. Training finished with stretching the engaged muscle groups for 5 min. The duration of the whole training was 60 min. The training engaged large muscle groups, whereas in subsequent exercises, through isolation of the practised exercise positions, the synergistic muscles of lower mass were activated. The training employed dumbbells, barbells, training devices, and the participant's own body mass. The progression of load (%) in the selected resistance exercises during the intervention and follow-up, calculated based on the data obtained in the force test 1 RM [32], compared to baseline are presented in Table 1 for EG2.

**Table 1.** The progression of load [%] in selected resistance exercises during the intervention and follow-up compared to baseline in the aerobic-resistance group EG2.

| Time of Observation | Barbell Bench Press | Lat Pull Down | Dumbbell Squat | Total Load of 3 Exercises |
|---|---|---|---|---|
| After 6 weeks of intervention | 15.32 | 11.76 | 16.77 | 15.50 |
| After 12 weeks of intervention | 23.84 | 23.02 | 25.41 | 24.35 |
| After 16 weeks, follow-up period | 26.92 | 25.70 | 26.30 | 26.50 |
| *p*-Value | 0.00 | 0.00 | 0.00 | 0.00 |

### *2.4. Statistical Analysis*

The distribution of results for the analyzed variables was checked by applying a Shapiro–Wilk test. Due to a skewed distribution of most variables, the differences between the study groups and the control group were assessed using the Kruskal-Wallis test.

To compare the impact of intervention on changes in the analyzed variables between EG and CG, the Friedman test with post hoc comparison (Wilcoxon-Nemenyi test) was used. The effect size (E.S.) was estimated for the Friedman test: $W = X2/N(K - 1)$; where W is the Kendall's W value, X2 is the Friedman test statistic value, N is the sample size, and K is the number of measurements per subject. The Kendall's W coefficient assumes a value from 0 (indicating no relationship) to 1 (indicating a perfect relationship). Kendalls uses the Cohen's interpretation guidelines of $0.1 \leq 0.3$ (small effect), $0.3 \leq 0.5$ (moderate effect) and $\geq 0.5$ (large effect) [33]. The Spearman correlation coefficient (r) was calculated.

In order to explain the variability in IL-6 and IR levels, multiple regression was applied. The models were prepared using an econometric linear model of multiple regression assessed by the method of least squares. In both models, the residual standard errors and test *p*-values were corrected using heteroscedasticity-adjusted robust standard errors.

In all analyses, the effects were assumed significant if their probability value *p* was lower than the accepted significance level $\alpha = 0.05$ ($p < 0.05$).

The ggplot2 package of RStudio IDE in R programming language was used to perform all calculations.

## 3. Results

There were no differences between EG1, EG2, and CG with respect to age, number of parameters of MetS confirmed in the examined males, and basic anthropometric parameters before the interventions (Table 2).

After applying the health training interventions both in EG1 ($p = 0.00$) and EG2 ($p = 0.00$), an increase in energy expenditure [kcal/week] was confirmed at each week of measurements in relation to the first week of tests. In CG, the total energy expenditure did not change significantly through the whole period of observation. The energy value of the diet during the intervention after 6 ($p = 0.53$) and 12 ($p = 0.22$) weeks did not change

in EG1, but a remarkable increase in delivered calories was noticed during the follow-up period ($p$ = 0.01) in the diet of the described group. Similarly, an increase in delivered calories in the diet was confirmed in EG2 ($p$ = 0.00). In CG, the energy value of the diet during the observation period did not change significantly ($p$ = 0.35) (Table 3).

**Table 2.** Characteristics of the research participants in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| Index | Group | | | $p$-Value |
|---|---|---|---|---|
| | EG1 | EG2 | CG | |
| Age [years] | 34.21 ± 6.06 | 37.37 ± 7.08 | 38.26 ± 7.43 | 0.20 |
| MetS criterion acc. to IDF | 3.07 ± 0.83 | 3.25 ± 0.86 | 3.47 ± 0.74 | 0.30 |
| BMI [kg/m$^2$] | 34.57 ± 4.58 | 33.14 ± 4.32 | 33.20 ± 4.31 | 0.62 |
| WC [cm] | 114.7 ± 10.93 | 114.8 ± 11.64 | 115.3 ± 10.54 | 0.93 |

MetS—number of metabolic syndrome parameters that meet the criteria of recognition by IDF (International Diabetes Federation), BMI—body mass index, WC—waist circumference, $p$-Value—Kruskal-Wallis test.

**Table 3.** Energy expenditure and energy value of the research participants' diets in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| | Gr. | Week 1 Baseline | | Week 6 Intervention | | Week 12 Intervention | | Week 16 Follow-Up | | $p$-Value | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Me | Q1; Q3 | Me | Q1; Q3 | Me | Q1; Q3 | Me | Q1; Q3 | F. T. (E.S.) | d 6-1 (E.S.) | d 12-1 (E.S.) | d 16-1 (E.S.) |
| Energy expenditure [kcal/ week] | EG1 | 3813.7 | 3329.3; 4714.2 | 5697.3 | 4777.5; 6217.7 | 5593.5 | 4495.1; 6249.7 | 4757.5 | 4486.6; 6720.4 | 0.00 (0.70) | 0.00 (0.88) | 0.00 (0.88) | 0.00 (0.83) |
| | EG2 | 3746.5 | 3412.3; 4465.5 | 5058.9 | 4419.3; 5903.6 | 5252.7 | 4249.9; 5632.8 | 5520.2 | 4609.0; 5648.4 | 0.00 (0.42) | 0.00 (0.86) | 0.00 (0.86) | 0.03 (0.64) |
| | CG | 4465.1 | 2978.1; 5811.5 | 3955.1 | 2760.3; 5497.6 | 4605.2 | 3425.4; 5481.4 | 4682.8 | 3473.8; 6137.9 | 0.73 (0.03) | 1.00 (0.00) | 0.68 (0.13) | 0.27 (0.34) |
| | T.K. | 0.90 | | 0.03 | | 0.13 | | 0.60 | | | | | |
| Energy value of diet [kcal/day] | EG1 | 2761.5 | 2085.8; 3107.0 | 2445.5 | 2222.5; 3032.3 | 2708.5 | 2327.0; 3336.0 | 3134.0 | 2415.5; 3447.5 | 0.00 (0.32) | 0.53 (0.17) | 0.22 (0.34) | 0.01 (0.66) |
| | EG2 | 2669.5 | 2325.5; 2786.0 | 2680.5 | 2531.8; 2996.8 | 2685.5 | 2612.3; 3127.0 | 2900.5 | 2671.0; 3251.3 | 0.00 (0.35) | 0.03 (0.63) | 0.01 (0.83) | 0.00 (0.86) |
| | CG | 2689.0 | 2411.5; 2975.5 | 2782.0 | 2653.8; 3055.0 | 2803.5 | 2683.8; 3138.3 | 3112.0 | 2855.0; 3274.0 | 0.35 (0.07) | 0.27 (0.34) | 0.43 (0.24) | 0.04 (0.59) |
| | T.K. | 0.81 | | 0.50 | | 0.77 | | 0.95 | | | | | |

EG1—aerobic group; EG2—aerobic-resistance group; CG—control group; d 6-1, d 12-1, d 16-1—differences in results obtained after 6 and 12 weeks of intervention and after 4 weeks of follow-up, respectively, in relation to measurements taken before intervention; Me—median; Q1—lower quartile; Q3—upper quartile; $p < 0.05$—statistically significant difference; $p \geq 0.05$—statistically insignificant difference; E.S.—effect size; T.K.—Kruskal-Wallis test; F.T.—Friedman test.

After applying 6 ($p$ = 0.00) and 12 ($p$ = 0.00) weeks of aerobic-resistance exercise intervention, a significant ($p$ = 0.00) increase in FFM was confirmed in the examined males (EG2). In contrast, no change in FFM was found in either EG1 or CG. Changes in total percentage of BF were found in EG1 ($p$ = 0.05) and EG2 ($p$ = 0.01) at 6, 12, and 16 weeks compared to the initial measurements. The highest decrease in BF level was observed in EG2 (Table 4), while a increase in BF level was confirmed between measurements at 6 and 12 weeks in CG (data not included).

Significant changes ($p$ = 0.03) in the level of INS were observed between measurements in EG2. A decrease in INS level took place between 1 and 16 weeks ($p$ = 0.03). A significant change in the concentration of GL was found in a single measurement: a decrease in GL concentration was confirmed between measurements at weeks 1 and 16 in EG1 ($p$ = 0.02) (Table 5).

**Table 4.** Body composition measured using densitometry in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| | Gr. | Week 1 Baseline | | Week 6 Intervention | | Week 12 Intervention | | Week 16 Follow-Up | | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Me | Q1; Q3 | Me | Q1; Q3 | Me | Q1; Q3 | Me | Q1; Q3 | T.F. (E.S.) | d 6-1 (E.S.) | d 12-1 (E.S.) | d 16-1 (E.S.) |
| FFM [kg] | EG1 | 70.30 | 67.06; 74.83 | 70.86 | 66.40; 73.15 | 69.80 | 66.01; 73.33 | 70.06 | 66.79; 75.20 | 0.72 (0.03) | 0.24 (0.34) | 0.69 (0.13) | 0.79 (0.09) |
| | EG2 | 67.75 | 60.39; 73.22 | 71.82 | 65.25; 76.00 | 69.66 | 63.49; 73.71 | 67.66 | 64.61; 74.27 | 0.00 (0.30) | 0.00 (0.89) | 0.00 (0.77) | 0.00 (0.89) |
| | CG | 67.78 | 62.69; 76.68 | 68.35 | 62.63; 77.42 | 71.25 | 63.45; 77.44 | 72.36 | 65.49; 76.25 | 0.77 (0.02) | 0.74 (0.14) | 0.57 (0.22) | 0.91 (0.06) |
| | T.K. | 0.46 | | 0.81 | | 0.86 | | 0.79 | | | | | |
| BF [%] | EG1 | 37.40 | 35.67; 40.25 | 37.25 | 35.07; 39.38 | 38.10 | 33.80; 39.90 | 36.95 | 33.18; 40.25 | 0.05 (0.18) | 0.05 (0.55) | 0.03 (0.61) | 0.02 (0.60) |
| | EG2 | 36.40 | 34.05; 39.7 | 35.80 | 33.80; 38.47 | 35.00 | 33.40; 37.80 | 33.90 | 33.15; 37.15 | 0.01 (0.27) | 0.01 (0.76) | 0.01 (0.79) | 0.00 (0.86) |
| | CG | 36.95 | 34.82; 40.73 | 37.20 | 34.53; 42.10 | 37.55 | 35.42; 42.12 | 38.55 | 36.53; 41.85 | 0.15 (0.11) | 0.16 (0.49) | 0.19 (0.46) | 0.25 (0.42) |
| | T.K. | 0.87 | | 0.60 | | 0.38 | | 0.26 | | | | | |

FFM [kg]—fat free mass; BF [%]—percentage of body fat; EG1—aerobic group; EG2—aerobic-resistance group; CG—control group; d 6-1, d 12-1, d 16-1—differences in results obtained after 6 and 12 weeks of interventions and after 4 weeks of follow-up, respectively, in relation to measurements taken before intervention; Me—median; Q1—lower quartile; Q3—upper quartile; $p < 0.05$—statistically significant difference; $p \geq 0.05$—statistically insignificant difference; E.S.—effect size; T.K.—Kruskal-Wallis test; F.T.—Friedman test.

**Table 5.** Concentrations of glucose (GL) and insulin (INS) in participants' blood in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| | Gr. | Week 1 Baseline | | Week 6 Intervention | | Week 12 Intervention | | Week 16 Follow-Up | | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Me | Q1; Q3 | Me | Q1; Q3 | Me | Q1; Q3 | Me | Q1; Q3 | T.F. (E.S.) | d 6-1 (E.S.) | d 12-1 (E.S.) | d 16-1 (E.S.) |
| INS [μIU/mL] | EG1 | 14.65 | 10.50; 21.70 | 10.45 | 7.60; 16.48 | 15.05 | 8.52; 24.3 | 12.35 | 8.68; 18.02 | 0.36 (0.08) | 0.23 (0.40) | 0.38 (0.31) | 0.13 (0.50) |
| | EG2 | 16.25 | 11.20; 22.12 | 18.75 | 13.32; 22.18 | 12.00 | 8.20; 14.9 | 10.75 | 7.66; 12.95 | 0.03 (0.19) | 0.08 (0.56) | 0.41 (0.29) | 0.03 (0.69) |
| | CG | 20.60 | 11.15; 22.90 | 18.70 | 13.62; 27.25 | 20.30 | 13.40; 28.4 | 16.80 | 11.80; 28.40 | 0.12 (0.12) | 0.34 (0.34) | 0.25 (0.42) | 0.91 (0.06) |
| | T.K. | 0.77 | | 0.06 | | 0.06 | | 0.13 | | | | | |
| GL [mmol/L] | EG1 | 5.16 | 4.75; 5.61 | 4.96 | 4.77; 5.16 | 4.84 | 4.70; 5.03 | 4.78 | 4.64; 5.07 | 0.12 (0.14) | 0.11 (0.39) | 0.17 (0.38) | 0.02 (0.66) |
| | EG2 | 5.13 | 4.94; 5.30 | 5.26 | 5.17; 5.42 | 5.06 | 4.86; 5.27 | 5.00 | 4.75; 5.20 | 0.12 (0.12) | 0.17 (0.45) | 0.73 (0.16) | 0.24 (0.42) |
| | CG | 5.31 | 4.99; 5.48 | 5.18 | 5.00; 5.41 | 4.96 | 4.84; 5.65 | 5.14 | 4.79; 5.38 | 0.23 (0.09) | 0.52 (0.20) | 0.20 (0.39) | 0.05 (0.57) |
| | T.K. | 0.38 | | 0.08 | | 0.18 | | 0.28 | | | | | |

EG1—aerobic group; EG2—aerobic-resistance group; CG—control group; d 6-1, d 12-1, d 16-1—differences in results obtained after 6 and 12 weeks of interventions and after 4 weeks of follow-up, respectively, in relation to measurements taken before interventions; Me—median; Q1—lower quartile; Q3—upper quartile; $p < 0.05$—statistically significant difference; $p \geq 0.05$—statistically insignificant difference; E.S.—effect size; T.K.—Kruskal-Wallis test; F.T.—Friedman test.

After applying aerobic exercise intervention in the examined males (EG1), an increase in IR concentration was confirmed ($p = 0.02$) (Figure 2). After aerobic-resistance exercise intervention (EG2), no changes were found in the concentration of IR, both after 6 and 12 weeks of intervention and after the follow-up period. In the control group (CG), no changes were found in the concentration of IR. After applying exercise intervention in both

EG1 ($p$ = 0.01) and EG2 ($p$ = 0.01), a decrease in the concentration of IL-6 was found, and mean concentrations of IL-6 were lower at each subsequent measurement in EG2 (Figure 3). Intergroup differences were confirmed after 6 ($p$ = 0.00) and 12 ($p$ = 0.00) weeks between EG1 and EG2 as well as between EG2 and CG, and after 16 weeks ($p$ = 0.01) between EG1 and EG2 and between EG2 and CG. In the control group (CG), no changes were found in the concentration of IL-6 (Table 6).

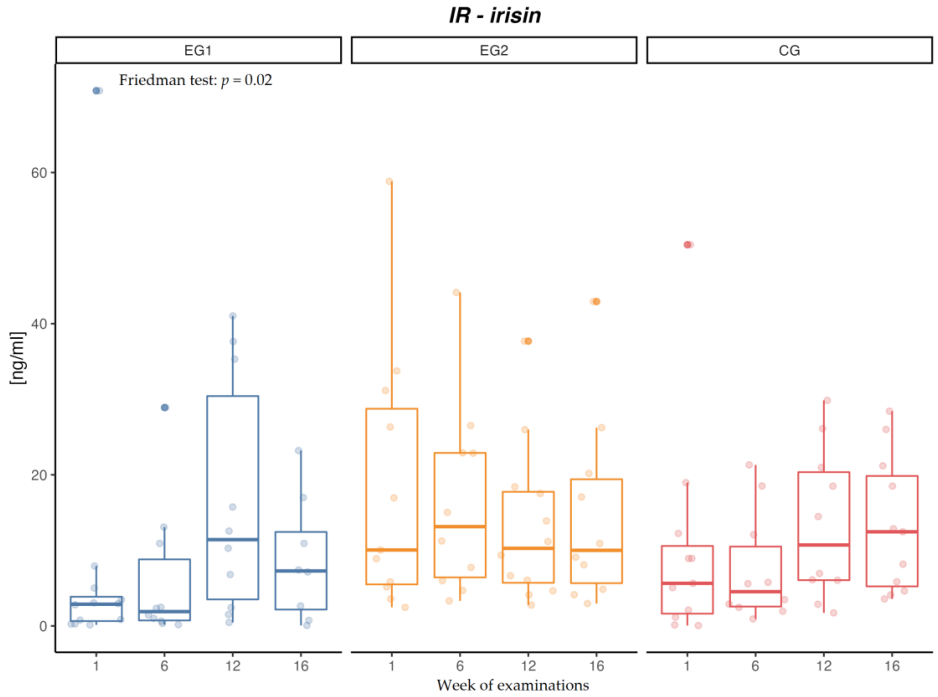


**Figure 2.** Changes in irisin (IR) concentration [ng/mL] in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG) during weeks of examinations.

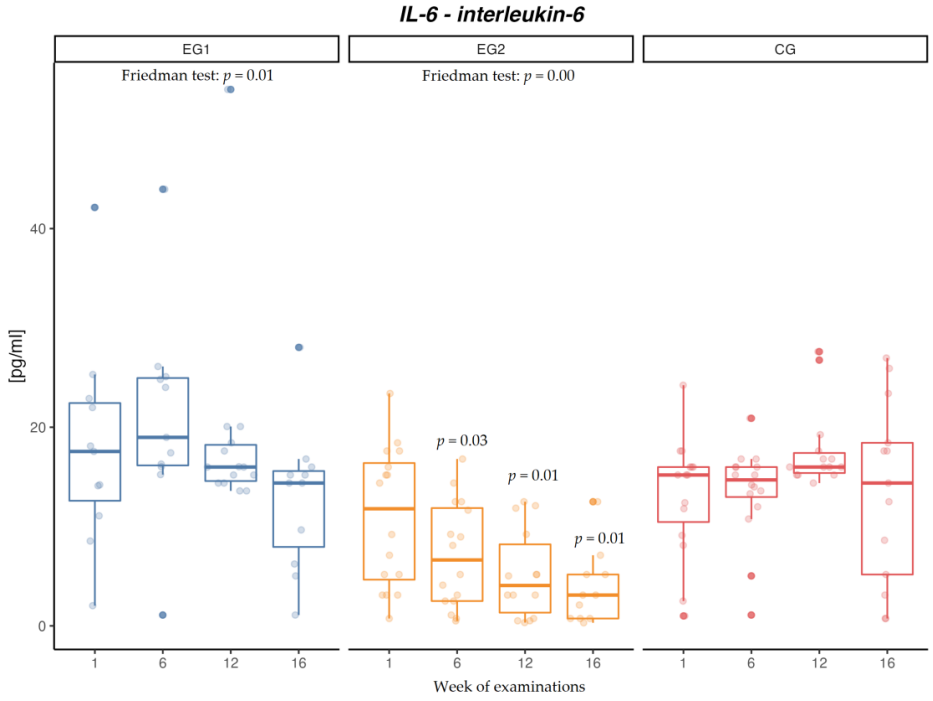


**Figure 3.** Changes in interleukin-6 (IL-6) concentration [pg/mL] in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG) during weeks of examinations.

**Table 6.** Concentrations of irisin (IR) and interleukin-6 (IL-6) in participants' blood plasma in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| | Gr. | Week 1 Baseline | | Week 6 Intervention | | Week 12 Intervention | | Week 16 Follow-Up | | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Me | Q1; Q3 | Me | Q1; Q3 | Me | Q1; Q3 | Me | Q1; Q3 | T.F. (E.S.) | d 6-1 (E.S.) | d 12-1 (E.S.) | d 16-1 (E.S.) |
| IR [ng/mL] | EG1 | 3.05 | 2.80; 5.01 | 2.40 | 1.34; 11.46 | 12.56 | 6.80; 35.31 | 7.41 | 4.89; 13.95 | 0.02 (0.24) | 0.06 (0.91) | 0.81 (0.18) | 0.06 (0.91) |
| | EG2 | 10.05 | 5.50; 28.74 | 13.14 | 6.43; 22.90 | 10.27 | 5.71; 17.75 | 10.00 | 5.66; 19.41 | 0.69 (0.03) | 0.16 (0.58) | 0.94 (0.06) | 0.58 (0.26) |
| | CG | 8.93 | 5.07; 12.24 | 4.53 | 2.57; 10.50 | 10.71 | 6.06; 20.35 | 12.46 | 5.23; 19.85 | 0.05 (0.20) | 0.58 (0.26) | 0.58 (0.26) | 0.30 (0.48) |
| | T.K. | 0.07 | | 0.14 | | 0.99 | | 0.36 | | | | | |
| IL-6 [pg/mL] | EG1 | 17.56 | 12.59; 22.44 | 18.98 | 16.16; 24.95 | 15.99 | 14.58; 18.23 | 14.38 | 7.94; 15.59 | 0.01 (0.29) | 0.21 (0.40) | 0.58 (0.19) | 0.10 (0.51) |
| | EG2 | 11.79 | 4.65; 16.40 | 8.10 | 2.80; 12.07 | 5.03 | 3.10; 9.22 | 3.10 | 1.08; 5.17 | 0.00 (0.32) | 0.03 (0.71) | 0.01 (0.85) | 0.01 (0.85) |
| | CG | 15.19 | 10.46; 15.99 | 14.70 | 12.97; 15.99 | 15.99 | 15.39; 17.41 | 14.38 | 5.17; 18.43 | 0.23 (0.09) | 0.10 (0.51) | 0.07 (0.51) | 0.97 (0.02) |
| | T.K. | 0.08 | | 0.00 | | 0.00 | | 0.01 | | | | | |

EG1—aerobic group; EG2—aerobic-resistance group; CG—control group; d 6-1, d 12-1, d 16-1—differences in results obtained after 6 and 12 weeks of interventions and after 4 weeks of follow-up, respectively, in relation to measurements taken before interventions; Me—median; Q1—lower quartile; Q3—upper quartile; $p < 0.05$—statistically significant difference; $p \geq 0.05$—statistically insignificant difference; E.S.—effect size; T.K.—Kruskal-Wallis test; F.T.—Friedman test.

Significant correlations (Table 7) were confirmed in EG1 between IR and energy expenditure (r = 0.27), FFM (r = 0.35), concentration of GL in blood (r = 0.44), INS (r = 0.37), and also between IL-6 and energy expenditure (r = 0.35), FFM (r = 0.44), GL (r = 0.31), and INS (r = 36). In EG2, correlations were found between the concentrations of IR and IL-6 (r = −0.31) and energy value of the diet (r = 0.27), as well as between IL-6 and energy expenditure (r = −0.35) and BF (r = 0.38). In CG, correlations were observed between IR and BF (r = −0.30), GL (r = −0.36), and INS (r = −0.42). No correlations were found between IL-6 and other parameters in CG (Table 7).

**Table 7.** Spearman's rank correlations for participants in the control group (CG), aerobic group (EG1), and aerobic-resistance group (EG2).

| | IR EG1 [ng/mL] | IR EG2 [ng/mL] | IR CG [ng/mL] | IL-6 EG1 [pg/mL] | IL-6 EG2 [pg/mL] | IL-6 CG [pg/mL] |
|---|---|---|---|---|---|---|
| Energy value of diet [kcal] | 0.23 | 0.27 * | 0.08 | −0.05 | −0.07 | 0.06 |
| Energy expenditure [kcal/week] | 0.27 * | 0.05 | 0.06 | 0.35 * | −0.35 * | −0.10 |
| BF [%] | −0.19 | −0.11 | −0.30 * | 0.19 | 0.38 * | 0.05 |
| FFM [kg] | 0.35 * | −0.05 | −0.06 | 0.44 * | −0.18 | 0.22 |
| IR [ng/mL] | 1.00 | 1.00 | 1.00 | 0.16 | −0.31 * | 0.10 |
| IL-6 [pg/mL] | 0.16 | −0.31 * | 0.10 | 1.00 | 1.00 | 1.00 |
| GL [mmol/L] | 0.44 * | −0.14 | −0.36 * | 0.31 * | 0.06 | −0.12 |
| INS [µIU/mL] | 0.37 * | −0.09 | −0.42 * | 0.36 * | 0.22 | −0.04 |

*—statistically significant value p < 0.05; IR EG1—concentrations of irisin in EG1 taken from the four timepoints; IR EG2—concentrations of irisin in EG2 taken from the four timepoints; IR CG—concentrations of irisin in CG taken from the four timepoints; IL-6 EG—concentrations of interleukin-6 in EG1 taken from the four timepoints; IL-6 EG2—concentrations of interleukin-6 in EG2 taken from the four timepoints; IL-6 CG—concentrations of interleukin-6 in CG taken from the four timepoints; FFM—fat free mass; BF—percentage of body fat; GL—glucose level; INS—insulin level.

The applied multiple regression model demonstrated that both BF and FFM were significantly connected with the concentration of IR ($p < 0.05$). Males in EG2 featured sig-

nificantly lower concentrations of IR than males in EG1. The analyzed variables explained 14% of variability in IR (value of $R^2$ model = 0.14) (Table 8).

**Table 8.** Parameters of multiple regression model of the irisin (IR) dependent variable.

| Dependent Variable | Parameter Assessment | Standard Error | t Value | *p*-Value |
|---|---|---|---|---|
| Free parameter | 11.83 | 10.34 | 1.14 | 0.25 |
| BF [%] | −0.72 | 0.21 | −3.45 | 0.00 |
| FFM [kg] | 0.43 | 0.12 | 3.48 | 0.00 |
| Dummy: EG2 | −6.40 | 3.08 | −2.08 | 0.04 |
| Dummy: CG | −3.62 | 2.55 | −1.42 | 0.16 |

BF—percentage of body fat, FFM—fat free mass, EG2—aerobic-resistance group, CG—control group.

The applied multiple regression model showed that BF, FFM, and the type of examined group together explained 32% of the variability in IL-6 (value of $R^2$ model = 0.32). Males in EG2 and CG were characterized by a significantly higher concentration of IL-6 than males in EG1 (Table 9).

**Table 9.** Parameters of multiple regression model of the IL-6 dependent variable.

| Dependent Variable | Parameter Assessment | Standard Error | t Value | *p*-Value |
|---|---|---|---|---|
| Free parameter | −15.26 | 7.33 | −2.08 | 0.04 |
| BF [%] | 0.25 | 0.11 | 2.23 | 0.03 |
| FFM [kg] | 0.19 | 0.09 | 2.06 | 0.04 |
| Dummy: EG2 | 9.90 | 1.52 | 6.51 | 0.00 |
| Dummy: CG | 6.63 | 1.27 | 5.21 | 0.00 |

BF—percentage of body fat, FFM—fat free mass, EG2—aerobic-resistance group, CG—control group.

## 4. Discussion

The main aim of the research was to assess the effects of 12 weeks of two different exercise interventions and 4 weeks of follow-up on the concentrations of IR and IL-6 in males with MetS.

While interpreting fluctuations in the concentrations of IR and IL-6, the moment of measuring the concentration of hormones in plasma should be taken into account. In this study, the measurements were taken at fasting 24 h after training. Under such conditions, the increased concentrations of Il-6 and IR may have resulted from increased synthesis in the adipose tissue. IL-6 and IR levels increase mainly under the influence of effort and skeletal muscle activation, and their measurement should be performed on the training day, preferably during training or immediately after finishing it [34,35]. It was demonstrated that IR levels instantly increase after the beginning of physical activity in adults with and without MetS [17,36,37]. The response of IR release depends on the intensity of the effort. Higher levels are observed after more intensive effort [38]. The concentration of circulating IL-6 increases exponentially in response to physical activity [34]. Concentrations of IL-6 in plasma may increase by 100 times in response to exercise [21]. The concentration of the hormone stabilizes 24 h after exercise intervention [35].

There are contradictory reports on the results of IR concentrations connected with long-term (≥8 weeks) intervention of physical activity. When both resistance and aerobic training were applied to groups with either normal body mass or obesity, the authors of a meta-analysis observed an increase in IR concentration and long-term results were obtained by people performing resistance training [39]. Additionally, in the study by Cosio et al. [40], an increased concentration of IR was found in people performing resistance training. In the meta-analysis by Qiu et al. [41], the authors registered a decrease in IR level in aerobic training intervention groups. Meanwhile, in an overview of studies on healthy adults, no significant changes were observed in the concentration of IR after performing long-term resistance or aerobic training [42].

IR is mainly produced in the tissue of skeletal muscles under the influence of physical effort, but it is also synthesized in adipocytes [43]. The occurrence of the 'IR resistance' phenomenon in patients with MetS and in an obese population was previously reported [16]. Another cause of the increased concentration of IR in the blood of obese patients may be the higher secretion of the hormone from adipose tissue [44]. A positive correlation between IR concentration and body mass, BMI, fat mass, and INS resistance was confirmed by Perakakis et al. Despite the fact that the concentration of IR was higher in obese patients, it was lower in patients with type 2 diabetes (T2DM) in some studies [45]. In the research of Norheim et al. [46], a 12-week training intervention decreased the concentrations of IR both in groups of healthy males and in those with INS resistance. Taking into consideration fluctuations of hormones connected with the issue of resistance, this study was expected to show increased concentrations of IR in the participants' blood and decreased levels influenced by intervention, correlated with the loss of body fat and an increase in fat free body mass. In the group with aerobic training, after 6 weeks of intervention, there was a decrease in the percentage of BF and a decrease in IR concentration, whereas no changes were observed in the level of FFM. The increased IR concentrations in EG1 could have resulted from changes associated with the physical exercise effect (energy expenditure, r = 0.27). IR released from muscles stimulates increased mRNA expression of uncoupling protein 1 (UCP1) in adipocytes, leading to the transformation of white adipose tissue into brown adipose tissue, causing energy expenditure and inducing thermogenesis and GL homeostasis. In this group, the concentration of GL gradually decreased and a significant decrease took place 16 weeks after beginning the intervention. In the aerobic group, a positive correlation between IR concentration and fat free mass was also confirmed. A positive correlation between IR concentration and muscle mass or FFM was also observed by other scientists [37,47,48]. The mechanisms underlying the positive energy balance in obese patients are numerous, complex, and multifactorial. They exist largely beyond conscious control and are only partially the same among patients [49].

In the aerobic-resistance group, no significant changes in IR concentration were observed after 12 weeks of intervention. However, a significant decrease in the percentage of adipose tissue (−6.9%) and increase in the percentage of FFM (6.0%) were confirmed, despite an increase in the energy value of the diet in the analyzed period of time. A possible cause of the increased energy value of the diet was an increase in the feeling of hunger among examined participants after introducing physical activity and higher energy expenditures.

In this study, the mean level of BMI was 33.63 kg/m$^2$ and the participants met at least 3 of 5 of the criteria of MetS. According to a previously published report [15], such a group has a high risk of IR resistance; therefore, a beneficial effect obtained through intervention is the lowering of IR concentrations, as found in EG1 during the first 6 weeks of observation. In a previous paper [13] investigating the relationship between IR and metabolic diseases, including obesity, type 2 diabetes, and hepatic steatosis, different test results were observed. It was shown that the concentration of IR was high in a group of obese people, whereas patients with type 2 diabetes and hepatic steatosis had lower concentrations of IR in relation to the control group. Researchers observed higher concentrations of IR and IL-6 in obese males with a tendency to suffer from MetS [19].

In this study, a gradual decrease in IL-6 concentrations was observed in the groups performing physical activity: in the aerobic-resistance group it amounted to −74% after 16 weeks and −18% was observed in the aerobic group. In the control group, no significant changes were found. The difference between groups indicated lower concentrations of IL-6 in the group performing aerobic-resistance training. The pathophysiology of obesity includes the occurrence of a chronic inflammatory condition with low intensity as a result of, among other factors, excessive synthesis of IL-6 by adipose tissue [50]. In the present work, a positive correlation was found between the percentage of adipose tissue and IL-6 level in EG2. Increased concentrations of IL-6 occur in patients with obesity and type 2 diabetes [51]. Myokine IL-6 is of significant importance to muscle efficiency

during a muscle contraction, while IL-6 synthesized in adipose tissue, especially when it is chronically increased, may lead to INS resistance in muscles. Despite the fact that IL-6 synthesized in muscles provides therapeutic potential for INS resistance, there appear to be challenges connected to distinguishing the source of IL-6 synthesis, i.e., adipose tissue or skeletal muscle [52,53]. Observing a significant decrease in INS concentrations in EG2, accompanied by the highest decrease in IL-6 concentrations and the highest increase in FFM level, suggests that the changes result from the decrease in adipose tissue content, leading to lowering of the inflammatory condition in the body and INS resistance connected with obesity. The presented multiple regression model confirmed that BF and FFM explained 14% of the variability in IR concentration and 32% of the IL-6 variability. The present work demonstrated a significant negative correlation between the concentrations of IR and IL-6 in EG2. IR features anti-inflammatory properties that can lead to the decreased secretion of inflammatory cytokines, such as TNF-alpha and IL-6 [54].

There is information on the relationship between IR, IL-6, and the metabolism of carbohydrates in previous reports; therefore, an analysis of GL and INS concentrations was performed at individual timepoints in the current study. In EG1 and CG, no changes in the concentration of INS were observed. In EG2, after 6 weeks of intervention, an increase in INS concentration was confirmed, and a significant decrease was found in subsequent measurements that amounted to −34% after 16 weeks. In the post-hoc test, a significant decrease in GL level was registered after 16 weeks of intervention in EG1 and there was also a change between 6 and 16 weeks of intervention in EG2 (data not included). The relationship between IR and INS resistance is not explicit. In the study by Park et al. [15], it was observed that the concentration of IR was higher in people with MetS and was closely connected with INS resistance. However, in the research by Choi et al. [55], it was found that concentrations of IR were lower in people with type 2 diabetes and no relation was observed between IR and INS resistance.

IR leads to the browning of adipose tissue, which may affect the metabolism of GL. In humans, brown adipose tissue features ten times higher GL uptake through INS after exposure to cold than white or visceral adipose tissue [56]. Moreover, IR induces the expression of glucotransporter 4 (GLUT4) in mature human adipocytes [57]. Introduction of recombinant IR to human skeletal cells significantly increased GL and fatty acid uptake (30–40%) for approximately 1 h. Such intervention provided similar results as the uptake observed after exposure to INS [58]. In humans, the synthesis of FNDC5 and secretion of IR are higher in the skeletal muscles of people with obesity but without T2DM, probably to maximize GL uptake by muscles and prevent hyperglycemia [59,60]. There are reports that INS may not have an influence on the secretion of IR, regardless of the concentration, in people with INS resistance or obesity. In people with T2DM, GL is an important regulator of IR secretion from skeletal muscle [60].

This study was not free from limitations. The focus of this study was to comprehensively investigate clinical and/or functional adaptations in a relatively non-invasive manner, whereas assessment of the detailed molecular mechanisms was not possible. The monitoring of physical activity was conducted using devices monitoring heart rate; however, more precise supervision could be obtained by measuring VO2 max [61]. The examined participants increased the energy value of their diet despite registering their dietary habits and recommendations to keep their previous nutritional standards. This study only included male participants, and finally, the group sample sizes were relatively small and as such, added to variability in our data.

In summary, it should be emphasized that the application of combined aerobic-resistance training led to a higher decrease in IL-6 and INS concentrations and advantageous changes in the body composition compared to performing only aerobic training in males with MetS.

**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm12010369/s1, Table S1: A detailed plan of aerobic-resistance training in aerobic-resistance group (EG2).

**Author Contributions:** Conceptualization, K.M. and A.S.; methodology, K.M., A.S., A.T., M.M. and A.H.; formal analysis, K.M.; investigation, K.M., A.S. and A.T.; data curation, K.M.; writing—original draft preparation, K.M.; writing—review and editing, K.M., A.S., A.T., M.M. and A.H.; supervision, A.S.; project administration, K.M. and A.S.; funding acquisition, K.M. and A.S. All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Regional Medical Chamber in Krakow (No. 90/KBL/OK/2020). This study is also registered as a clinical trial in ANZCTR (registration number 12622001394730).

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

**Data Availability Statement:** Data are available on request from the corresponding author.

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## References

1. Fahed, G.; Aoun, L.; Bou Zerdan, M.; Allam, S.; Bou Zerdan, M.; Bouferraa, Y.; Assi, H.I. Metabolic Syndrome: Updates on Pathophysiology and Management in 2021. *Int. J. Mol. Sci.* **2022**, *23*, 786. [CrossRef] [PubMed]
2. Fathi Dizaji, B. The investigations of genetic determinants of the metabolic syndrome. *Diabetes Metab. Syndr.* **2018**, *12*, 783–789. [CrossRef] [PubMed]
3. Matsuzawa, Y.; Funahashi, T.; Nakamura, T. The concept of metabolic syndrome: Contribution of visceral fat accumulation and its molecular mechanism. *J. Atheroscler. Thromb.* **2011**, *18*, 629–639. [CrossRef]
4. Suder, A. Socioeconomic and lifestyle determinants of body fat distribution in young working males from Cracow, Poland. *Am. J. Hum. Biol.* **2008**, *20*, 100–109. [CrossRef]
5. Suder, A. Body fatness and its social and lifestyle determinants in young working males from Cracow, Poland. *J. Bios. Sci.* **2009**, *41*, 139–154. [CrossRef] [PubMed]
6. Pedersen, B.K. Physical activity and muscle-brain crosstalk. *Nat. Rev. Endocrinol.* **2019**, *15*, 383–392. [CrossRef] [PubMed]
7. Das, D.K.; Graham, Z.A.; Cardozo, C.P. Myokines in skeletal muscle physiology and metabolism: Recent advances and future perspectives. *Acta Physiol.* **2020**, *228*, e13367. [CrossRef] [PubMed]
8. Huh, J.Y. The role of exercise-induced myokines in regulating metabolism. *Arch. Pharmacal Res.* **2018**, *41*, 14–29. [CrossRef] [PubMed]
9. Yu, Q.; Kou, W.; Xu, X.; Zhou, S.; Luan, P.; Li, H.; Zhuang, J.; Wang, J.; Zhao, Y.; Xu, Y.; et al. FNDC5/Irisin inhibits pathological cardiac hypertrophy. *Clin. Sci.* **2019**, *133*, 611–627. [CrossRef]
10. Roca-Rivada, A.; Castelao, C.; Senin, L.L.; Landrove, M.O.; Baltar, J.; Crujeiras, A.B.; Seoane, L.M.; Casanueva, F.F.; Pardo, M. FNDC5/irisin is not only a myokine but also an adipokine. *PLoS ONE* **2013**, *8*, e60563. [CrossRef]
11. Boström, P.; Wu, J.; Jedrychowski, M.P.; Korde, A.; Ye, L.; Lo, J.C.; Rasbach, K.A.; Boström, E.A.; Choi, J.H.; Long, J.Z.; et al. A PGC1-α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. *Nature* **2012**, *481*, 463–468. [CrossRef] [PubMed]
12. Xin, C.; Liu, J.; Zhang, J.; Zhu, D.; Wang, H.; Xiong, L.; Lee, Y.; Ye, J.; Lian, K.; Xu, C.; et al. Irisin improves fatty acid oxidation and glucose utilization in type 2 diabetes by regulating the AMPK signaling pathway. *Int. J. Obes.* **2016**, *40*, 443–451. [CrossRef] [PubMed]
13. Polyzos, S.A.; Anastasilakis, A.D.; Efstathiadou, Z.A.; Makras, P.; Perakakis, N.; Kountouras, J.; Mantzoros, C.S. Irisin in metabolic diseases. *Endocrine* **2018**, *59*, 260–274. [CrossRef] [PubMed]
14. Chen, N.; Li, Q.; Liu, J.; Jia, S. Irisin, an exercise-induced myokine as a metabolic regulator: An updated narrative review. *Diabetes Metab. Res. Rev.* **2016**, *32*, 51–59. [CrossRef] [PubMed]

15. Park, K.H.; Zaichenko, L.; Brinkoetter, M.; Thakkar, B.; Sahin-Efe, A.; Joung, K.E.; Tsoukas, M.A.; Geladari, E.V.; Huh, J.Y.; Dincer, F.; et al. Circulating irisin in relation to insulin resistance and the metabolic syndrome. *J. Clin. Endocrinol. Metab.* **2013**, *98*, 4899–4907. [CrossRef]
16. Jia, J.; Yu, F.; Wei, W.P.; Yang, P.; Zhang, R.; Sheng, Y.; Shi, Y.Q. Relationship between circulating irisin levels and overweight/obesity: A meta-analysis. *World J. Clin. Cases* **2019**, *7*, 1444–1455. [CrossRef]
17. Huh, J.Y.; Siopi, A.; Mougios, V.; Park, K.H.; Mantzoros, C.S. Irisin in response to exercise in humans with and without metabolic syndrome. *J. Clin. Endocrinol. Metab.* **2015**, *100*, 453–457. [CrossRef] [PubMed]
18. Pal, M.; Febbraio, M.A.; Whitham, M. From cytokine to myokine: The emerging role of interleukin-6 in metabolic regulation. *Immunol. Cell Biol.* **2014**, *92*, 331–339. [CrossRef]
19. Werida, R.H.; El-Gharbawy, N.M.; Mostafa, T.M. Circulating IL-6, clusterin and irisin in obese subjects with differentgrades of obesity: Association with insulin resistance and sexual dimorphism. *Arch. Endocrinol. Metab.* **2021**, *65*, 126–136. [CrossRef]
20. Nash, D.; Hughes, M.G.; Butcher, L.; Aicheler, R.; Smith, P.; Cullen, T.; Webb, R. IL-6 signaling in acute exercise and chronic training: Potential consequences for health and athletic performance. *Scand. J. Med. Sci. Sports* **2022**, *33*, 4–19. [CrossRef]
21. Fischer, C.P. Interleukin-6 in acute exercise and training: What is the biological relevance? *Exerc. Immunol. Rev.* **2006**, *12*, 6–33. [PubMed]
22. Gonzalez-Gil, A.M.; Elizondo-Montemayor, L. The Role of Exercise in the Interplay between Myokines, Hepatokines, Osteokines, Adipokines, and Modulation of Inflammation for Energy Substrate Redistribution and Fat Mass Loss: A Review. *Nutrients* **2020**, *12*, 1899. [CrossRef] [PubMed]
23. Turcotte, L.P.; Fisher, J.S. Skeletal muscle insulin resistance: Roles of fatty acid metabolism and exercise. *Phys. Ther.* **2008**, *88*, 1279–1296. [CrossRef] [PubMed]
24. Gleeson, M.; Bishop, N.C.; Stensel, D.J.; Lindley, M.R.; Mastana, S.S.; Nimmo, M.A. The anti-inflammatory effects of exercise: Mechanisms and implications for the prevention and treatment of disease. *Nat. Rev. Immunol.* **2011**, *11*, 607–615. [CrossRef] [PubMed]
25. Vincent, H.K.; Raiser, S.N.; Vincent, K.R. The aging musculoskeletal system and obesity-related considerations with exercise. *Ageing. Res. Rev.* **2012**, *11*, 361–373. [CrossRef]
26. Jurca, R.; Lamonte, M.J.; Barlow, C.E.; Kampert, J.B.; Church, T.S.; Blair, S.N. Association of muscular strength with incidence of metabolic syndrome in men. *Med. Sci. Sports Exerc.* **2005**, *37*, 1849–1855. [CrossRef]
27. Alberti, K.G.; Zimmet, P.; Shaw, J. Metabolic syndrome—A new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabet. Med.* **2006**, *23*, 469–480. [CrossRef]
28. Craig, C.L.; Marshall, A.J.; Sjöström, M.; Bauman, A.E.; Booth, M.L.; Ainsworth, B.E.; Pratt, M.; Ekelund, U.; Yngve, A.; Sallis, J.F.; et al. International Physical Activity Questionnaire: 12-country reliability and validity. *Med. Sci. Sports Exerci.* **2003**, *35*, 1381–1395. [CrossRef]
29. Garber, C.E.; Blissmer, B.; Deschenes, M.R.; Franklin, B.A.; Lamonte, M.J.; Lee, I.M.; Nieman, D.C.; Swain, D.P.; American College of Sports Medicine; American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Med. Sci. Sports. Exerc.* **2011**, *43*, 1334–1359. [CrossRef]
30. Grgic, J.; Lazinica, B.; Schoenfeld, B.J.; Pedisic, Z. Test-Retest Reliability of the One-Repetition Maximum (1RM) Strength Assessment: A Systematic Review. *Sports Med. Open.* **2020**, *6*, 31. [CrossRef]
31. Ainsworth, B.E.; Haskell, W.L.; Herrmann, S.D.; Meckes, N.; Bassett, D.R., Jr.; Tudor-Locke, C.; Greer, J.L.; Vezina, J.; Whitt-Glover, M.C.; Leon, A.S. 2011 Compendium of Physical Activities: A second update of codes and MET values. *Med. Sci. Sports Exerc.* **2011**, *43*, 1575–1581. [CrossRef] [PubMed]
32. Levinger, I.; Goodman, C.; Hare, D.L.; Jerums, G.; Toia, D.; Selig, S. The reliability of the 1RM strength test for untrained middle-aged individuals. *J. Sci. Med. Sport.* **2009**, *12*, 310–316. [CrossRef]
33. Fritz, C.O.; Morris, P.E.; Richler, J.J. Effect size estimates: Current use, calculations, and interpretation. *J. Exp. Psychol. Gen.* **2012**, *141*, 2–18. [CrossRef] [PubMed]
34. Steensberg, A.; van Hall, G.; Osada, T.; Sacchetti, M.; Saltin, B.; Klarlund Pedersen, B. Production of interleukin-6 in contracting human skeletal muscles can account for the exercise-induced increase in plasma interleukin-6. *J. Physiol.* **2000**, *529*, 237–242. [CrossRef]
35. Wiecek, M.; Szymura, J.; Maciejczyk, M.; Kantorowicz, M.; Szygula, Z. Acute Anaerobic Exercise Affects the Secretion of Asprosin, Irisin, and Other Cytokines—A Comparison Between Sexes. *Front. Physiol.* **2018**, *9*, 1782. [CrossRef] [PubMed]
36. Kraemer, R.; Shockett, P.; Webb, N.; Shah, U.; Castracane, V.A. Transient Elevated Irisin Blood Concentration in Response to Prolonged, Moderate Aerobic Exercise in Young Men and Women. *Horm. Metab. Res.* **2013**, *46*, 150–154. [CrossRef]
37. Löffler, D.; Müller, U.; Scheuermann, K.; Friebe, D.; Gesing, J.; Bielitz, J.; Erbs, S.; Landgraf, K.; Wagner, I.V.; Kiess, W.; et al. Serum Irisin Levels Are Regulated by Acute Strenuous Exercise. *J. Clin. Endocrinol. Metab.* **2015**, *100*, 1289–1299. [CrossRef]
38. Daskalopoulou, S.S.; Cooke, A.B.; Gomez, Y.H.; Mutter, A.F.; Filippaios, A.; Mesfum, E.T.; Mantzoros, C.S. Plasma irisin levels progressively increase in response to increasing exercise workloads in young, healthy, active subjects. *Eur. J. Endocrinol.* **2014**, *171*, 343–352. [CrossRef]
39. Kazeminasab, F.; Sadeghi, E.; Afshari-Safavi, A. Comparative Impact of Various Exercises on Circulating Irisin in Healthy Subjects: A Systematic Review and Network Meta-Analysis. *Oxidative Med. Cell. Longev.* **2022**, *22*, 8235809. [CrossRef]

40. Cosio, P.L.; Crespo-Posadas, M.; Velarde-Sotres, Á.; Pelaez, M. Effect of Chronic Resistance Training on Circulating Irisin: Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Int. J. Environ. Res. Public Health.* **2021**, *18*, 2476. [CrossRef]
41. Qiu, S.; Cai, X.; Sun, Z.; Schumann, U.; Zügel, M.; Steinacker, J.M. Chronic Exercise Training and Circulating Irisin in Adults: A Meta-Analysis. *Sports Med.* **2015**, *45*, 1577–1588. [CrossRef] [PubMed]
42. Rodrigues, A.C.; Ferreira, E.F.; Carneiro-Júnior, M.A.; Natalia, A.J.; Bressanc, J. Effects of exercise on the circulating concentrations of irisin in healthy adult individuals: A review. *Sci. Sports* **2016**, *31*, 251–260. [CrossRef]
43. Rodriguez, A.; Becerril, S.; Ezquerro, S.; Mendez-Gimenez, L.; Fruhbeck, G. Crosstalk between adipokines and myokines in fat browning. *Acta Physiol.* **2017**, *219*, 362–381. [CrossRef] [PubMed]
44. Moreno-Navarrete, J.M.; Ortega, F.; Serrano, M.; Guerra, E.; Pardo, G.; Tinahones, F.; Ricart, W.; Fernández-Real, J.M. Irisin is expressed and produced by human muscle and adipose tissue in association with obesity and insulin resistance. *J. Clin. Endocrinol. Metab.* **2013**, *98*, 769–778. [CrossRef]
45. Perakakis, N.; Triantafyllou, G.A.; Fernández-Real, J.M.; Huh, J.Y.; Park, K.H.; Seufert, J.; Mantzoros, C.S. Physiology and role of irisin in glucose homeostasis. *Nat. Rev. Endocrinol.* **2017**, *13*, 324–337. [CrossRef]
46. Norheim, F.; Langleite, T.M.; Hjorth, M.; Holen, T.; Kielland, A.; Stadheim, H.K.; Gulseth, H.L.; Birkeland, K.I.; Jensen, J.; Drevon, C.A. The effects of acute and chronic exercise on PGC-1α, irisin and browning of subcutaneous adipose tissue in humans. *FEBS J.* **2014**, *281*, 739–749. [CrossRef]
47. Mai, S.; Grugni, G.; Mele, C.; Vietti, R.; Vigna, L.; Sartorio, A.; Aimaretti, G.; Scacchi, M.; Marzullo, P. Irisin levels in genetic and essential obesity: Clues for a potential dual role. *Sci. Rep.* **2020**, *10*, 1020. [CrossRef]
48. Stengel, A.; Hofmann, T.; Goebel-Stengel, M.; Elbelt, U.; Kobelt, P.; Klapp, B.F. Circulating levels of irisin in patients with anorexia nervosa and different stages of obesity-correlation with body mass index. *Peptides* **2013**, *39*, 125–130. [CrossRef]
49. Hebebrand, J.; Holm, J.C.; Woodward, E.; Baker, J.L.; Blaak, E.; Durrer Schutz, D.; Farpour-Lambert, N.J.; Frühbeck, G.; Halford, J.G.C.; Lissner, L.; et al. A Proposal of the European Association for the Study of Obesity to Improve the ICD-11 Diagnostic Criteria for Obesity Based on the Three Dimensions Etiology, Degree of Adiposity and Health Risk. *Obes. Facts* **2017**, *10*, 284–307. [CrossRef]
50. Hotamisligil, G.S. Inflammation and metabolic disorders. *Nature* **2006**, *444*, 860–867. [CrossRef]
51. Scheja, L.; Heeren, J. The endocrine function of adipose tissues in health and cardiometabolic disease. *Nat. Rev. Endocrinol.* **2019**, *15*, 507–524. [CrossRef] [PubMed]
52. Raschke, S.; Eckel, J. Adipo-myokines: Two sides of the same coin-mediators of inflammation and mediators of exercise. *Mediat. Inflamm.* **2013**, *2013*, 320724. [CrossRef] [PubMed]
53. Park, S.E.; Park, C.Y.; Sweeney, G. Biomarkers of insulin sensitivity and insulin resistance: Past, present and future. *Crit. Rev. Clin. Lab. Sci.* **2015**, *52*, 180–190. [CrossRef] [PubMed]
54. Mazur-Bialy, A.I.; Pochec, E.; Zarawski, M. Anti-Inflammatory Properties of Irisin, Mediator of Physical Activity, Are Connected with TLR4/MyD88 Signaling Pathway Activation. *Int. J. Mol. Sci.* **2017**, *18*, 701. [CrossRef] [PubMed]
55. Choi, Y.K.; Kim, M.K.; Bae, K.H.; Seo, H.A.; Jeong, J.Y.; Lee, W.K.; Kim, J.G.; Lee, I.K.; Park, K.G. Serum irisin levels in new-onset type 2 diabetes. *Diabetes Res. Clin. Pract.* **2013**, *100*, 96–101. [CrossRef] [PubMed]
56. Orava, J.; Nuutila, P.E.; Lidell, M.; Oikonen, V.; Noponen, T.; Viljanen, T.; Scheinin, M.; Taittonen, M.; Niemi, T.; Enerbäck, S.A.; et al. Different metabolic responses of human brown adipose tissue to activation by cold and insulin. *Cell Metab.* **2011**, *14*, 272–279. [CrossRef] [PubMed]
57. Huh, J.Y.; Dincer, F.; Mesfum, E.; Mantzoros, C.S. Irisin stimulates muscle growth-related genes and regulates adipocyte differentiation and metabolism in humans. *Int. J. Obes.* **2014**, *38*, 1538–1544. [CrossRef] [PubMed]
58. Huh, J.Y.; Mougios, V.; Kabasakalis, A.; Fatouros, I.; Siopi, A.; Douroudos, I.; Filippaios, A.; Panagiotou, G.; Park, K.H.; Mantzoros, C.S. Exercise-induced irisin secretion is independent of age or fitness level and increased irisin may directly modulate muscle metabolism through AMPK activation. *J. Clin. Endocrinol. Metab.* **2014**, *99*, E2154–E2161. [CrossRef]
59. Huh, J.Y.; Panagiotou, G.; Mougios, V.; Brinkoetter, M.; Vamvini, M.T.; Schneider, B.E.; Mantzoros, C.S. FNDC5 and irisin in humans: I. Predictors of circulating concentrations in serum and plasma and II mRNA expression and circulating concentrations in response to weight loss and exercise. *Metabolism* **2012**, *61*, 1725–1738. [CrossRef]
60. Kurdiova, T.; Balaz, M.; Vician, M.; Maderova, D.; Vlcek, M.; Valkovic, L.; Srbecky, M.; Imrich, R.; Kyselovicova, O.; Belan, V.; et al. Effects of obesity, diabetes and exercise on Fndc5 gene expression and irisin release in human skeletal muscle and adipose tissue: In vivo and in vitro studies. *J. Physiol.* **2014**, *592*, 1091–1107. [CrossRef]
61. Smirmaul, B.P.; Bertucci, D.R.; Teixeira, I.P. Is the VO2max that we measure really maximal? *Front. Physiol.* **2013**, *5*, 4–203. [CrossRef] [PubMed]

**Table S1. A detailed plan of aerobic-resistance training** in **aerobic-resistance group (EG2).**

| | **Trainings 1-3** | **Trainings 4-6** | **Trainings 6<** |
|---|---|---|---|
| Intensity of aerobic training [% HR max] | 50 | 70 | 70 |
| Duration of aerobic training [min] | 20 | 15 | 10 |
| Intensity of resistance training [% 1 RM] | 50 | 70 | 70 |
| Duration of resistance training [min] | 30 | 35 | 40 |
| Volume of resistance training [exercises x series x repetitions] | 3 x 4 x 15 | 6 x 3 x 12 | 9 x 3 x 12 |
| Breaks between series [min] | 2 | 1.5 | 1 |
| Type of training | Whole body training | Training of antagonistic parts | Training of antagonistic parts |
| Specialised exercises | 1. Supported push-ups (Smith machine)<br>2. One arm dumbbell row<br>3. Squads<br>4. Front support | 5. Barbell bench press<br>6. Standing dumbbell press<br>7. Bent dumbbell row<br>8. Reverse grip lat pulldown<br>9. Hip thrust lying | 10. Cable triceps extension<br>11. Standing dumbbell curl<br>12. Deadlift |

1RM – one repetition maximum, HR max – maximal heart rate.

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# Impact of Two Types of Exercise Interventions on Leptin and Omentin Concentrations and Indicators of Lipid and Carbohydrate Metabolism in Males with Metabolic Syndrome

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**Abstract:** Leptin (LEP) and omentin (OMEN) are proteins whose concentrations change with the development of the metabolic syndrome (MetS). There are few intervention studies using various forms of physical activity in people with MetS that aim to determine the impact of physical exercise on the fluctuations of the presented hormones, and their results are contradictory. The present study aimed to examine the effect of two types of exercise intervention on LEP and OMEN concentrations and indicators of lipid and carbohydrate metabolism in males with MetS. The study included 62 males with MetS (age 36.6 ± 6.9 years, body mass 110.31 ± 17.37 kg), randomly allocated to EG1, the examined group with aerobic training ($n$ = 21); EG2, the examined group with combined aerobic and resistance training ($n$ = 21), both for 12 weeks, and the control group (CG) without interventions ($n$ = 20). Anthropometric measurements, body composition (body fat [BF], android body fat [ANDR]), as well as a biochemical blood analysis (omentin [OMEN], leptin [LEP], quantitative insulin sensitivity check index [QUICKI], high-density lipoprotein cholesterol [HDL-C] and nonHDL-C) were performed at baseline, and at 6 and 12 weeks of interventions and after 4 weeks after ending intervention (follow-up). Intergroup and intragroup comparisons were performed. In the intervention groups EG1 and EG2, a decrease in BF was observed as well as an improvement in carbohydrate metabolism parameters. In the EG1 group, the level of ANDR was reduced. In EG2 a decrease in LEP concentration between measurements was confirmed. However, no significant changes were found in the concentration of OMEN in any groups. Combined aerobic and resistance exercises led to a higher reduction of LEP concentration than applying only aerobic training in males with MetS.

**Keywords:** omentin; leptin; exercise; metabolic syndrome; obesity; physical activity; QUICKI



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## 1. Introduction

The metabolic syndrome (MetS) is diagnosed in patients who are affected by several mutually connected disorders leading to an increased risk of cardiovascular disease development, mainly atherosclerosis, insulin resistance and type 2 diabetes, and vascular and neurological complications such as cerebrovascular incidents [1]. Metabolic disorders become a syndrome if three out of five criteria are confirmed in a patient: abdominal

obesity, low high-density lipoprotein cholesterol (HDL-C), high triglyceride levels, high glucose level, high blood pressure, or treatment for a specific disorder is conducted. The main, indirect cause of MetS is obesity which is always connected with the risk of type 2 diabetes, cancers and other chronic diseases that are components of the MetS [2,3]. Insulin resistance is thought to be the direct cause of diseases that the MetS consists of, mainly due to strong correlations with obesity and accompanying comorbidity [4]. Obesity favours the accumulation of visceral fat, which is connected with the occurrence of systemic inflammation of low intensity and adds to the development of metabolic disorders [5]. In a population of obese people at risk of the MetS, a dysregulated production of adipokines may lead to disorders in the functioning of insulin and glucose homeostasis [6]. Changes in adipokines levels, especially those produced in visceral fat tissue, may reflect systemic complications linked to obesity [7–9]. During the research overview it was found that white and brown adipose tissue communicate with skeletal muscles and the heart through the secretion of leptin (LEP) and omentin (OMEN) whose concentrations significantly alter with the development of obesity [10,11]. Concentrations of circulating biomarkers of inflammation condition, insulin resistance and LEP are significantly higher in people with MetS compared to the control group [12], whereas in the same population lowered levels of OMEN were observed [13].

Leptin (LEP) is an adipokine that due to its influence on the regulation of appetite and energy homeostasis attracts interest among researchers dealing with obesity and MetS [14]. Insulin and LEP act as the key signals regulating energy balance through direct influence on their related receptors in hypothalamus neurons affecting the control of food intake and energy expenditure [15]. Moreover, LEP plays many roles in the body, including a considerable role in immunology and respiratory systems, and it influences the regulation of sex hormones [16–19]. In obesity patients and in patients with MetS, the phenomenon of leptin resistance takes place [12,20]. The concentration of LEP level in serum is proportional to the level of obesity and it reflects the energy state of the body. The BMI threshold when the concentration of LEP starts increasing is 24.6 $kg/m^2$ [11]. Leptin resistance is the main factor that leads to a progression of the MetS and understanding of the mechanism of leptin resistance development requires further research [4]. An improper level of LEP may result in the development of type 2 diabetes (T2DM) [21], cardiovascular diseases [22] and some cancers [23,24].

Omentin (OMEN) occurs in two forms: OMEN-1 and OMEN-2 [25]. OMEN-1 is the main protein among isoforms that exists in the human body [13,26]. Unlike most adipokines, OMEN is not produced in subcutaneous fat tissue [27]. It is mainly synthesized in visceral fat tissue [25]. Despite this, its lowered concentrations are observed in a population of obese people and its decrease leads to metabolic disorders such as insulin resistance and glucose intolerance. People with proper body weight feature a much higher concentration of OMEN in serum than those overweight [13]. There are also differences in OMEN concentrations in the case of different sex—women have higher concentrations of OMEN than men [13]. The level of OMEN may allow us to predict metabolic consequences or diseases co-existing with obesity [13]. In relation to other adipokines, it was demonstrated that OMEN is positively connected with the level of adiponectin in serum and negatively with levels of LEP [13]. Low concentrations of OMEN in serum are also found in patients with type 1 and type 2 diabetes [28,29]. Secretion of OMEN-1 is stimulated in response to applying physical activity. Physiological adaptation of skeletal muscles to physical activity can also be related to the action of OMEN [30]. Conducting intervention research with the use of aerobic or resistance training leading to the reduction of adipose tissue offers opportunities for a better understanding of how the discussed adipokine works.

Regular physical activity is an important element of a lifestyle that prevents metabolic complications [31]. The American College of Sports Medicine recommends introducing 200–300 min of moderate physical activity weekly for obese and overweight people in order to achieve a clinically significant reduction of body mass [32]. The researchers highlight benefits resulting from applying aerobic-resistance training as an element of intervention

in health condition improvement in people with a surplus of adipose tissue. An important area of the positive influence of resistance training on health conditions in people with surplus body mass comprises beneficial hormonal changes in the levels of adiponectin, leptin and insulin and improvement of MetS parameters [33]. Resistance training does not always lead to body mass loss, but it can increase fat-free mass and decrease adipose tissue, and changes in proportion in the presented tissues are connected with the improvement of health conditions, reducing, among others, the level of insulin resistance, inflammation and atherogenic lipids [34].

A better understanding of roles played by LEP and OMEN in MetS may help choose more precise therapeutic interventions by the selection of proper training methods leading to maximum effects from attempts to reduce body mass and improve health [35–37]. Modification of lifestyle by introducing physical activity may lower insulin resistance. However, test results do not indicate clear results connected with changes in adipokine concentrations influenced by physical activity in patients with MetS so the authors suggest that more research should be conducted in the field [38].

The aim of the project was to evaluate the influence of applying two types of physical training for 12 weeks (aerobic vs. combined aerobic-resistance) and four weeks of follow-up on the concentration of LEP and OMEN and changes in indicators of lipid and carbohydrate metabolism in males with MetS. We hypothesize that combined aerobic-resistance training through the development of muscle mass and loss of adipose tissue brings more beneficial changes in concentrations of LEP and OMEN than aerobic training.

## 2. Materials and Methods

### *2.1. Materials*

The research is part of a project whose methodology has already been described in the paper presenting the effects of exercise interventions on the concentration of irisin and interleukin-6 [39]. Below, the description of the research methodology was supplemented with elements related to the present paper.

The research, planned as a prospective, randomized, and controlled trial study, was to examine the results of applying two kinds of physical training for 12 weeks (aerobic vs. combined aerobic-resistance) in male subjects with metabolic syndrome (MetS). The study examined the effects on their body composition, changes in leptin (LEP) and omentin (OMEN) levels as well as indexes of the MetS in comparison to men with MetS, contained in the control group, who did not take part in the interventions. After the training period finished, the subjects from all the groups were monitored for the subsequent 4 weeks as a follow-up phase.

In order to prevent bias, the laboratory staff, statisticians and analysts were not informed about the subjects' group allocation, but because of the type of intervention, we did not employ the blind trial. The research was registered in the clinical trials registry on the ANZCTR platform (Australian New Zealand Clinical Trials Registry): ACTRN 12622001394730 and received the approval of the Ethics Committee of the Regional Medical Chamber in Cracow (90/KBL/OK/2020). Figure 1 presents the study course.

The study involved 62 men aged 30–45 (mean age 37 $\pm$ 7) years with elevated waist circumference (WC) $\geq$ 94 cm and with 2 out of the 4 MetS criteria recognised: hypertriglyceridemia under treatment or concentration of triglycerides > 150 mg/dl (1.7 mmol/l); concentration of HDL-C < 40 mg/dl (1.03 mmol/l)—in men or the lipid disorder under treatment; systolic blood pressure (SBP) $\geq$ 130 mm Hg or diastolic (DBP) $\geq$ 85 mm Hg, or treatment of previously diagnosed hypertension; fasting level of GL in blood plasma $\geq$ 100 mg/dl (5.6 mmol/l) or pharmacological treatment of diabetes type 2 (IDF, International Diabetes Federation, 2006 [40]). The exclusion criteria involved a lack of medical statements concerning no contraindications to undertake aerobic-resistance exercise and others described in the former article in the field [39].

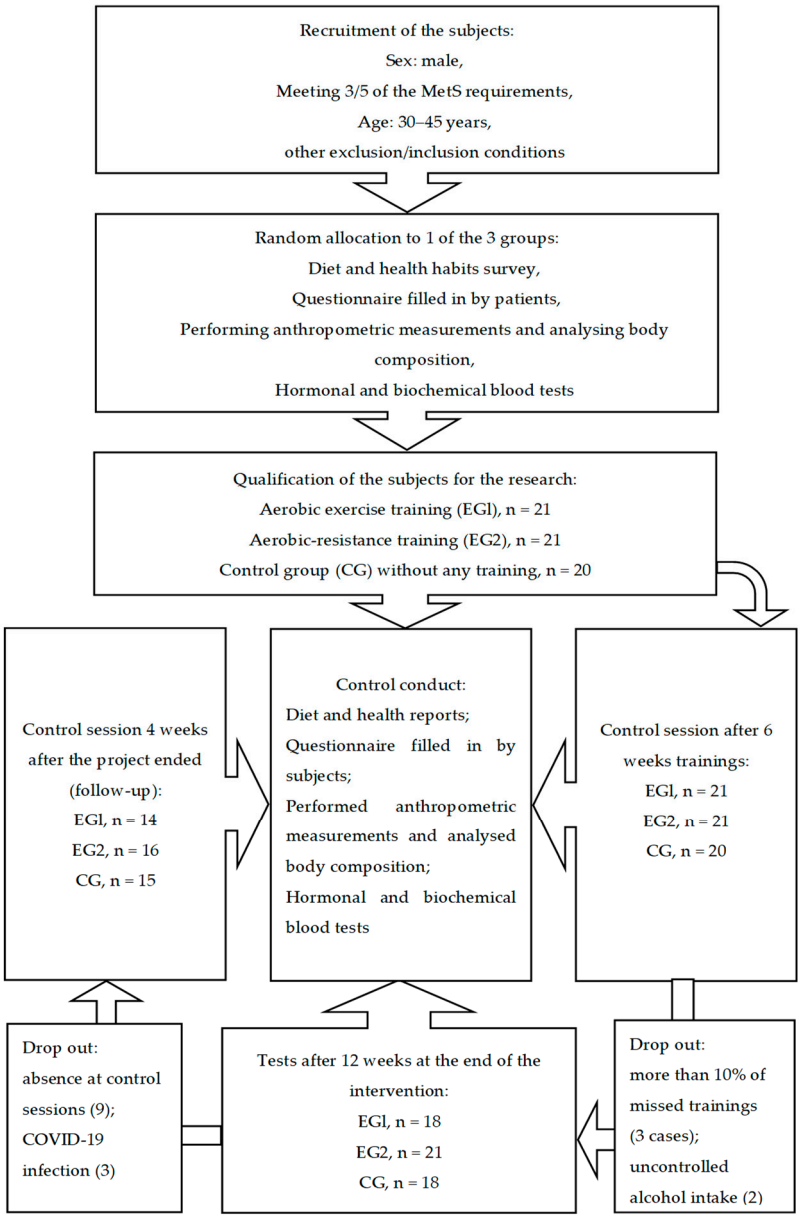


**Figure 1.** The course of the study.

The subjects were allocated randomly into 3 groups; the assignment relied on simple randomization following the sealed opaque envelopes:

the experimental group (EG1) of men with MetS ($n$ = 21) realizing aerobic training (age: 34.21 ± 6.06; body mass index, BMI: 34.57 ± 4.58; waist circumference, WC: 114.7 ± 10.93; waist to height ratio, WHtR: 63.37 ± 6.22);

the experimental group (EG2) of men with MetS ($n$ = 21) realizing combined aerobic-resistance training (age: 37.37 ± 7.08; BMI: 33.14 ± 4.32; WC: 114.8 ± 11.64; WHtR: 63.90 ± 5.97);

the control group (CG) of men with MetS ($n$ = 20) not realizing any training (age: 38.26 ± 7.43; BMI: 33.20 ± 4.31; WC: 115.3 ± 10.54; WHtR: 63.72 ± 4.99). There were no differences between age and basic anthropological parameters before the interventions.

The subjects received detailed information about the procedures and aim of the study and about the option to give up the interventions at any stage. There were cases of patients resigning from the training and of exclusion of participants due to: more than 10% of missed training (3 cases), uncontrolled alcohol intake (2), absence at control sessions (9),

and COVID-19 infection (3). The subjects declared not to change their diet, administered remedies, and spare time activity while participating in the research. They all submitted written consent to take part in the project and accepted using their data and the study results for academic aims.

### 2.2. Methods

The assessments found below were conducted in all the subjects and took place four times: before the training started, during the project (after 6 weeks and after 12 weeks of training) and 4 weeks after the end of the training sessions (follow-up):

#### 2.2.1. Anthropometry

Body height (BH) [cm], body mass (BM) [kg] and waist circumference (WC) [cm] were measured for the needs of the study. BH was taken without shoes, in a standing position to the nearest 1 mm, with the head in the Frankfurt plane, with a stadiometer (Seca 231 stadiometer, Hamburg, Germany). BM was measured in the standing position with a standardized medical scale (Beurer PS 240, Budapest, Hungary), with an accuracy of 50 g. Waist circumference (WC) was taken to the nearest 1 mm with an anthropometric tape between the lower edge of the costal arch and the upper edge of the iliac crest with the subject in a standing position and registered at the end of a gentle expiration. Waist-to-height ratio (WHtR) was obtained by dividing waist circumference (in cm) by height (in cm).

#### 2.2.2. Body Composition

Body fat (BF) [kg], android body fat (ANDR) [%] and body mass index (BMI) [kg/m$^2$] were assessed with the use of Dual-Energy X-ray Absorptiometry (DEXA). Measurements were done with the Lunar Prodigy Primo PR+352163 (Chicago, IL, USA) device following the manufacturer's manual.

#### 2.2.3. Hormonal Blood Indexes

Samples of blood were taken in the morning after a 12-h fast and after a 24-h break from training, from the basilic, cephalic, or median cubital vein into test tubes (Vacumed® system, F.L. Medical, Torreglia, Italy) by experienced nurses. They were then immediately centrifuged (RCF 1000× *g*) for 15 min at 4 °C (MPW-351R, MPW Med. Instruments, Warsaw, Poland) and plasma was collected and stored at −80 °C until further study (BIO Memory 690L, Froilabo, Paris, France). Leptin and omentin concentrations were assessed with ELISA kits according to the manufacturer's guidelines. The human Leptin Sandwich ELISA Kit (catalogue number EIA-2395) was provided by DRG Instruments GmbH (Marburg, Germany). The human omentin ELISA kit (catalogue number 201-12-0156) was bought from Shanghai Sunred Biological Technology Co. (Shanghai, China). An ELx 808 spectrophotometric microplate reader (BioTek, Winooski, VT, USA) was applied to specify the optical density at 450 nm. Marking was performed in the Laboratory of Genetics and Molecular Biology at the Department of Physiology, Jagiellonian University Medical College, Cracow, Poland.

#### 2.2.4. Biochemical Blood Indexes

Sensitivity to insulin was determined applying the quantitative insulin sensitivity check index (QUICKI) [41], following the formula:

$$\text{QUICKI} = 1/[\log \text{INS}\ (\mu\text{IU/ml}) + \log \text{GL}\ (\text{mmol/l})]$$

Plasma insulin (INS) [μIU/ml] concentration was assessed using electrochemiluminescence (ECLIA) with the Cobas e801 apparatus (Roche Diagnostics International Ltd., Mannheim, Germany). Glucose (GL) [mmol/l] concentration in the blood plasma was conducted by the enzymatic method with the Cobas c701/702 biochemical analyser (Roche Diagnostics International Ltd., Mannheim, Germany). The assessments were realized in

conformity with the manufacturer protocol using reagents dedicated to the GLUC3 and Elecsys Insulin analysers, respectively.

The plasma levels of total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) were specified with the spectrophotometric method relying on guidelines of the clinical chemistry analyser Architect ci-4100 (Abbott Laboratories). The intra- and interassay coefficients of variation (CV) for the assays were 0.9–1.2 and 1.2–1.8%, respectively. Non-HDL cholesterol (nonHDL-C) fraction was determined following the formula:

$$\text{nonHDL-C [mmol/l} - 1] = \text{TC [mmol/l} - 1] - \text{HDL-C [mmol/l} - 1]$$

#### 2.2.5. Evaluation of Energy Expenditure and Energy Value of Diet

The International Physical Activity Questionnaire (IPAQ) was performed to estimate total physical activity. The calculation of the total estimation of activity relied on the MET (metabolic equivalent of a task) formula expressed as a value of for example 3 MET (intensity of slow cycling) × 30 min (duration per day) × 2 times per week (frequency) = 3 [MET] × 30 [min] × 2 [week] [MET min/week] and based on the sum of non-exercise activity thermogenesis (NEAT) assessed with the use of the IPAQ and energy expenditures connected with training sessions in EG1 and EG2 [42].

A quantitative assessment of the diet and the monitoring of changes in it while taking part in the project were realised based on the 24 h interview with nutrition record that was conducted by an experienced nutritionist. The results were elaborated in the DietaPro program (version 4.0, Institute of Food and Nutrition, Warsaw, Poland). The energy value of the diet was calculated as [kJ/day].

### *2.3. Exercise Interventions*

Monitoring of intensity in both forms of interventions of aerobic character as well as the amount of load in resistance intervention were detrained individually, according to guidelines of the American College of Sports Medicine [43]. Following the project assumptions, the subjects realized three training sessions weekly that were converted into 3 × 6 MET of energy expenditure per week for aerobic training and 3 × 5.5 MET for the resistance one [42]. The physical activity interventions took place in a fitness club in Cracow. Each training was supervised by the same personal coach, at the same daytime (6–9 pm), at the same temperature (22 Centigrade) and humidity. The subjects' presence at the training sessions was registered and consequently, participants were eliminated from observation and statistics due to their absenteeism being higher than 10% during the 12-week course of training.

Before the resistance training, the test of 1 repetition maximum (1RM) was determined. The subjects took the 1 RM test before the intervention and after 6, 12 and 16 weeks. The obtained load and number of repetitions were converted into 1 RM based on a 1 RM calculator [44]. The exact course of the 1RM test is described in the Supplement.

#### 2.3.1. Aerobic Training

The aerobic training sessions (Figure S1, Supplement) were performed in max 5-person groups, 3 times a week, starting with a 5-min warm-up, not exceeding 50% maximal heart rate (HR max). After they warmed up, the intensity was elevated to 70% HR max due to higher treadmill speed or angle (treadmill walk, Technogym New Excite Run Now 500, Cesena, Italy), resistance on upright bikes (Technogym Artis, Cesena, Italy) and movement range or resistance on X-trainer (Precor EFX556i Elipsa, Woodinville, WA, USA). The subjects could use these three devices alternately. HR was monitored by a running watch Polar M200 GPS with a wrist HR sensor (Kempele, Finland). The aerobic training duration was 45 min. It was continuous with constant HR. The stretching phase of the engaged muscle groups lasted 10 min.

#### 2.3.2. Combined Aerobic-Resistance Training

The aerobic-resistance training (Table S1, Supplement) was performed in max 5-person groups, 3 times a week. Initially, a 5-min aerobic warm-up in the form of a treadmill walk was applied (Technogym New Excite Run Now 500, Cesena, Italy), to reach 50% HR max. In the first phase of resistance training, 3 complex exercises engaging the whole body (FBW—full body workout) were applied in 4 series with 120 s breaks between them. In the second week 3 series with 6 exercises each and 90 s breaks were introduced. Starting with the third week, the training included 3 series with 9 exercises each and 60 s breaks.

The load was initially set at 50% of 1 RM and after 4 weeks it was increased to 70%. After resistance exercises, there was an aerobic training element: the participants trained on a treadmill (Technogym New Excite Run Now 500, Cesena, Italy), upright bike (Technogym Artis, Cesena, Italy) or x-trainer (Precor EFX556i Elipsa, Woodinville, WA, USA) with an intensity of 50% HR max in the first week and 70% HR max from the second week of intervention. Duration of the resistance training was respectively 30, 35 and 40 min (1st, 2nd and 3rd week), and then respectively 20, 15 and 10 min for the aerobic one. The stretching phase was 5 min. The duration of the aerobic-resistance intervention was 60 min. Progression of load (kg) in selected resistance exercises calculated based on 1 RM [45] for EG2 was statistically significant in the analysed period (Table S2, Supplement).

### *2.4. Statistical Analysis*

Statistical significance concerning the number of subjects relied on previous studies in the area found in the literature. Calculation of the sample size applied an error probability ($\alpha$) of 0.05, power ($1 - \beta$) of 0.80, and an average effect size (d) of 0.8 and for the tested sample was $n = 54$.

The Shapiro-Wilk test was used to check the distribution of the results for the analysed variables. Because of a normal distribution of most variables, the differences between the examined groups and the control one were assessed with the one-way analysis of variance for independent groups. A comparison of the intervention influence on changes in the analysed variables between EG and CG was performed with the ANOVA test for dependent groups with post-hoc comparison (Tukey test). The size effect (ES) was assessed for the ANOVA test:

$$\eta^2 = \frac{SS_{effect}}{SS_{total}}$$

where squared eta ($\eta$) is the ratio of the sum of squares ($SS$) for the effect divided by the total sum of squares ($SS$). Squared eta applies interpretation guidelines by Cohen $0.1 \leq 0.3$ (low effect), $0.3 \leq 0.5$ (moderate effect) and $\geq 0.5$ (high effect) [46]. Pearson correlation coefficient (r) was calculated.

Multiple regression was used to explain the variation in LEP levels. The model was prepared with the use of the econometric linear multiple regression model assessed by the least squares method. In the model, the residual standard errors and test $p$-values were corrected using robust standard errors corrected for heteroscedasticity.

In all analyses, effects were considered significant if their probability value $p$ was lower than the assumed significance level $\alpha = 0.05$ ($p < 0.05$). The ggplot2 package of the RStudio IDE in the R programming language was used to perform all calculations.

## 3. Results

After applying health training intervention both in EG1 ($p = 0.04$) and EG2 ($p < 0.001$) a significant increase of MET [min/week] was confirmed between the initial measurements and measurements in 6th ($p < 0.001$) and 12th ($p < 0.001$) weeks of intervention (Table 1). In follow-up, an increase of MET was also confirmed in EG1 ($p = 0.03$) and EG2 ($p = 0.04$). No significant changes were found in MET in CG. The intergroup analyses confirmed differences ($p < 0.001$) in the 6th week of observation between EG1 and CG ($p < 0.001$), and EG2 and CG ($p = 0.04$) (Table 1).

**Table 1.** Metabolic equivalent of task (MET) and energy value of the research participants' diet in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| | Group | Week 1 Baseline | Week 6 Intervention | Week 12 Intervention | Week 16 Follow up | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | Test ANOVA (ES) | d 6-1 (ES) | d 12-1 (ES) | d 16-1 (ES) |
| MET [min/week] | EG1 | 2214.40 ± 681.75 | 3127.22 ± 578.50 | 3134.06 ± 639.22 | 3204.26 ± 1507.68 | 0.04 (0.17) | <0.001 (−5.09) | <0.001 (−1.99) | 0.03 (−0.66) |
| | EG2 | 2225.22 ± 522.06 | 2899.62 ± 412.91 | 3246.25 ± 1726.13 | 3264.50 ± 1740.83 | <0.001 (0.12) | <0.001 (−2.18) | <0.001 (−0.63) | 0.04 (−0.57) |
| | CG | 2423.69 ± 705.72 | 2379.42 ± 693.42 | 2428.00 ± 674.38 | 2533.33 ± 724.75 | 0.67 (0.00) | 0.70 (0.79) | 0.84 (0.85) | 0.23 (0.23) |
| | *p*-value | 0.60 | 0.00 * | 0.13 | 0.34 | | | | |
| Energy value of diet [kJ/day] | EG1 | 11,286.50 ± 1376.01 | 12,124.84 ± 1386.59 | 12,184.03 ± 1701.68 | 12,203.01 ± 1858.68 | 0.02 (0.55) | 0.68 (0.13) | 0.24 (−0.33) | 0.01 (−0.77) |
| | EG2 | 10,732.99 ± 872.50 | 11,486.72 ± 1194.02 | 11,671.27 ± 1760.909 | 11,867.81 ± 1706.025 | <0.001 (0.06) | 0.02 (−0.77) | <0.001 (−1.13) | <0.001 (−1.56) |
| | CG | 11,158.80 ± 1565.82 | 11,248.34 ± 1444.98 | 11,462.44 ± 1372.21 | 11,695.18 ± 1442.73 | 0.12 (0.05) | 0.90 (−0.04) | 0.38 (−0.26) | 0.05 (−0.65) |
| | *p*-value | 0.79 | 0.57 | 0.92 | 0.97 | | | | |

* post-hoc: EG1-CG: $p < 0.001$, EG2-CG: $p = 0.04$; d 6-1, d 12-1, d 16-1—differences in results after 6 and 12 weeks of training, respectively, and after 4 weeks of follow-up compared to measurements obtained before training, $\overline{X}$—mean, SD—standard deviation, $p < 0.05$—statistically significant difference, ES—effect size.

The energy value of the diet [kJ] during the intervention after 6 ($p$ = 0.68), and 12 ($p$ = 0.24) weeks did not change in EG1. In follow-up, an increase in calorie intake was registered ($p$ = 0.01). In EG2 a gradual increase of consumed calories in the diet between measurements was observed ($p$ < 0.001). In CG, the energy value of the diet during the observation period did not change significantly ($p$ = 0.12) (Table 1).

After the intervention in EG1, there was a decrease in body mass ($p$ < 0.001) between measurements, the largest reduction in body mass occurred after 6 weeks of intervention −2.6 kg ($p$ < 0.001) (Table 2). There were no significant changes in body mass in the EG2 and CG groups.

A decrease in BF [kg] in EG1 ($p$ = 0.01) and in EG2 ($p$ < 0.001) was confirmed (Table 2). The largest decrease in BF (average −1.47 kg) took place in EG1 after 6 weeks of intervention ($p$ < 0.001) and in EG2 (average reduction of −2.2 kg) after 12 weeks of intervention ($p$ = 0.01). No significant changes were observed in the level of adipose tissue in CG.

The decrease in the percentage of visceral fat (ANDR) [%] was confirmed in EG1 ($p$ = 0.04), with the largest changes occurring after 12 weeks of intervention; an average decrease of −3.4% ANDR ($p$ = 0.03). In EG2, a decrease in ANDR was also observed, but these changes were not significant. Statistically significant changes in ANDR were not confirmed in the CG group (Table 2).

The applied intervention with aerobic physical activity increased the value of QUICKI ($p$ = 0.02) in EG1 (Table 3). In EG2, an initial decrease in QUICKY after 6 weeks of intervention ($p$ = 0.04) was confirmed, followed by an increase in QUICKI ($p$ < 0.001) between measurements. No significant changes in CG were observed.

No changes in nonHDL-C levels were confirmed in any of the groups as a response to the intervention (Table 3). After 6 weeks of intervention, a decrease in HDL-C concentration in EG1 was observed, followed by an increase above baseline between weeks 6 and 16 of the study ($p$ = 0.04) (data not included). In the EG2 group, a gradual increase in the mean HDL-C value was observed, but it was not statistically significant. Changes in HDL-C concentration in CG were insignificant (Table 3).

The obtained results indicate changes in LEP concentration between measurements in all observed groups (Table 4, Figure 2). In EG1, after an initial increase ($p$ = 0.01), a significant decrease was confirmed at week 12 ($p$ = 0.01) of the intervention. In the follow-up period, the LEP concentration increased again ($p$ = 0.01). In EG2, a gradual decrease in LEP concentration was observed during the intervention period—after 12 weeks, LEP concentration was reduced by an average of −2.53 ng/ml ($p$ = 0.02). In the follow-up period, a slight increase in LEP concentration was also observed ($p$ = 0.05). In the CG group, there was a significant increase ($p$ = 0.03) in LEP concentration after 6 weeks of observation. Differences between the EG2 and CG groups ($p$ = 0.03) were confirmed in the 6th week of observation and in the follow-up period between EG1 and EG2 ($p$ = 0.03).

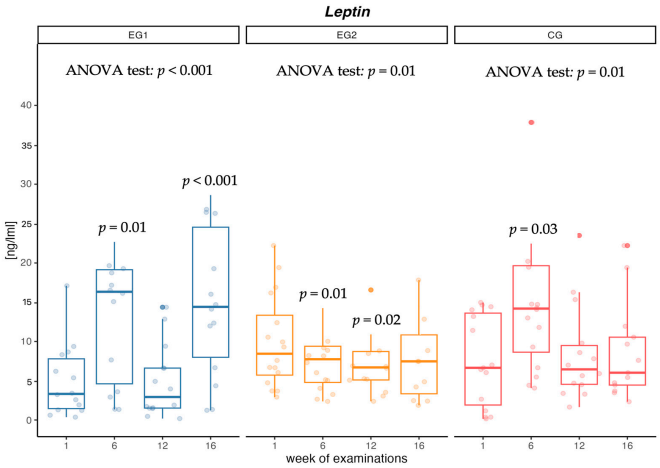


**Figure 2.** Changes in leptin (LEP) concentration [ng/ml] in aerobic group (EG1), aerobic-resistance group (EG2) and control group (CG) during weeks of examinations.

**Table 2.** Body composition: body mass (BM), body fat (BF) and android body fat (ANDR) in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| | Group | Week 1 Baseline | Week 6 Intervention | Week 12 Intervention | Week 16 Follow up | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | Test ANOVA (ES) | d 6-1 (ES) | d 12-1 (ES) | d 16-1 (ES) |
| BM [kg] | EG1 | 113.6 ± 16.8 | 111.0 ± 16.85 | 111.3 ± 17.47 | 111.4 ± 18.09 | <0.001 (0.36) | <0.001 (1.07) | 0.01 (0.88) | 0.03 (0.71) |
| | EG2 | 107.2 ± 17.36 | 107.1 ± 16.41 | 105.2 ± 16.68 | 107.3 ± 17.19 | 0.29 (0.00) | 0.50 (0.30) | 0.37 (0.24) | 0.32 (0.41) |
| | CG | 109.0 ± 17.78 | 111.5 ± 19.09 | 113.7 ± 9.12 | 115.3 ± 19.33 | 0.25 (0.00) | 0.67 (0.66) | 0.13 (0.26) | 0.22 (0.11) |
| | *p*-value | 0.34 | 0.60 | 0.29 | 0.54 | | | | |
| ANDR [%] | EG1 | 48.56 ± 5.97 | 47.32 ± 6.09 | 46.87 ± 6.67 | 46.71 ± 5.43 | 0.04 (0.02) | 0.05 (0.61) | 0.03 (0.67) | 0.02 (0.72) |
| | EG2 | 46.23 ± 6.35 | 45.10 ± 5.92 | 43.82 ± 6.41 | 44.70 ± 6.47 | 0.22 (0.01) | 0.27 (0.37) | 0.10 (0.58) | 0.69 (0.13) |
| | CG | 47.54 ± 6.64 | 48.00 ± 6.36 | 48.80 ± 6.85 | 48.52 ± 8.35 | 0.75 (0.00) | 0.41 (0.29) | 0.41 (0.29) | 0.61 (0.18) |
| | *p*-value | 0.60 | 0.40 | 0.16 | 0.41 | | | | |
| BF [kg] | EG1 | 42.48 ± 11.05 | 41.01 ± 11.12 | 40.96 ± 11.56 | 40.67 ± 11.26 | 0.01 (0.01) | <0.001 (1.05) | 0.01 (0.77) | 0.01 (0.84) |
| | EG2 | 39.52 ± 10.95 | 39.10 ± 10.34 | 37.32 ± 9.73 | 37.28 ± 10.31 | <0.001 (0.01) | 0.02 (0.92) | 0.01 (1.07) | <0.001 (1.36) |
| | CG | 39.82 ± 10.00 | 41.24 ± 11.67 | 42.77 ± 11.67 | 43.92 ± 11.68 | 0.33 (0.00) | 0.76 (0.11) | 0.10 (−0.62) | 0.90 (−0.05) |
| | p-value | 0.72 | 0.86 | 0.44 | 0.37 | | | | |

d 6-1, d 12-1, d 16-1—differences in results after 6 and 12 weeks of training, respectively, and after 4 weeks of follow-up compared to measurements obtained before training sessions, $\overline{X}$—mean, SD—standard deviation, $p < 0.05$—statistically significant difference, ES—effect size.

**Table 3.** Concentrations of quantitative insulin sensitivity check index (QUICKI), nonHDL-C and HDL-C cholesterol in the participants' blood in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| | Group | Week 1 Baseline | Week 6 Intervention | Week 12 Intervention | Week 16 Follow up | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | Test ANOVA (ES) | d 6-1 (ES) | d 12-1 (ES) | d 16-1 (ES) |
| QUICKI | EG1 | 0.32 ± 0.03 | 0.33 ± 0.04 | 0.32 ± 0.03 | 0.34 ± 0.03 | 0.02 (0.03) | 0.04 (−0.78) | 0.04 (−0.77) | 0.01 (−0.98) |
| | EG2 | 0.32 ± 0.03 | 0.315 ± 0.04 | 0.34 ± 0.03 | 0.34 ± 0.03 | <0.001 (0.05) | 0.04 (0.77) | 0.24 (−0.40) | 0.09 (−0.61) |
| | CG | 0.31 ± 0.04 | 0.31 ± 0.02 | 0.31 ± 0.03 | 0.32 ± 0.04 | 0.13 (0.08) | 0.19 (0.34) | 0.21 (0.49) | 0.50 (0.30) |
| | *p*-value | 0.60 | 0.07 | 0.06 | 0.12 | | | | |
| nonHDL-C [mmol/l] | EG1 | 3.88 ± 1.34 | 3.53 ± 1.34 | 3.40 ± 1.28 | 4.01 ± 1.55 | 0.05 (0.02) | 0.14 (0.51) | 0.10 (0.58) | 0.83 (−0.07) |
| | EG2 | 4.05 ± 0.79 | 3.80 ± 0.64 | 3.92 ± 0.87 | 4.06 ± 0.76 | 0.70 (0.01) | 0.19 (0.45) | 0.37 (0.30) | 0.60 (0.17) |
| | CG | 4.56 ± 0.80 | 4.54 ± 0.97 | 4.58 ± 1.10 | 4.50 ± 0.97 | 0.71 (0.01) | 0.62 (0.06) | 0.53 (0.14) | 0.49 (0.14) |
| | *p*-value | 0.17 | 0.03 * | 0.03 ** | 0.52 | | | | |
| HDL-C [mmol/l] | EG1 | 1.20 ± 0.29 | 1.15 ± 0.19 | 1.22 ± 0.36 | 1.27 ± 0.34 | 0.07 (0.04) | 0.03 (0.83) | 0.78 (−0.09) | 0.75 (−0.11) |
| | EG2 | 1.09 ± 0.22 | 1.14 ± 0.26 | 1.15 ± 0.26 | 1.18 ± 0.32 | 0.57 (0.01) | 0.59 (−0.18) | 0.63 (−0.16) | 0.30 (−0.35) |
| | CG | 1.15 ± 0.19 | 1.16 ± 0.19 | 1.13 ± 0.23 | 1.18 ± 0.27 | 0.38 (0.03) | 0.86 (0.06) | 0.70 (0.14) | 0.15 (−0.53) |
| | *p*-value | 0.47 | 0.96 | 0.98 | 0.72 | | | | |

* post-hoc: EG1-CG: $p = 0.03$; ** post-hoc: EG1-CG: $p = 0.04$, QUICKI—quantitative insulin sensitivity check index, nonHDL-C—non-high-density lipoprotein, HDL-C—high-density lipoprotein, d 6-1, d 12-1, d 16-1—differences in results after 6 and 12 weeks of training, respectively, and after 4 weeks of follow-up compared to measurements obtained before training sessions, $\overline{X}$—mean, SD—standard deviation, $p < 0.05$—statistically significant difference, ES—effect size.

**Table 4.** Concentrations of leptin (LEP) and omentin (OMEN) in participants' blood plasma in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| | Group | Week 1 Baseline | Week 6 Intervention | Week 12 Intervention | Week 16 Follow up | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | $\overline{X} \pm$ SD | Test ANOVA (ES) | d 6-1 (ES) | d 12-1 (ES) | d 16-1 (ES) |
| LEP [ng/ml] | EG1 | 4.96 ± 4.63 | 13.41 ± 8.35 | 4.80 ± 4.58 | 15.03 ± 9.6 | <0.001 (0.32) | 0.01 (0.70) | 0.92 (0.08) | <0.001 (0.76) |
| | EG2 | 9.89 ± 5.93± | 7.93 ± 4.48 | 7.36 ± 4.06 | 7.53 ± 5.14 | 0.01 (0.06) | 0.01 (0.70) | 0.02 (0.67) | 0.05 (0.56) |
| | CG | 7.54 ± 5.77 | 16.18 ± 11.53 | 8.35 ± 6.07 | 8.54 ± 6.15 | 0.01 (0.21) | 0.03 (0.52) | 0.79 (0.02) | 0.87 (0.20) |
| | *p*-value | 0.06 | 0.03 * | 0.16 | 0.03 ** | | | | |
| OMEN [ng/ml] | EG1 | 276.03 ± 108.72 | 316.24 ± 132.97 | 334.76 ± 153.53 | 339.05 ± 123.09 | 0.53 (0.04) | 0.33 (0.13) | 0.32 (0.29) | 0.19 (0.34) |
| | EG2 | 303.93 ± 248.13 | 362.77 ± 262.40 | 345.86 ± 291.12 | 282.00 ± 248.14 | 0.24 (0.03) | 0.14 (−0.51) | 0.26 (−0.38) | 0.54 (0.20) |
| | CG | 340.92 ± 176.91 | 322.88 ± 177.32 | 381.32 ± 240.40 | 269.07 ± 172.61 | 0.92 (0.01) | 0.83 (0.08) | 0.90 (0.14) | 0.61 (0.27) |
| | *p*-value | 0.65 | 0.79 | 0.86 | 0.58 | | | | |

* post-hoc: EG2-CG: $p = 0.03$; ** post-hoc: EG1-EG2: $p = 0.04$; d 6-1, d 12-1, d 16-1—differences in results after 6 and 12 weeks of training, respectively, and after 4 weeks of follow-up compared to measurements obtained before training sessions, $\overline{X}$—mean, SD—standard deviation, $p < 0.05$—statistically significant difference, ES—effect size.

No changes in OMEN concentration were observed both between groups and between measurements. Despite the lack of statistically significant changes, it was shown that in the intervention groups (EG1 and EG2) the level of OMEN increased after 6 and 12 weeks in relation to the initial values (Table 4).

Significant correlations (Table 5) were confirmed in EG1 between LEP and MET (r = −0.37), the energy value of diet (r = 0.28), BM (r = 0.28), BF (r = 39), ANDR (r = 0.39), QUCIKI (r = −0.45) and for cholesterol fraction nonHDL-C (r = 0.50) and HDL-C (r = −0.43). No significant correlations were found in EG1 for OMEN. In addition, significant correlations were confirmed in EG1 between QUCIKI and MET (r = 0.29), the energy value of diet (r = −0.35), HDL-C (r = 0.72) and components of body composition: BM (r = −0.67), BF (r = −0.61), ANDR (r = −0.56). In the EG2 group, very strong correlations were confirmed between LEP and components of body composition: BM (0.73), BF (r = 0.88), ANDR (r = 0.87), and the QUICKI carbohydrate metabolism index (r = −0.45). In the EG2 group, a negative correlation between OMEN and nonHDL-C was confirmed (r = −0.39). As in the EG1 group, in the EG2 group there were strong correlations between QUICKI and components of body composition: BM (r = −0.64), BF (r = −0.55), ANDR (r = −0.44). In CG, LEP level was associated with BF (r = 0.51), ANDR (r = −0.47), and BM (r = 0.42). In the case of OMEN, correlations were confirmed for BM (r = −0.39) and HDL-C (r = 0.31). Correlations in CG for QUICKI occurred between BM (r = −0.41), BF (r = −0.33) and HDL-C (r = 0.28).

**Table 5.** The value of the Pearson correlation for variables in the aerobic group (EG1), aerobic-resistance group (EG2), and control group (CG).

| | MET [1] [min/week] | Energy Value of Diet [1] [kJ/day] | BM [1] [kg] | BF [1] [kg] | ANDR [1] [%] | QUICKI [1] | nonHDL-C [1] [mmol/l] | HDL-C [1] [mmol/l] | LEP [1] [ng/ml] | OMEN [1] [ng/ml] |
|---|---|---|---|---|---|---|---|---|---|---|
| LEP EG1 [ng/ml] | −0.37 * | 0.28 * | 0.28 * | 0.39 * | 0.39 * | −0.45 * | 0.50 * | −0.43 * | 1.00 | 0.16 |
| LEP EG2 [ng/ml] | −0.21 | 0.09 | 0.73 * | 0.88 * | 0.87 * | −0.53 * | −0.28 | −0.09 | 1.00 | 0.03 |
| LEP CG [ng/ml] | −0.25 | 0.26 | 0.42 * | 0.51 * | 0.47 * | −0.20 | −0.09 | −0.02 | 1.00 | −0.01 |
| OMEN EG1 [ng/ml] | −0.14 | 0.14 | 0.09 | 0.14 | 0.13 | −0.07 | 0.25 | −0.06 | 0.16 | 1.00 |
| OMEN EG2 [ng/ml] | 0.27 | 0.32 | 0.19 | 0.08 | 0.18 | −0.27 | −0.39 * | 0.15 | 0.03 | 1.00 |
| OMEN CG [ng/ml] | −0.15 | −0.03 | −0.39 * | −0.36 | −0.25 | 0.27 | −0.34 | 0.31 * | −0.01 | 1.00 |
| QUICKI EG1 | 0.29 * | −0.35 * | −0.67 * | −0.61 * | −0.56 * | 1.00 | −0.30 | 0.72 * | −0.45 * | −0.07 |
| QUICKI EG2 | 0.20 | −0.22 | −0.64 * | −0.55 * | −0.44 * | 1.00 | 0.44 | 0.27 | −0.53 * | −0.27 |
| QUICKI CG | 0.10 | 0.04 | −0.41 * | −0.33* | −0.25 | 1.00 | −0.24 | 0.28* | −0.20 | 0.27 |

*—statistically significant value $p < 0.05$; LEP EG1—concentrations of leptin in EG1 taken from the four timepoints; LEP EG2—concentrations of leptin in EG2 taken from the four timepoints; LEP CG—concentrations of leptin in CG taken from the four timepoints; OMEN EG1—concentrations of omentin in EG1 taken from the four timepoints; OMEN EG2—concentrations of omentin in EG2 taken from the four timepoints; OMEN CG—concentrations of omentin CG taken from the four timepoints, MET—metabolic equivalent of task, BM—body mass, BF—body fat, ANDR—android body fat, QUICKI—quantitative insulin sensitivity check index, nonHDL-C—non-high-density lipoprotein, HDL-C—high-density lipoprotein, [1]—taken from the four timepoints, corresponding to the group and measurement week in column 1.

The applied multiple regression model showed a significant connection of BF with the concentration of LEP ($p < 0.05$). The variability of LEP was explained by the analysed variables in 10% (value of $R^2$ model = 0.10) (Table 6).

**Table 6.** Parameters of multiple regression model of the leptin (LEP) dependent variable.

| Dependent Variable | Parameter Assessment | Standard Error | t Value | *p*-Value |
|---|---|---|---|---|
| Free parameter | 5.98 | 6.42 | 0.93 | 0.35 |
| BF [kg] | 0.31 | 0.06 | 4.98 | <0.001 |
| QUICKI | −28.05 | 14.88 | −1.89 | 0.06 |

Free parameter—intercept, BF—body fat, QUICKI—quantitative insulin sensitivity check index.

## 4. Discussion

The aim of the study was to assess the influence of two types of physical training (aerobic vs. combined aerobic-resistance) realised for 12 weeks in a group of males with MetS on changes in body composition, concentrations of leptin (LEP) and omentin (OMEN), and MetS indexes in comparison with the control group. The research results confirmed significant changes occurring in the level of LEP under the influence of the applied exercise interventions, but also in the control group fluctuations of the hormone were observed. The obtained results indicate a significant correlation between LEP and the place of its synthesis, i.e., adipose tissue, including visceral fat and the change taking place in the fat tissue during the interventions. The favourable influence of aerobic and combined aerobic-resistance training was also confirmed on the insulin resistance index QUICKI whose changes were significantly related to changes occurring in LEP. The required level of significance needed to confirm changes in the levels of OMEN, HDL-C and nonHDL-C was not achieved.

The present study confirmed the variability in LEP concentration between measurements in all groups, however, the biological behaviour of the hormone differed in each of the analysed groups. After 6 weeks of intervention, there was an increase in LEP concentration in the aerobic group, but the extension of the intervention time to 12 weeks was associated with a downward trend in LEP concentration in our study. In a meta-analysis Yu et al. presented several reports that aerobic exercise has a significant effect on lowering serum LEP levels [47]. In the study by Klempel et al. [48], it was shown that even a small weight loss (4–5%) can have a beneficial effect on LEP concentration. In the case of a weight loss of 2.4%, there was a decrease in serum LEP concentration [49]. In our study, despite the initial weight loss, the LEP concentration increased in the EG1 group after 6 weeks of intervention. The increase in LEP levels despite the use of aerobic training could be the result of other factors beyond our control. The study was conducted during the COVID-19 pandemic and, among others, increased anxiety levels due to the ongoing lockdown [50], less sleep [51], and increased stress levels [52] are factors connected with the fluctuation of hormones [53].

However, in the group with the aerobic-resistance intervention, a decrease in LEP concentration was confirmed both after 6 and 12 weeks of the intervention. LEP values in the EG2 group were significantly lower after 6 weeks compared to the CG group and after 16 weeks compared to the EG1 group. Due to the observed decreases in the LEP value in the EG2 group between measurements and differences between the groups, our results indicate a more beneficial effect of aerobic-resistance training than aerobics alone or no physical activity on the level of LEP. Such changes may relate to inflammation reduction in response to resistance-aerobic training [39]. Different results were obtained by the authors in the population study of people with MetS, in which Nordic Walking (NW) training at the level of 65–75% HR max or resistance training for a period of 12 weeks was used. Researchers did not confirm a change in LEP concentration in people practising resistance training, but they confirmed a decrease in LEP level by 27% in a group using NW [49]. Such direction of changes can result from the lack of changes in fat free mass (FFM) in any of the groups and a higher reduction of fat tissue in the NW group. Other studies have shown that LEP concentration decreased by 21% during a 3-month dynamic resistance training program [53] and by 14% during a 6-month program combining diet with moderate activity [54]. The scientists found out that LEP ameliorates the level of mRNA peroxisome proliferator-activated receptor gamma co-activator 1 (PGC-1) in the skeletal muscles and exercise of higher intensity can influence the adaptive decrease of LEP level [55,56].

In our research, an increase in the level of LEP concentration in CG was registered, which may be associated with the development of leptin resistance in individual people with MetS, not undertaking physical activity.

Our study showed positive correlations between LEP concentration and BF in each group, which confirms the reports that serum LEP concentration depends mainly on adipose tissue mass [57]. Despite reports that subcutaneous adipocytes secrete more LEP than visceral adipocytes [58], our study confirmed positive correlations between LEP and the level of ANDR in each group. Correlation values between LEP and BF and ANDR are very similar, which may indicate a similar level of LEP synthesis in subcutaneous and visceral adipose tissue in the population of people with MetS.

Negative correlations between LEP and QUICKI and statistical variability in both groups in the case of LEP and QUICKI confirm a highly probable cause-and-effect relationship of the effect of LEP on the level of insulin resistance in people with MetS. A similar correlation between LEP and QUICKI in MetS was confirmed by other researchers [59].

The obtained results confirm a strict relationship between LEP and the level of total and visceral adipose tissues which are the place of its synthesis [60]. The process of leptin resistance, occurring in obesity, plays the key role in complications connected with its course [61]. The results of our research confirm a high concentration of LEP in the population of people with MetS and obesity as well as a correlation between LEP and QUICKI. The therapeutic potential resulting from applying aerobic training and the combination of resistance and aerobic training, offers perspectives in treating and preventing MetS and obesity through influencing the reduction of the adipose tissue level and, consequently, a decrease of LEP level and insulin resistance.

The results of our work indicate a growing trend of mean concentrations of omentin (OMEN) in subsequent weeks of the aerobic intervention, however, the changes in OMEN values did not reach statistical significance. In the study of de Souza Batista et al. the authors emphasize the influence of exercise intervention in increasing OMEN concentrations [13]. An increase in the concentration of circulating omentin was also observed in people who underwent a 12-week aerobic training and whose level of fat content in the body decreased [62].

The main site of OMEN synthesis is visceral fat [25], therefore, in order to understand the variability of the presented hormone, we used the results estimated by the DEXA method. Analysing the level of visceral fat in the group subjected to aerobic intervention, its gradual decrease of 3.8% over 16 weeks was confirmed. In the group with aerobic-resistance intervention, its decrease in the same period by 3.3% was also confirmed, but it was not a significant change. Despite reports of a negative correlation between the level of OMEN and BMI, waist circumference and the level of visceral fat [13], our study did not confirm the correlation between the level of OMEN and the level of total and visceral fat in any of the groups. A possible reason for not achieving a significant increase in the OMEN concentration in the intervention groups may be insufficient loss of visceral fat. Weight loss is considered a key factor in an intervention to reduce pro-inflammatory cytokine levels and increase anti-inflammatory cytokine levels [63,64]. Achieving greater weight loss in individuals with MetS could result in clinically beneficial changes in OMEN concentrations. Similar relationships were confirmed by researchers in the case of other adipokines. Among patients achieving a weight loss of 4–5%, no significant changes in the concentrations of adiponectin, IL-6 and RBP4 were confirmed, while the concentration of LEP decreased [48]. The effect of lowering the OMEN concentration was achieved, among others, in a study with dietary intervention, where a low-energy diet (deficit of 500–1000 kcal per day) was used for 4 months. As a result of the intervention, a reduction in body weight of 13.8% was obtained. Researchers confirmed a decrease in LEP concentration by 60.6% and a significant increase in OMEN concentration by 22.1% [65].

Our study did not confirm the correlation between OMEN and LEP concentration and insulin resistance indices. The positive relationship between HDL-C and the level of OMEN was confirmed in CG. Despite the fact that OMEN is considered an adipokine

whose important function is to influence the level of insulin resistance [18,30], no correlation between omentin and QUICKI was confirmed in any of the analysed groups. The significant correlations between visceral and total adipose tissue and the index of insulin resistance can be explained by the fact that the disproportionate accumulation of fat in the abdominal region is associated with reduced insulin-mediated glucose transport. Increased pancreatic beta cell apoptosis, necrosis or autophagy may be involved in beta cell dysfunction in MetS [66].

The results of our study indicate that HDL-C level increased by 5.8% in the aerobic intervention group and by 8.3% in the aerobic-resistance group over 16 weeks, although the changes were not significant. In the meta-analysis of studies analysing the impact of physical activity on lipid parameters, it was confirmed that the use of a combination of resistance and aerobic training over 12 weeks led to an increase in HDL-C from 3.5% to 23% [67]. The meta-analysis of studies on the subject of the lipid profile in people using resistance training also showed beneficial changes in nonHDL-C and HDL-C in people with the intervention [68]. Despite numerous reports on the beneficial effect of physical exercise on the level of nonHDL-C, no significant beneficial changes in the described parameter were observed in our studies. An increase in HDL-C concentration and a decrease in nonHDL-C concentration have been confirmed in other intervention studies using physical activity in the treatment of MetS [69]. Undertaking resistance training can lead to a 6% decrease in nonHDL-C levels and an increase in HDL-C levels by 1%. In the case of aerobic training, a decrease in nonHDL-C by 2.5% and an increase by 4% in HDL-C were confirmed [70]. No changes in HDL-C and nonHDL-C levels despite the intervention could result from the proportion of fatty acids supplied in the diet [71].

The study is not free from some limitations. The presented results show changes in LEP, OMEN concentrations and biochemical parameters under the influence of intervention in the form of physical activity, however, people participating in the study may have been exposed to other factors, such as increased stress levels, a limited amount of sleep, etc. that may affect the level of the presented parameters. Due to the long period of the study, the initial number of participants was reduced, which could have resulted in the lack of statistical significance in some measured parameters. During the follow-up procedure, the VO2 max test was not performed, which would allow monitoring of training adaptation in the intervention groups. Despite the initial assumptions of maintaining the current diet and constant control of the diet of the study participants, the amount of energy supplied in food increased. Describing the diet, no detailed analysis of fatty acids that could affect the lipid profile of the study participants was made.

To summarise, the use of a combination of resistance and aerobic training in men with MetS leads to a decrease in LEP concentration. Obtaining results is more beneficial when using a combination of two forms of exercise compared to using aerobic training alone. Taking up physical activity did not lead to significant changes in the concentration of OMEN in men with MetS. The use of aerobic training as well as a combination of aerobic and resistance training results in beneficial changes in the level of insulin resistance and body composition. However, a combination of aerobic and resistance training led to greater benefits in reducing the level of BF, BM, and ANDR. Leptin is an important adipokine whose significant relations with body composition and the level of insulin resistance in the population of males with MetS indicate that application of physical training in order to improve health conditions features a therapeutic potential. The use of a combination of aerobic and resistance training had a direct impact on the decrease in leptin levels during the 12-week intervention period. Explaining the role of OMEN in the process of MetS treatment support through introducing physical exercise requires a higher number of tests.

**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/jcm12082822/s1, Figure S1: A comprehensive strategy for aerobic program intended for a group engaged in aerobic activities (EG1). Table S1: A comprehensive strategy for a combined aerobic and resistance training program intended for a group engaged in aerobic-resistance activities (EG2). Table S2: The progressions of loads [kg] in selected resistance exercises

during the intervention and follow-up in comparison to baseline in the aerobic-resistance group EG2. References [44,72] are cited in Supplementary Materials.

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**Institutional Review Board Statement:** The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Regional Medical Chamber in Cracow, No. 90/KBL/OK/2020. This study is also registered as a clinical trial in ANZCTR 12622001394730 (registration number).

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

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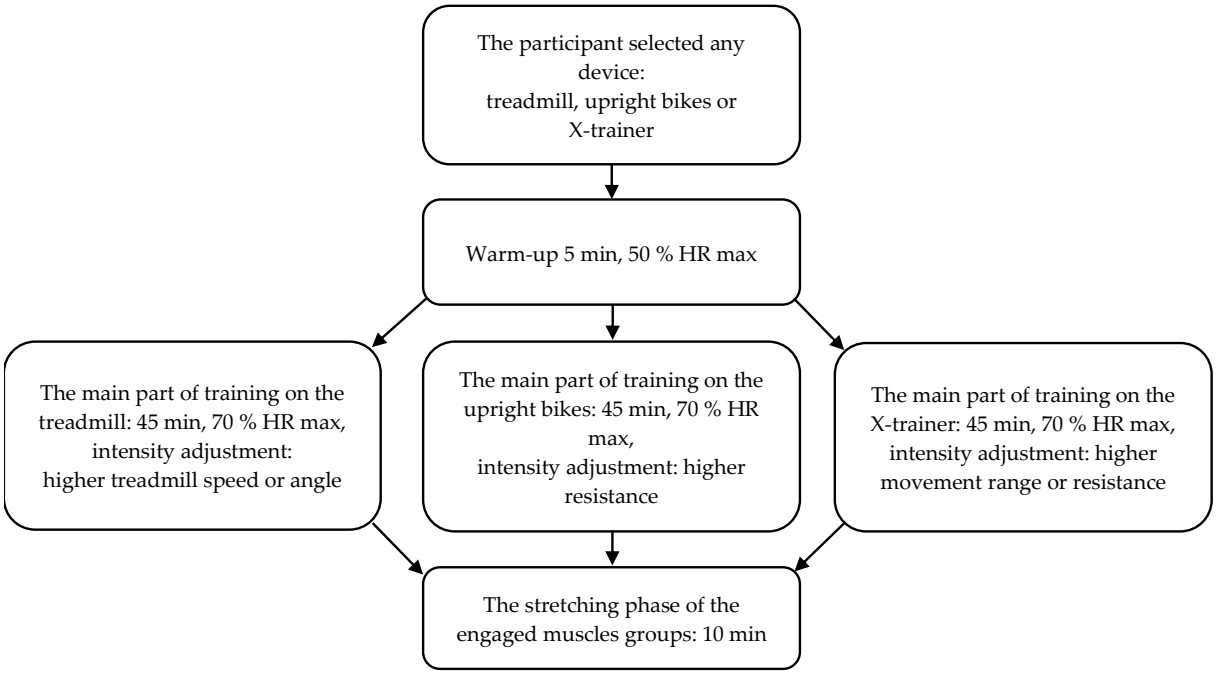
## References

1. Swarup, S.; Goyal, A.; Grigorova, Y.; Zeltser, R. Metabolic Syndrome. In *StatPearls*; StatPearls Publishing: Treasure Island, FL, USA, 2022.
2. Wolin, K.Y.; Carson, K.; Colditz, G.A. Obesity and cancer. *Oncologist* **2010**, *15*, 556–565. [CrossRef] [PubMed]
3. Ohashi, K.; Shibata, R.; Murohara, T.; Ouchi, N. Role of anti-inflammatory adipokines in obesity-related diseases. *Trends Endocrinol. Metab.* **2014**, *25*, 348–355. [CrossRef] [PubMed]
4. Unger, R.H.; Scherer, P.E. Gluttony, sloth and the metabolic syndrome: A roadmap to lipotoxicity. *Trends Endocrinol. Metab.* **2010**, *21*, 345–352. [CrossRef]
5. Ouchi, N.; Parker, J.L.; Lugus, J.J.; Walsh, K. Adipokines in inflammation and metabolic disease. *Nat. Rev. Immunol.* **2011**, *11*, 85–97. [CrossRef] [PubMed]
6. Blüher, M. Vaspin in obesity and diabetes: Pathophysiological and clinical significance. *Endocrine* **2012**, *41*, 176–182. [CrossRef] [PubMed]
7. Fève, B.; Bastard, C.; Fellahi, S.; Bastard, J.-P.; Capeau, J. New adipokines. In *Annales D'endocrinologie*; Elsevier: Amsterdam, The Netherlands, 2016. [CrossRef]
8. Sahin-Efe, A.; Katsikeris, F.; Mantzoros, C.S. Advances in adipokines. *Metab. Clin. Exp.* **2012**, *61*, 1659–1665. [CrossRef]
9. Suder, A. Socioeconomic and lifestyle determinants of body fat distribution in young working males from Cracow, Poland. *Am. J. Hum. Biol.* **2008**, *20*, 100–109. [CrossRef]
10. Rodríguez, A.; Becerril, S.; Hernández-Pardos, A.W.; Frühbeck, G. Adipose tissue depot differences in adipokines and effects on skeletal and cardiac muscle. *Curr. Opin. Pharmacol.* **2020**, *52*, 1–8. [CrossRef]
11. Owecki, M.; Nikisch, E.; Miczke, A.; Pupek-Musialik, D.; Sowinski, J. Leptin, soluble leptin receptors, free leptin index, and their relationship with insulin resistance and BMI: High normal BMI is the threshold for serum leptin increase in humans. *Horm. Metab. Res.* **2010**, *42*, 585–589. [CrossRef]
12. Bremer, A.A.; Devaraj, S.; Afify, A.; Jialal, I. Adipose tissue dysregulation in patients with metabolic syndrome. *J. Clin. Endocrinol. Metab.* **2011**, *96*, E1782–E1788. [CrossRef]
13. de Souza Batista, C.M.; Yang, R.Z.; Lee, M.J.; Glynn, N.M.; Yu, D.Z.; Pray, J.; Ndubuizu, K.; Patil, S.; Schwartz, A.; Kligman, M.; et al. Omentin plasma levels and gene expression are decreased in obesity. *Diabetes* **2007**, *56*, 1655–1661. [CrossRef] [PubMed]
14. Chan, J.L.; Heist, K.; DePaoli, A.M.; Veldhuis, J.D.; Mantzoros, C.S. The role of falling leptin levels in the neuroendocrine and metabolic adaptation to short-term starvation in healthy men. *J. Clin. Investig.* **2003**, *111*, 1409–1421. [CrossRef] [PubMed]
15. Coppari, R.; Ramadori, G.; Elmquist, J.K. The role of transcriptional regulators in central control of appetite and body weight. *Nat. Rev. Endocrinol.* **2009**, *5*, 160–166. [CrossRef] [PubMed]
16. Malli, F.; Papaioannou, A.I.; Gourgoulianis, K.I.; Daniil, Z. The role of leptin in the respiratory system: An overview. *Respir. Res.* **2010**, *11*, 152. [CrossRef] [PubMed]
17. Veniant, M.M.; LeBel, C.P. Leptin: From animals to humans. *Curr. Pharm. Des.* **2003**, *9*, 811–818. [CrossRef]

18. Wabitsch, M.; Ballauff, A.; Holl, R.; Blum, W.F.; Heinze, E.; Remschmidt, H.; Hebebrand, J. Serum leptin, gonadotropin, and testosterone concentrations in male patients with anorexia nervosa during weight gain. *J. Clin. Endocrinol. Metab.* **2001**, *86*, 2982–2988. [CrossRef]
19. Suder, A.; Płonka, M.; Jagielski, P.; Piórecka, B.; Głodzik, J. Physiological and environmental factors associated with central fat distribution in pubertal girls. *J. Physiol. Pharmacol.* **2015**, *66*, 463–470.
20. Martin, S.S.; Qasim, A.; Reilly, M.P. Leptin resistance: A possible interface of inflammation and metabolism in obesity-related cardiovascular disease. *J. Am. Coll. Cardiol.* **2008**, *52*, 1201–1210. [CrossRef]
21. Tabak, A.G.; Brunner, E.J.; Miller, M.A.; Karanam, S.; McTernan, P.G.; Cappuccio, F.P.; Witte, D.R. Low serum adiponectin predicts 10-year risk of type 2diabetes and HbA1c independently of obesity, lipids, and inflammation: Whitehall II study. *Horm. Metab. Res.* **2009**, *41*, 626–629. [CrossRef]
22. Mattu, H.S.; Randeva, H.S. Role of adipokines in cardiovascular disease. *J. Endocrinol.* **2013**, *216*, T17–T36. [CrossRef]
23. Liao, L.M.; Schwartz, K.; Pollak, M.; Graubard, B.I.; Li, Z.; Ruterbusch, J.; Rothman, N.; Davis, F.; Wacholder, S.; Colt, J.; et al. Serum Leptin and Adiponectin Levels and Risk of Renal Cell Carcinoma. *Obesity* **2013**, *21*, 1478–1485. [CrossRef]
24. Arditi, J.D.; Venihaki, M.; Karalis, K.P.; Chrousos, G.P. Antiproliferative effect of adiponectin on MCF7 breast cancer cells: A potential hormonal link between obesity and cancer. *Horm. Metab. Res.* **2007**, *39*, 9–13. [CrossRef] [PubMed]
25. Yang, R.Z.; Lee, M.J.; Hu, H.; Pray, J.; Wu, H.B.; Hansen, B.C.; Shuldiner, A.R.; Fried, S.K.; McLenithan, J.C.; Gong, D.W. Identification of omentin as a novel depot-specific adipokine in human adipose tissue: Possible role in modulating insulin action. *Am. J. Physiol. Endocrinol. Metab.* **2006**, *290*, E1253–E1261. [CrossRef] [PubMed]
26. Li, Z.G.; Zhao, D.; Xia, C.J.; Wang, T.N.; Liu, Y.P.; Zhang, Y.; Wang, B.J. Decreased synovial fluid omentin-1 concentrations reflect symptomatic severity in patients with knee osteoarthritis. *Scand. J. Clin. Lab. Investig.* **2012**, *72*, 623–628. [CrossRef] [PubMed]
27. Fu, M.; Gong, D.W.; Damcott, C.; Sabra, M.; Yang, R.; Pollin, T. Systematic analysis of omentin 1 and omentin 2 on 1q23 as candidate genes for type 2 diabetes in the old order amish. *Diabetes* **2004**, *53*, 59.
28. Tan, B.K.; Pua, S.; Syed, F.; Lewandowski, K.C.; O'Hare, J.P.; Randeva, H.S. Decreased plasma omentin-1 levels in Type 1 diabetes mellitus. *Diabet. Med.* **2008**, *25*, 1254–1255. [CrossRef]
29. Yan, P.; Liu, D.; Long, M.; Ren, Y.; Pang, J.; Li, R. Changes of Serum Omentin Levels and Relationship between Omentin and Adiponectin Concentrations in Type 2 Diabetes Mellitus. *Exp. Clin. Endocrinol. Diabetes* **2011**, *119*, 257–263. [CrossRef]
30. Wilms, B.; Ernst, B.; Gerig, R.; Schultes, B. Plasma omentin-1 levels are related to exercise performance in obese women and increase upon aerobic endurance training. *Exp. Clin. Endocrinol. Diabetes* **2015**, *123*, 187–192. [CrossRef]
31. Suder, A. Body fatness and its social and lifestyle determinants in young working males from Cracow, Poland. *J. Biosoc. Sci.* **2009**, *41*, 139–154. [CrossRef]
32. Donnelly, J.E.; Blair, S.N.; Jakicic, J.M.; Manore, M.M.; Rankin, J.W.; Smith, B.K. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Med. Sci. Sports Exerc.* **2009**, *41*, 459–471. [CrossRef]
33. Dieli-Conwright, C.M.; Courneya, K.S.; Demark-Wahnefried, W.; Sami, N.; Lee, K.; Buchanan, T.A.; Spicer, D.V.; Tripathy, D.; Bernstein, L.; Mortimer, J.E. Effects of Aerobic and Resistance Exercise on Metabolic Syndrome, Sarcopenic Obesity, and Circulating Biomarkers in Overweight or Obese Survivors of Breast Cancer: A Randomized Controlled Trial. *J. Clin. Oncol.* **2018**, *36*, 875–883. [CrossRef] [PubMed]
34. Myers, J.; Kokkinos, P.; Nyelin, E. Physical Activity, Cardiorespiratory Fitness, and the Metabolic Syndrome. *Nutrients* **2019**, *11*, 1652. [CrossRef]
35. Bray, G.A.; Heisel, W.E.; Afshin, A.; Jensen, M.D.; Dietz, W.H.; Long, M.; Kushner, R.F.; Daniels, S.R.; Wadden, T.A.; Tsai, A.G.; et al. The science of obesity management: An endocrine society scientific statement. *Endocr. Rev.* **2018**, *39*, 79–132. [CrossRef] [PubMed]
36. Golbidi, S.; Laher, I. Exercise induced adipokine changes and the metabolic syndrome. *J. Diabetes Res.* **2014**, *2014*, 726861. [CrossRef] [PubMed]
37. You, T.; Nicklas, B.J.; Ding, J.; Penninx, B.W.J.H.; Goodpaster, B.H.; Bauer, D.C.; Tylavsky, F.A.; Harris, T.B.; Kritchevsky., S.B. The metabolic syndrome is associated with circulating adipokines in older adults across a wide range of adiposity. *J. Gerontol. Ser. A Biol. Sci. Med. Sci.* **2008**, *63*, 414–419. [CrossRef]
38. Parameshwar, A.; Maiya, G.A.; Kamath, S.U.; Shastry, B.A. Lifestyle Modification with Physical Activity Promotion on Leptin Resistance and Quality of Life in Metabolic Syndrome—A Systematic Review with Meta-Analysis. *Curr. Diabetes Rev.* **2021**, *17*, 345–355. [CrossRef]
39. Makiel, K.; Suder, A.; Targosz, A.; Maciejczyk, M.; Haim, A. Effect of exercise interventions on irisin and interleukin-6 concentrations and indicators of carbohydrate metabolism in males with metabolic syndrome. *J. Clin. Med.* **2023**, *12*, 369. [CrossRef] [PubMed]
40. Alberti, K.G.; Zimmet, P.; Shaw, J. Metabolic syndrome—A new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabet. Med.* **2006**, *23*, 469–480. [CrossRef]
41. Katz, A.; Nambi, S.S.; Mather, K.; Baron, A.D.; Follmann, D.A.; Sullivan, G.; Quon, M.J. Quantitative insulin sensitivity check index: A simple, accurate method for assessing insulin sensitivity in humans. *J. Clin. Endocrinol. Metab.* **2000**, *85*, 2402–2410. [CrossRef]

42. Ainsworth, B.E.; Haskell, W.L.; Herrmann, S.D.; Meckes, N.; Bassett, D.R., Jr.; Tudor-Locke, C.; Greer, J.L.; Vezina, J.; Whitt-Glover, M.C.; Leon, A.S. 2011 Compendium of Physical Activities: A second update of codes and MET values. *Med. Sci. Sports Exerc.* **2011**, *43*, 1575–1581. [CrossRef]
43. Garber, C.E.; Blissmer, B.; Deschenes, M.R.; Franklin, B.A.; Lamonte, M.J.; Lee, I.M.; Nieman, D.C.; Swain, D.P. American College of Sports Medicine. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Med. Sci. Sports Exerc.* **2011**, *43*, 1334–1359. [CrossRef] [PubMed]
44. Grgic, J.; Lazinica, B.; Schoenfeld, B.J.; Pedisic, Z. Test–Retest Reliability of the One-Repetition Maximum (1RM) Strength Assessment: A Systematic Review. *Sports Med. Open* **2020**, *6*, 31. [CrossRef] [PubMed]
45. Levinger, I.; Goodman, C.; Hare, D.L.; Jerums, G.; Toia, D.; Selig, S. The reliability of the 1RM strength test for untrained middle-aged individuals. *J. Sci. Med. Sport* **2009**, *12*, 310–316. [CrossRef]
46. Fritz, C.O.; Morris, P.E.; Richler, J.J. Effect size estimates: Current use, calculations, and interpretation. *J. Exp. Psychol. Gen.* **2012**, *141*, 2–18. [CrossRef] [PubMed]
47. Yu, N.; Ruan, Y.; Gao, X.; Sun, J. Systematic Review and Meta-Analysis of Randomized, Controlled Trials on the Effect of Exercise on Serum Leptin and Adiponectin in Overweight and Obese Individuals. *Horm. Metab. Res.* **2017**, *49*, 164–173. [CrossRef]
48. Klempel, M.C.; Varady, K.A. Reliability of leptin, but not adiponectin, as a biomarker for diet-induced weight loss in humans. *Nutr. Rev.* **2011**, *69*, 145–154. [CrossRef] [PubMed]
49. Venojärvi, M.; Wasenius, N.; Manderoos, S.; Heinonen, O.J.; Hernelahti, M.; Lindholm, H.; Surakka, J.; Lindström, J.; Aunola, S.; Atalay, M.; et al. Nordic walking decreased circulating chemerin and leptin concentrations in middle-aged men with impaired glucose regulation. *Ann. Med.* **2013**, *45*, 162–170. [CrossRef]
50. Cénat, J.M.; Blais-Rochette, C.; Kokou-Kpolou, C.K.; Noorishad, P.G.; Mukunzi, J.N.; McIntee, S.E.; Dalexis, R.D.; Goulet, M.A.; Labelle, P.R. Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: A systematic review and meta-analysis. *Psychiatry Res.* **2021**, *295*, 113599. [CrossRef]
51. Lin, J.; Jiang, Y.; Wang, G.; Meng, M.; Zhu, Q.; Mei, H.; Liu, S.; Jiang, F. Associations of short sleep duration with appetite-regulating hormones and adipokines: A systematic review and meta-analysis. *Obes. Rev.* **2020**, *21*, e13051. [CrossRef]
52. Bouillon-Minois, J.B.; Trousselard, M.; Thivel, D.; Benson, A.C.; Schmidt, J.; Moustafa, F.; Bouvier, D.; Dutheil, F. Leptin as a Biomarker of Stress: A Systematic Review and Meta-Analysis. *Nutrients* **2021**, *13*, 3350. [CrossRef]
53. Klimcakova, E.; Polak, J.; Moro, C.; Hejnova, J.; Majercik, M.; Viguerie, N.; Berlan, M.; Langin, D.; Stich, V. Dynamic strength training improves insulin sensitivity without altering plasma levels and gene expression of adipokines in subcutaneous adipose tissue in obese men. *J. Clin. Endocrinol. Metab.* **2006**, *91*, 5107–5112. [CrossRef] [PubMed]
54. Monzillo, L.U.; Hamdy, O.; Horton, E.S.; Ledbury, S.; Mullooly, C.; Jarema, C.; Porter, S.; Ovalle, K.; Moussa, A.; Mantzoros, C.S. Effect of lifestyle modification on adipokine levels in obese subjects with insulin resistance. *Obes. Res.* **2003**, *11*, 1048–1054. [CrossRef] [PubMed]
55. Casuso, R.A.; Plaza-Díaz, J.; Ruiz-Ojeda, F.J.; Aragón-Vela, J.; Robles-Sanchez, C.; Nordsborg, N.B.; Hebberecht, M.; Salmeron, L.M.; Huertas, J.R. High-intensity high-volume swimming induces more robust signaling through PGC-1$\alpha$ and AMPK activation than sprint interval swimming in m. triceps brachii. *PLoS ONE* **2017**, *12*, e0185494. [CrossRef] [PubMed]
56. Hsu, W.H.; Lee, B.H.; Pan, T.M. Leptin-induced mitochondrial fusion mediates hepatic lipid accumulation. *Int. J. Obes.* **2015**, *39*, 1750–1756. [CrossRef] [PubMed]
57. Williams, K.W.; Scott, M.M.; Elmquist, J.K. From observation to experimentation: Leptin action in the mediobasal hypothalamus. *Am. J. Clin. Nutr.* **2009**, *89*, 985S–990S. [CrossRef]
58. Van Harmelen, V.; Reynisdottir, S.; Eriksson, P.; Thörne, A.; Hoffstedt, J.; Lönnqvist, F.; Arner, P. Leptin secretion from subcutaneous and visceral adipose tissue in women. *Diabetes* **1998**, *47*, 913–917. [CrossRef] [PubMed]
59. Gannagé-Yared, M.H.; Khalife, S.; Semaan, M.; Fares, F.; Jambart, S.; Halaby, G. Serum adiponectin and leptin levels in relation to the metabolic syndrome, androgenic profile and somatotropic axis in healthy non-diabetic elderly men. *Eur. J. Endocrinol.* **2006**, *155*, 167–176. [CrossRef] [PubMed]
60. Obradovic, M.; Sudar-Milovanovic, E.; Soskic, S.; Essack, M.; Arya, S.; Stewart, A.J.; Gojobori, T.; Isenovic, E.R. Leptin and Obesity: Role and Clinical Implication. *Front. Endocrinol.* **2021**, *12*, 585887. [CrossRef]
61. Izquierdo, A.G.; Crujeiras, A.B.; Casanueva, F.F.; Carreira, M.C. Leptin, Obesity, and Leptin Resistance: Where Are We 25 Years Later? *Nutrients* **2019**, *8*, 2704. [CrossRef]
62. Saremi, A.; Asghari, M.; Ghorbani, A. Effects of aerobic training on serum omentin-1 and cardiometabolic risk factors in overweight and obese men. *J. Sports Sci.* **2010**, *28*, 993–998. [CrossRef]
63. Puglisi, M.J.; Fernandez, M.L. Modulation of C-reactive protein, tumor necrosis factor-alpha, and adiponectin by diet, exercise, and weight loss. *J. Nutr.* **2008**, *138*, 2293–2296. [CrossRef] [PubMed]
64. Belza, A.; Toubro, S.; Stender, S.; Astrup, A. Effect of diet-induced energy deficit and body fat reduction on high-sensitive CRP and other inflammatory markers in obese subjects. *Int. J. Obes.* **2009**, *33*, 456–464. [CrossRef] [PubMed]
65. Moreno-Navarrete, J.M.; Catalán, V.; Ortega, F.; Gómez-Ambrosi, J.; Ricart, W.; Frühbeck, G.; Fernández-Real, J.M. Circulating omentin concentration increases after weight loss. *Nutr. Metab.* **2010**, *7*, 27. [CrossRef]

66. Endukuru, C.K.; Gaur, G.S.; Yerrabelli, D.; Sahoo, J.; Vairappan, B. Cut-off Values and Clinical Utility of Surrogate Markers for Insulin Resistance and Beta-Cell Function to Identify Metabolic Syndrome and Its Components among Southern Indian Adults. *J. Obes. Metab. Syndr.* **2020**, *29*, 281–291. [CrossRef] [PubMed]
67. Tambalis, K.; Panagiotakos, D.B.; Kavouras, S.A.; Sidossis, L.S. Responses of blood lipids to aerobic, resistance, and combined aerobic with resistance exercise training: A systematic review of current evidence. *Angiology* **2009**, *60*, 614–632. [CrossRef] [PubMed]
68. Kelley, G.A.; Kelley, K.S. Impact of progressive resistance training on lipids and lipoproteins in adults: A meta-analysis of randomized controlled trials. *Prev. Med.* **2009**, *48*, 9–19. [CrossRef]
69. Zając-Gawlak, I.; Pelclová, J.; Groffik, D.; Přidalová, M.; Nawrat-Szołtysik, A.; Kroemeke, A.; Gába, A.; Sadowska-Krępa, E. Does physical activity lower the risk for metabolic syndrome: A longitudinal study of physically active older women. *BMC Geriatr.* **2021**, *21*, 11. [CrossRef]
70. Gordon, B.; Chen, S.; Durstine, J.L. The effects of exercise training on the traditional lipid profile and beyond. *Curr. Sports Med. Rep.* **2014**, *13*, 253–259. [CrossRef]
71. Mensink, R.P.; Zock, P.L.; Kester, A.D.; Katan, M.B. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: A meta-analysis of 60 controlled trials. *Am. J. Clin. Nutr.* **2003**, *77*, 1146–1155. [CrossRef]
72. Brzycki, M. Strength Testing—Predicting a One-Rep Max from Reps-to-Fatigue. *J. Phys. Educ. Recreat. Dance* **1993**, *64*, 88–90. [CrossRef]




HR max – maximal heart rate

**Figure S1.** A comprehensive strategy for aerobic program intended for a group engaged in aerobic activities (EG1).

**Table S1.** A comprehensive strategy for a combined aerobic and resistance training program intended for a group engaged in aerobic-resistance activities (EG2).

| | **Trainings 1 - 3** | **Trainings 4 - 6** | **Trainings 6 <** |
|---|---|---|---|
| Type of training | Whole body training | Training of antagonistic parts | Training of antagonistic parts |
| Volume of resistance training [exercises x series x repetitions] | 3 x 4 x 15 | 6 x 3 x 12 | 9 x 3 x 12 |
| Intensity of resistance training [% 1 RM] | 50 | 70 | 70 |
| Breaks between series [min] | 2 | 1.5 | 1 |
| Duration of resistance training [min] | 30 | 35 | 40 |
| Duration of aerobic training [min] | 20 | 15 | 10 |
| Intensity of aerobic | 50 | 70 | 70 |

| | | | |
|---|---|---|---|
| training [% HR max] | | | |
| Specialised exercises | One arm row with dumbbell<br>Supported push-ups (Smith machine)<br>Supported sit-ups (with bar)<br>Front support (plank) | Standing dumbbell press<br>Barbell bench press<br>Reverse grip lat pulldown<br>Hip thrust lying<br>Bent dumbbell row | Dumbbell deadlift<br>Cable tricep extension<br>Standing dumbbell curl |

HR max – maximal heart rate, 1RM – one repetition maximum.

**Table S2.** The progressions of loads [kg] in selected resistance exercises during the intervention and follow-up in comparison to baseline in the aerobic-resistance group EG2.

| Time of Observation | Barbell Bench Press [kg] | Lat Pull Down [kg] | Dumbbell Squat [kg] |
|---|---|---|---|
| Baseline | 63.36 ± 12.92 | 11.58 ± 2.56 | 44.51 ± 8.26 |
| After 6 weeks of intervention | 72.78 ± 14.77 | 13.15 ± 2.84 | 51.77 ± 9.84 |
| After 12 weeks of intervention | 76.65 ± 15.04 | 14.89 ± 2.64 | 56.78 ± 9.77 |
| After 16 weeks, follow up period | 79.32 ± 17.29 | 14.91 ± 2.02 | 57.74 ± 10.78 |
| *p*- value | 0.00 | 0.00 | 0.00 |

*p*-value – ANOVA test.

The course of 1RM:

The examined participants underwent the 1 RM test before the examination, and after 6, 12, and 16 weeks.

The personal coach carried out the warm-up on the treadmill (Technogym New Excite Run Now 500, Cesena, Italy) for 5 min at 60% HR. The subjects warmed-up in two series of 10 repetitions using about 50% of their 1 RM estimated load before the beginning of the test protocol.

After 5 min break, the subjects were instructed to do the selected test exercise till the lack of possibility to continue the series of exercise maintaining the proper technique (failure).

For the 1RM bench press test, the subjects were instructed to maintain 5-point body contact (i.e., head, back, and hips with the bench, and both feet with the floor) during the test, the barbell had to touch the chest when lowered.

In the 1RM squat test, subjects were instructed to move from a standing position to a position of 90 degrees of flexion at the knee joints.

The pull-down test was performed on a training atlas. The repetition was passed when the subject made a full extension of the arms during the eccentric phase and touching the bar to the chest during the concentric phase.

A qualified personal coach controlled the range of motion to verify the correctness of the test

The last repetition of a series occurred when the participant could not continue to exercise maintaining the proper technique.

The obtained load and number of repetitions were converted into 1 RM based on the 1 RM calculator [1], applying the Brzycki formula [2].

1. Grgic, J.; Lazinica, B.; Schoenfeld, B.J.; Pedisic, Z. Test-Retest Reliability of the One-Repetition Maximum (1RM) Strength Assessment: a Systematic Review. Sports Med. Open. 2020, 6, 31. doi: https://10.1186/s40798-020-00260-z.
2. Brzycki, M. Strength Testing—Predicting a One-Rep Max from Reps-to-Fatigue. J. Phys. Educ. Recreat. Dance. 1993, 64, 88-90. doi: https://10.1080/07303084.1993.10606684

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# Exercise-Induced Alternations of Adiponectin, Interleukin-8 and Indicators of Carbohydrate Metabolism in Males with Metabolic Syndrome

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**Abstract:** Adiponectin (ADIPO) and interleukin-8 (IL-8) are proteins that play a significant, albeit opposing, role in metabolic syndrome (MetS). The reported data on the effect of physical activity on the levels of these hormones in the population of people with MetS are conflicting. The aim of the study was to evaluate the changes in hormone concentrations, insulin-resistance indices and body composition after two types of training. The study included 62 men with MetS (age 36.6 ± 6.9 years, body fat [BF] = 37.53 ± 4.5%), randomly assigned to: an experimental group EG1 (n = 21) with aerobic exercise intervention, an experimental group EG2 (n = 21) with combined aerobic and resistance exercise intervention, both for 12 weeks, and a control group CG (n = 20) without interventions. Anthropometric measurements and body composition (fat-free mass [FFM], gynoid body fat [GYNOID]), as well as a biochemical blood analysis (adiponectin [ADIPO], interleukin-8 [IL-8], homeostatic model assessment—adiponectin (HOMA-AD) and homeostatic model assessment—triglycerides (HOMA-TG) were performed at baseline, and at 6 and 12 weeks of intervention and 4 weeks after the intervention (follow-up). Intergroup (between groups) and intragroup (within each group) changes were statistically evaluated. In the experimental groups EG1 and EG2, no significant changes were observed in the ADIPO concentration, but a decrease of GYNOID and insulin-resistance indices was confirmed. The aerobic training led to favorable changes in IL-8 concentration. The use of combined resistance and aerobic training led to improved body composition, decreased waist circumference and better insulin-resistance indices in men with MetS.

**Keywords:** adiponectin; interleukin-8; metabolic syndrome; obesity; physical activity; HOMA-AD; HOMA-TG



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## 1. Introduction

The criteria of metabolic syndrome (MetS) include central obesity, high blood pressure, lipid disorders and hyperglycemia [1]. MetS leads to many health consequences, including type 2 diabetes, gout [2], cardiovascular diseases (CVD), acute coronary syndrome, stroke, malignancies [3] and sleep apnea [4]. The scale of the MetS problem affects 20–25% of the adult urban population [5]. Obesity, especially central obesity, plays an important role in the development of MetS [6] and is associated with an increased risk of CVD, T2D and some cancers [7]. Each of the components of MetS can predispose patients to CVD, and the risk increases when a number of these components co-occur in one person [8,9].

The process of MetS and obesity treatment begins with lifestyle modification [10,11]. The key changes are the modification of the diet [12] and increased physical activity (PA). Insufficient levels of PA and a sedentary lifestyle are among the most important factors determining the development of MetS [13,14]. Physical exercise itself has a health-promoting effect, independent of weight loss, by acting on several mechanisms, including the inhibition of pro-inflammatory processes and the stimulation of anti-inflammatory pathways, as well as by affecting the synthesis of adipokines that regulate insulin sensitivity. High-intensity activity seems to give the best results, particularly the combination of aerobic and resistance exercises, which have achieved a significant anti-inflammatory effect in patients with type 2 diabetes and MetS [15], influencing the metabolism of the adipose tissue and skeletal muscles.

Both the adipose tissue and skeletal muscles are endocrine organs that conduct a specific dialogue, releasing cytokines, adipokines and myokines—hormones that reach their receptors, playing an important role in the homeostasis of the body [16,17]. They regulate, among other things, the energy and metabolic processes of the body [18,19]. The adipose tissue and skeletal muscles are key regulators of carbohydrate tolerance [20,21].

An example of information transferred from the adipose tissue to skeletal muscles is the production of adiponectin (ADIPO)—synthesized mainly in adipose tissue, whose Adipo1 receptors are located in the skeletal muscles. ADIPO also journeys to the Adipo2 receptor located in the liver [22]. It is responsible for fatty acids oxidation in skeletal muscles and the inhibition of glucose production in the liver, improving the energy homeostasis of the whole body. ADIPO has an anti-inflammatory function, reducing inflammation in various types of tissues [23]. Low levels of ADIPO have been observed in the population of people with MetS and abdominal obesity [24]. ADIPO has anti-atherosclerotic and insulin-sensitizing properties [25]. With respect to insulin sensitization, ADIPO has been shown to reduce blood glucose levels by inhibiting hepatic gluconeogenesis and enhancing insulin signaling in skeletal muscles [26].

As a marker of adipose tissue dysfunction, an index based on the ADIPO/LEP ratio (ADIPO/LEP ratio) has been introduced [27]. To calculate the ADIPO/LEP ratio, the concentration of circulating leptin (LEP) is used—a protein produced mainly by the adipose tissue in amounts proportional to the level of obesity. LEP is involved in the regulation of food intake, energy homeostasis and other physiological processes [28]. In obesity and MetS, the concentration of leptin increases, which is also a marker of inflammation [29]. The ADI-PO/LEP ratio is therefore a marker illustrating the pathophysiological function of both adipokines [27]. In addition, the ADIPO/LEP ratio decreases with an increase in the number of MetS risk factors [30]. An increase in the ADIPO/LEP ratio was associated in epidemiological studies with a reduced risk of atherosclerosis, as well as with a reduced risk of some types of cancer [27].

The cytokine interleukin-8 (IL-8), responsible for the increase of pro-inflammatory macrophages (M1) in adipose tissue, acts in opposition to ADIPO [31]. IL-8 is a pro-inflammatory cytokine synthesized, among others, in adipocytes, and its excessive production can lead to insulin resistance, type 2 diabetes and atherosclerosis [32–34]. Elevated levels of IL-8 have been observed among people with MetS [35], although there are reports indicating the opposite relationship [36]. Researchers have noted that exercise does not typically increase circulating IL-8 [37], despite evidence suggesting that IL-8 is released from skeletal muscle during exercise and acts locally [38].

Current knowledge on the impact of physical activity on the level of ADIPO, ADIPO/LEP ratio and IL-8 does not give clear conclusions and requires more studies, preferably clinical, randomized and with a group of more than 20 people [39]. Based on the fact that physical activity is beneficial for health [40], the aim of the study was to investigate how two types of 12-week exercise training affected the parameters of body composition, ADIPO concentrations, ADIPO/LEP ratio and IL-8, as well as indicators of insulin resistance in men with MetS and how the tested parameters changed after a 4-week observation without scheduled training. We hypothesized that aerobic–resistance training would be associated

with more favorable changes in hormone concentrations, i.e., an increase in ADIPO and a decrease in IL-8, with a decrease of insulin-resistance indices and an improvement in body composition, i.e., an increase in fat-free mass and a decrease in body fat and waist circumference, compared to aerobic training.

## 2. Materials and Methods

### *2.1. Study Design*

The study was designed as a randomized, prospective controlled study. A detailed description of the research methods was presented in previous papers [41,42]. The aim of this study was to compare the 12-week effect of two types of physical training on ADIPO and IL-8 levels and carbohydrate metabolism indices in men with metabolic syndrome (MetS), compared to men with MetS not undertaking physical activity (control group CG). The interventions involved applying aerobic training (EG1) and training combining resistance and aerobic exercise (EG2). Body composition parameters and selected indicators of the MetS were used to monitor changes. After 12 weeks of intervention, a period of 4 weeks of observation without scheduled training took place, in which the participants of the groups themselves decided on the number of training sessions or lack thereof.

The process of assigning to groups was carried out randomly; each of the study participants chose an opaque envelope with the group number. During the statistical analysis of the results and the performance of the biochemical determinations, the staff were unaware of the group assignment. Due to the form of the intervention or its absence, no blind trial was used.

The study involved 62 Caucasian men aged 30 to 45 (mean age 36.6 $\pm$ 6.9) who met the main selection criterion, concerning an increased waist circumference (WC) above 94 cm (which is one of the criteria for the diagnosis of MetS) and two of the other four MetS criteria for men: systolic (SBP) $\geq$ 130 mmHg or diastolic (DBP) $\geq$ 85 mmHg; HDL C < 1.03 mmol/L; triglycerides > 1.7 mmol/L; fasting plasma GL $\geq$ 5.6 mmol/L or drug treatment for the disorder presented (International Diabetes Federation, IDF) [43].

Participants were randomly assigned to 3 groups:

1. Experimental group: EG1 of men (age: 34.21 $\pm$ 6.06) with MetS (n = 21) performing aerobic exercise (BMI: 34.57 $\pm$ 4.58; BF: 38.03 $\pm$ 4.82);
2. Experimental group: EG2 of men (age: 37.37 $\pm$ 7.08) with MetS (n = 21) performing combined aerobic–resistance exercise (BMI: 33.14 $\pm$ 4.32; BF: 37.33 $\pm$ 4.30);
3. Control group: CG of men (age: 38.26 $\pm$ 7.43) with MetS (n = 20) who did not engage in any physical activity (BMI: 33.20 $\pm$ 4.31; BF: 37.22 $\pm$ 4.37).

There were no differences between age and basic somatic parameters before the interventions.

Apart from being male and meeting the MetS diagnosis, the following criteria were included in the study: age 30–45, medical certificate of no contraindications to undertake aerobic–resistance health training, and written consent for voluntary participation in the research project.

The exclusion criteria for the research project comprised: medical contraindications to resistance and aerobic training, too-low attendance at trainings in intervention groups (minimum attendance above 90%) and others, thoroughly presented in a previous paper [41].

The volunteers underwent training and received a written description of the objectives, procedures and the planned course of the research project. Each of the participants could withdraw from the study at any time without any consequences. During the project, there were situations leading to a reduction in the number of study participants. The main exclusion factor was absence during control measurements—9 participants. As a result of introducing excessive changes in diet (alcohol intake), 2 participants were excluded; as a result of infectious diseases, 3 participants were excluded; and as a result of too-low attendance during training, 3 patients were excluded (<90% attendance).

All subjects were trained by the same personal coach and asked not to change their diet, not to undertake physical activity other than with a trainer, and to maintain their

regimen of medications and dietary supplements during the observation. All participants of the study gave written consent to the processing of personal data, voluntary participation in the study and the use of the obtained results for scientific purposes. The research project was approved by the Ethics Committee of the District Medical Chamber in Krakow (90/KBL/OK/2020). The studies were registered in the register of clinical trials on the ANZCTR (Australian New Zealand Clinical Trials Registry) platform: ACTRN 12622001394730. The flowchart of the study is presented in Figure 1.

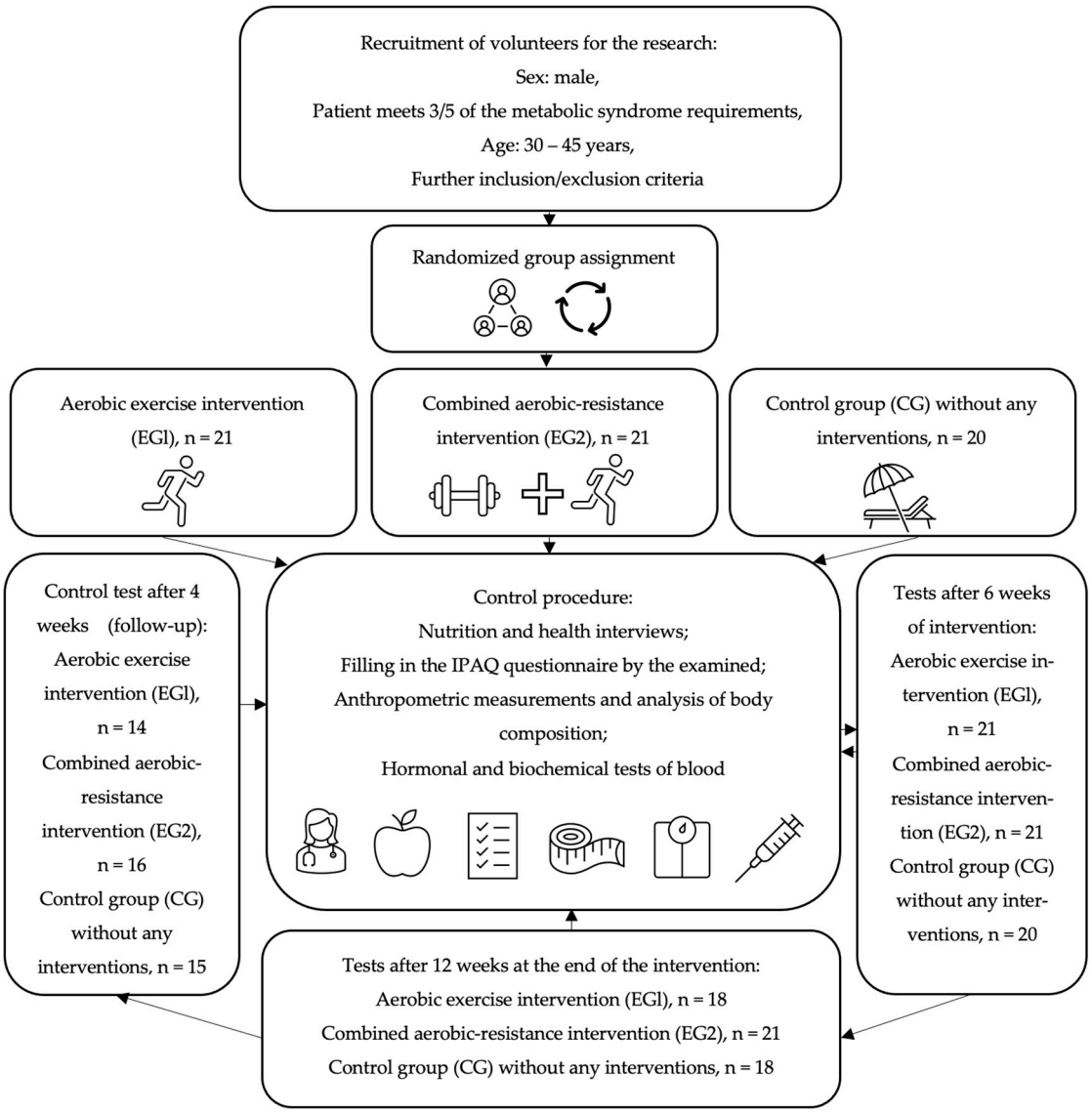


**Figure 1.** The flowchart of the study.

### *2.2. Methods*

The research project took 16 weeks, during which the evaluation was carried out 4 times: before the intervention, after 6 weeks of training, after 12 weeks of training and after 16 weeks of the project—the last 4 weeks was the period of observation without scheduled training. The following parameters were assessed during the control weeks.

#### 2.2.1. Anthropometry

Body mass (BM) [kg], body height (BH) [cm] and waist circumference (WC) [cm] were used in the study. BM, BH and WC were measured in a standing position, in underwear, with the head in the Frankfurt plane. BM was measured with a medical scale (Beurer PS

240, Budapest, Hungary) with an accuracy of 50 g. BH was measured with an accuracy of 1 mm with a stadiometer (Seca 231 stadiometer, Hamburg, Germany). Waist circumference (WC) was measured last during free exhalation using an anthropometric tape, between the upper edge of the iliac crest and the lower edge of the costal arch. Based on the obtained BM and BH, the body mass index (BMI) [kg/m$^2$] was calculated.

#### 2.2.2. Body Composition

Dual-Energy X-ray Absorptiometry (DEXA) was applied to assess body composition: fat-free mass (FFM) [%], body fat (BF) [%] and gynoid body fat (GYNOID) [%]. Evaluation of body composition was carried out with the Lunar Prodigy Primo PR+352163 (Chicago, IL, USA) device according to the manufacturer's guidelines.

#### 2.2.3. Hormones

Fasting blood samples were collected after a one day break from workout, in the morning, from the basilic, cephalic or median cubital vein into test tubes (Vacumed® system, F.L. Medical, Torreglia, Italy) by experienced nurses. The collected blood was centrifuged (RCF 1.000× *g*) immediately after collection for 15 min at 4 °C (MPW-351R, MPW Med. Instruments, Warsaw, Poland) and serum was collected and stored at −80 °C until further study (BIO Memory 690L, Froilabo, Paris, France).

The concentrations of adiponectin (ADIPO), leptin (LEP) and interleukin-8 (IL-8) were measured using commercially available ELISA kits according to the manufacturer's protocol. The human Adiponectin ELISA Kit (catalogue number E09) was purchased from Mediagnost (Reut-Lingen, Germany). The human Leptin Sandwich ELISA Kit (catalogue number EIA-2395) was purchased from DRG Instruments GmbH (Marburg, Germany). The IL-8 ELISA kit (catalogue number EIA-4700) was purchased from DRG Instruments GmbH (Marburg, Germany). An ELx 808 spectrophotometric microplate reader (BioTek, Winooski, VT, USA) was used to determine the optical density at 450 nm. Marking was performed in the Laboratory of Genetics and Molecular Biology at the Department of Physiology, Jagiellonian University Medical College, Cracow, Poland.

Index of adiponectin-to-leptin ratio (ADIPO/LEP ratio) was calculated based on the formula:

$$\text{ADIPO/LEP ratio} = \text{ADIPO (}\mu\text{g/mL)/LEP (}\mu\text{g/mL)}$$

#### 2.2.4. Biochemical Blood Indices

Fasting plasma glucose (FPG) [mmol/L] was determined via the enzymatic method using a Cobas c701/702 biochemical analyzer (Roche Diagnostics International Ltd., Mannheim, Germany). Serum insulin concentration (INS) [μIU/mL] was determined via the electrochemiluminescence method (ECLIA) using the Cobas e801 apparatus (Roche Diagnostics International Ltd., Mannheim, Germany). The determinations were performed in accordance with the manufacturer's instructions using reagents dedicated to the GLUC3 and Elecsys Insulin analyzers, respectively.

Using the specifications of the Architect ci-4100 clinical chemistry analyzer (Abbott Laboratories), serum triglyceride (TG) [mg/dl] levels were determined via spectrophotometry.

Evaluation of sensitivity to insulin was performed with the use of the homeostatic model assessment—adiponectin (HOMA-AD) [44] and homeostatic model assessment—triglycerides (HOMA-TG) [45], calculated based on the formula:

$$\text{HOMA-AD} = \text{INS (}\mu\text{U/mL)} \times \text{FPG (mmol/L)/ADIPO (}\mu\text{g/mL);}$$

$$\text{HOMA-TG} = \text{INS (}\mu\text{U/mL)} \times \text{FPG (mmol/L)/TG (mg/dL)}$$

#### 2.2.5. Evaluation of Total Energy Expenditure and Energy Value of Diet

The International Physical Activity Questionnaire (IPAQ) [46] was employed to evaluate the daily energy expenditures. The total energy expenditure (TEE), measured in

kilocalories per day, was computed as the sum of non-exercise activity thermogenesis (NEAT) assessed through the IPAQ questionnaire and the energy expenditures associated with the interventions implemented in the EG1 and EG2 groups.

To evaluate the energy value of the participants' diets, a clinical dietician conducted a 24 h nutrition interview using the nutrition record method. The data were analyzed using the DietaPro program (version 4.0, Institute of Food and Nutrition, Warsaw, Poland) to quantitatively assess the nutrition habits and monitor any changes in the diet during the intervention. Based on the obtained results, a report of dietary nutrients was generated: proteins [g], carbohydrates [g] and fats [g].

### 2.3. Exercise Interventions

The exercise interventions were conducted at a fitness club and supervised by a personal coach. The training sessions were carried out at the same time of day (evening, 6–9 pm) by the same personal coach, in a room with consistent temperature (22 degrees Celsius) and humidity. Adherence to the intervention was monitored using a session attendance checklist, and participants who dropped out from more than 10% of the training sessions for 12 weeks were excluded from the analysis.

Individualized planning and monitoring of aerobic and resistance training intensity were based on the guidelines of the American College of Sports Medicine [47]. The One Repetition Maximum (1 RM) was determined before resistance training (Supplement). The load and number of repetitions were recorded and converted into 1 RM based on the 1 RM calculator using Brzycki's formula [48,49].

The intervention aimed to achieve 3 training sessions per week, which resulted in $3 \times 5.5$ MET for a week equivalent to resistance training, and $3 \times 6$ MET for running [50].

#### 2.3.1. Aerobic Training

The aerobic training intervention (Figure S1, Supplement) involved three sessions per week in groups of up to five participants at a fitness club. The training started with a five-minute warm-up on a treadmill (Technogym New Excite Run Now 500, Cesena, Italy) at 50% of maximal heart rate (HR max). HR max was calculated based on the formula: $208 - 0.7 \times$ age (years) [51]. Heart rate during training was monitored using the Polar M200 GPS Running Watch with Wrist-Based Heart Monitor (Kempele, Finland).

Next, the participants increased the intensity of their workout to 70% HR max by adjusting their velocity or angle on the treadmill, resistance on the upright bikes (Technogym Artis, Cesena, Italy) or range of motion or resistance on the x-trainer (Precor EFX556i Elipsa, Woodinville, WA, USA). The aerobic exercises mainly consisted of fast walking or jogging on the treadmill; however, in the case of reporting pain from the musculoskeletal system, the participants had an option to change the device. The training was continuous and maintained a steady HR, with a duration of 45 min. Following the aerobic training, participants stretched the muscle groups they had engaged for 10 min.

#### 2.3.2. Combined Aerobic–Resistance Training

The aerobic–resistance intervention (Table S1, Supplement) was conducted three times per week in groups of up to five participants under the supervision of a personal coach. One session of exercises lasted 60 min. The training started with a 5 min aerobic warm-up on a treadmill to reach an intensity of 50% HRmax.

The initial resistance training comprised three complex exercises involving the whole body, such as one-arm dumbbell row, squats and push-ups, with four sets and 120 s breaks between them. Due to the body's adaptation to training, in the second week of intervention, the resistance training procedure was changed to push–pull and the training volume was changed to 3 sets of 6 exercises with 90 s breaks. After 3 weeks of intervention, the training was performed in 3 series of 9 exercises with 60 s breaks. The load was gradually increased from the first week, from 50% 1RM to 70% 1RM in the second and the remaining 10 weeks of intervention [52]. The progression of load of the resistance exercises during

the intervention and follow-up for EG2 was statistically significant in the analyzed period (Table S2, Supplement).

After resistance exercises, there was an aerobic training element: the participants trained with an intensity of 50% HR max in the first week and 70% HR max from the second week of intervention on a treadmill (Technogym New Excite Run Now 500, Cesena, Italy), upright bike (Technogym Artis, Cesena, Italy) or x-trainer (Precor EFX556i Elipsa, Woodinville, WA, USA). To avoid overloading the joints of the lower extremities, the subjects could use these three devices alternately.

The duration of the resistance training sessions was 30, 35 and 40 min, respectively, followed by 20, 15 and 10 min of aerobic training, respectively. The training session ended with the stretching phase (5 min).

### *2.4. Statistical Analysis*

The Shapiro–Wilk test was used to examine the distribution of the variables being analyzed. To compare the effects of an intervention on changes in the analyzed variables in the experimental groups and control group, the one-way ANOVA test with repeated measures and post hoc comparison (Tukey's test) was employed. Homogeneity of variance within the groups was tested with Levene's test.

The size effect (ES) for the ANOVA test was calculated using the $\eta^2$ coefficient, which is the ratio of the sum of squares ($SS$) for the effect to the total sum of squares ($SS$). The squared eta coefficient interpretation follows Cohen's guidelines: $0.1 \leq 0.3$ (low effect), $0.3 \leq 0.5$ (moderate effect) and $\geq 0.5$ (high effect) [53].

$$\eta^2 = \frac{SS_{effect}}{SS_{total}}$$

Pearson's correlation coefficient (r) was used to calculate correlations between LEP, IL-8 and HOMA-AD and other measured parameters. The interpretation of the Pearson correlation in the range < 0–1 > was made as follows: $0 \leq r < 0.3$, no or very weak correlation; $0.3 \leq r < 0.5$, moderate correlation; $0.5 \leq r < 0.7$, strong correlation; $0.7 \leq r \leq 1$, very strong correlation [54].

To explain the variation in ADIPO concentrations, multiple regression was employed, utilizing an econometric linear multiple regression model assessed by the least-squares method. In the model, the residual standard errors and test $p$-values were corrected using robust standard errors corrected for heteroscedasticity.

The number of participants required to demonstrate statistical significance was based on previously published studies in the field. Probability of error ($\alpha$) 0.05, power ($1 - \beta$) 0.80 and mean effect size (d) 0.8 were used to calculate the sample size and the tested sample was n = 54.

In all the analyses, effects were considered significant if their probability value $p$ was less than the assumed significance level $\alpha = 0.05$ ($p < 0.05$). The ggplot2 package in the RStudio IDE of the R programming language was applied to perform all calculations.

## 3. Results

After performing health training intervention both in EG1 ($p = 0.02$) and EG2 ($p = 0.01$), a significant increase of total energy expenditure (TEE) [kcal/day] was confirmed between the initial measurements and measurements in the $6^{th}$ ($p < 0.001$) week of intervention (Table 1). In the 12th week of intervention, the significance level of EG1 was $p < 0.001$ and EG2 was $p = 0.04$. In follow-up, an increase of TEE was also confirmed in EG1 ($p < 0.001$) and in EG2 ($p = 0.03$). No significant changes were found in TEE in CG. A significant difference in TEE between the intervention groups and the CG in the 6th week of observation was confirmed ($p = 0.03$).

**Table 1.** Total energy expenditure (TEE) and diet nutrients: proteins, carbohydrates and fats in the aerobic group (EG1), aerobic–resistance group (EG2) and control group (CG).

| | Group | Week 1 Baseline | Week 6 Intervention | Week 12 Intervention | Week 16 Follow-Up | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\overline{X} \pm SD$ | $\overline{X} \pm SD$ | $\overline{X} \pm SD$ | $\overline{X} \pm SD$ | Test ANOVA (ES) | d 6-1 (ES) | d 12-1 (ES) | d 16-1 (ES) |
| TEE [kcal/day] | EG1 | 597.46 ± 195.93 | 823.37 ± 175.76 | 835.18 ± 234.05 | 838.00 ± 350.75 | 0.02 (0.15) | <0.001 (−3.28) | <0.001 (−1.37) | <0.001 (0.69) |
| | EG2 | 553.84 ± 85.63 | 735.17 ± 119.64 | 797.89 ± 383.25 | 749.17 ± 430.71 | 0.01 (0.12) | <0.001 (−2.01) | 0.04 (−0.67) | 0.03 (−0.50) |
| | CG | 634.06 ± 221.38 | 627.97 ± 197.18 | 652.36 ± 186.92 | 690.23 ± 205.14 | 0.56 (0.00) | 0.87 (−0.05) | 0.77 (−0.09) | 0.18 (−0.41) |
| | *p*-value | 0.45 | 0.03 * | 0.20 | 0.53 | | | | |
| Proteins [g] | EG1 | 125.50 ± 53.37 | 126.50 ± 39.20 | 120.93 ± 29.63 | 134.93 ± 44.13 | 0.46 (0.02) | 0.92 (−0.03) | 0.63 (0.13) | 0.18 (−0.38) |
| | EG2 | 144.06 ± 34.09 | 137.31 ± 25.45 | 125.00 ± 21.06 | 154.67 ± 40.64 | <0.001 (0.11) | 0.34 (0.29) | 0.05 (0.63) | 0.01 (−0.91) |
| | CG | 148.80 ± 39.74 | 135.06 ± 21.90 | 126.14 ± 19.87 | 152.85 ± 35.07 | 0.04 (0.11) | 0.18 (0.42) | 0.07 (0.57) | 0.86 (−0.05) |
| | *p*-value | 0.32 | 0.57 | 0.83 | 0.38 | | | | |
| Carbo -hydrates [g] | EG1 | 295.79 ± 67.74 | 294.29 ± 68.92 | 310.29 ± 70.32 | 346.21 ± 81.50 | 0.04 (0.08) | 0.95 (0.02) | 0.47 (−0.20) | 0.01 (−0.87) |
| | EG2 | 304.38 ± 79.41 | 319.00 ± 70.14 | 338.00 ± 69.59 | 356.83 ± 81.90 | 0.04 (0.03) | 0.60 (-0.15) | 0.04 (−0.70) | 0.01 (−1.01) |
| | CG | 316.20 ± 65.40 | 304.81 ± 73.44 | 320.21 ± 50.77 | 347.69 ± 77.61 | 0.16 (0.03) | 0.22 (0.37) | 0.59 (0.16) | 0.24 (−0.36) |
| | *p*-value | 0.74 | 0.63 | 0.52 | 0.94 | | | | |
| Fats [g] | EG1 | 110.43 ± 43.78 | 104.43 ± 29.79 | 122.21 ± 34.85 | 117.79 ± 40.99 | 0.03 (0.03) | 0.43 (0.22) | 0.05 (−0.57) | 0.13 (−0.43) |
| | EG2 | 92.38 ± 22.99 | 103.44 ± 18.23 | 106.57 ± 18.30 | 103.25 ± 22.73 | 0.08 (0.07) | 0.04 (−0.67) | 0.03 (−0.73) | 0.01 (−0.94) |
| | CG | 99.20 ± 25.82 | 113.56 ± 21.63 | 121.57 ± 19.96 | 113.38 ± 26.22 | 0.01 (0.23) | 0.03 (−0.72) | <0.001 (−1.09) | 0.04 (−0.69) |
| | *p*-value | 0.30 | 0.42 | 0.20 | 0.50 | | | | |

* post hoc EG1-CG: $p = 0.03$; d 6-1, d 12-1, d 16-1—differences in results obtained after 6 and 12 weeks of interventions, respectively, and after 4 weeks of follow-up in relation to measurements taken before interventions, $\overline{X}$—mean, SD—standard deviation, $p < 0.05$—statistically significant difference, ES—effect size.

When analyzing the balance of nutrients during the study, no changes in the level of protein supplied in the diet in the EG1 group were confirmed (Table 1). In EG2, changes in the level of supplied proteins were observed ($p < 0.001$), but a visible increase in consumption occurred only at the follow-up stage ($p = 0.01$). CG confirmed the variability in protein intake between measurements ($p = 0.04$).

In the EG1 and EG2 intervention groups, carbohydrate consumption increased between measurements ($p = 0.04$) (Table 1). In both groups, the highest intake was confirmed in the follow-up period ($p = 0.01$).

Significant changes in consumption also occurred in the case of fats supplied in the diet (Table 1). Changes between measurements in EG1 ($p = 0.03$) and CG ($p = 0.01$) were confirmed. The increase in fat consumption was noticeable in the EG2 group after 6 ($p = 0.04$), 12 ($p = 0.03$) and 16 ($p = 0.01$) weeks compared to the measurement before the intervention. Similar relationships were observed in the CG group; despite the lack of intervention, fat consumption increased in the 6th ($p = 0.03$), 12th ($p < 0.001$) and 16th ($p = 0.04$) weeks of observation (Table 1).

Analyzing the body composition of the people participating in the study, the most beneficial changes regarding FFM increase, GYNOID and WC decrease were confirmed in the EG2 group (Table 2). No changes in FFM were confirmed in the case of the EG1 and CG groups, while in the EG2 group there was a significant increase in FFM between measurements ($p < 0.001$); after 16 weeks, the observed increase was 5.8% ($p < 0.001$).

**Table 2.** Body composition: fat-free mass (FFM), gynoid body fat (GYNOID) and waist circumference (WC) in the aerobic group (EG1), aerobic–resistance group (EG2) and control group (CG).

| | Group | Week 1 Baseline | Week 6 Intervention | Week 12 Intervention | Week 16 Follow-Up | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\overline{X}\pm$ SD | $\overline{X}\pm$ SD | $\overline{X}\pm$ SD | $\overline{X}\pm$ SD | Test ANOVA (ES) | d 6-1 (ES) | d 12-1 (ES) | d 16-1 (ES) |
| FFM [%] | EG1 | 63.09 ± 4.81 | 63.74 ± 5.04 | 63.85 ± 5.26 | 64.56 ± 4.95 | 0.13 (0.00) | 0.07 (−0.58) | 0.05 (−0.64) | 0.07 (−0.58) |
| | EG2 | 62.56 ± 5.23 | 65.14 ± 5.44 | 65.63 ± 4.69 | 66.17 ± 4.30 | <0.001 (0.06) | <0.001 (−1.60) | <0.001 (−1.32) | <0.001 (−1.82) |
| | CG | 59.23 ± 16.97 | 54.90 ± 22.00 | 62.51 ± 4.96 | 61.57 ± 4.80 | 0.19 (0.13) | 0.17 (0.45) | 0.50 (0.21) | 0.14 (0.49) |
| | *p*-value | 0.58 | 0.11 | 0.28 | 0.07 | | | | |
| GYNOID [%] | EG1 | 37.36 ± 5.57 | 36.21 ± 5.85 | 36.74 ± 6.33 | 36.04 ± 5.10 | 0.07 (0.01) | 0.03 (0.68) | 0.23 (0.35) | 0.05 (0.59) |
| | EG2 | 35.91 ± 4.88 | 34.49 ± 4.62 | 35.08 ± 4.36 | 33.84 ± 4.60 | <0.001 (0.04) | 0.02 (0.95) | 0.24 (0.39) | 0.00 (1.59) |
| | CG | 35.91 ± 6.22 | 35.90 ± 6.62 | 36.18 ± 5.99 | 36.24 ± 6.84 | 0.16 (0.00) | 0.42 (0.29) | 0.15 (−0.57) | 0.51 (−0.23) |
| | *p*-value | 0.73 | 0.68 | 0.75 | 0.53 | | | | |
| WC [cm] | EG1 | 114.7 ± 10.93 | 113.8 ± 12.01 | 114.0 ± 12.87 | 113.7 ± 12.56 | 0.53 (0.02) | 0.14 (0.43) | 0.44 (0.21) | 0.25 (0.32) |
| | EG2 | 114.8 ± 11.64 | 113.2 ± 11.55 | 111.0 ± 10.33 | 111.3 ± 11.08 | <0.001 (0.00) | 0.01 (1.10) | 0.01 (1.15) | 0.01 (1.15) |
| | CG | 115.3 ± 10.54 | 117.4 ± 11.22 | 119.1 ± 11.09 | 119.3 ± 12.26 | 0.50 (0.05) | 0.49 (−0.25) | 0.07 (−0.57) | 0.21 (−0.24) |
| | *p*-value | 0.99 | 0.55 | 0.18 | 0.24 | | | | |

EG1—aerobic group, EG2—aerobic–resistance group, CG—control group, d 6-1, d 12-1, d 16-1—differences in results obtained after 6 and 12 weeks of interventions, respectively, and after 4 weeks of follow-up in relation to measurements taken before interventions, $\overline{X}$—mean, SD—standard deviation, $p < 0.05$—statistically significant difference, ES—effect size.

In the case of GYNOID, it decreased after 6 weeks of intervention in the EG1 group ($p = 0.03$) (Table 2). A significant change between measurements occurred in the EG2 group ($p < 0.001$), in which decreases in GYNOID levels were confirmed after 6 ($p = 0.02$) and 16 ($p < 0.001$) weeks. No significant changes were observed in the CG group.

After the WC analysis, changes in EG1 and CG were not confirmed (Table 2). However, in the EG2 group, changes were found both between measurements ($p < 0.001$) and in each of the analyzed measurement moments ($p = 0.01$). The decrease in WC was 3.8 cm after 12 weeks of intervention ($p = 0.01$).

By analyzing changes in insulin resistance indices, changes between measurements ($p = 0.02$) in HOMA-AD values in the EG2 group were confirmed (Table 3). There was an increase after 6 weeks ($p = 0.03$), followed by a decrease in HOMA-AD in subsequent measurements. No significant changes in HOMA-AD values were observed in the EG1 and CG groups.

In the case of the HOMA-TG index, changes between measurements in the EG1 ($p = 0.04$) and EG2 ($p = 0.03$) intervention groups were confirmed (Table 3). The greatest changes were observed in the EG2 group, where after 16 weeks the decrease was 39% ($p = 0.04$). There were no significant changes in the CG.

Observations of ADIPO fluctuations did not confirm significant changes in the concentration of the analyzed hormone both within groups and between groups (Table 4). However, changes in the ADIPO/LEP ratio in the EG1 group were found between the measurements ($p < 0.001$) and after 6 ($p = 0.01$) and 16 ($p < 0.001$) weeks.

When analyzing changes in the concentration of IL-8 cytokine, no changes in concentrations between measurements in the EG1 and EG2 intervention groups were confirmed. In the EG1 group, there was a decrease in the concentration of IL-8 in the first 6 weeks of the intervention ($p = 0.04$). In contrast, in CG there was a significant increase in IL-8 concentration ($p = 0.01$) between measurements of 36% over 16 weeks. Additionally, at

week 16, a significant difference in IL-8 concentration between CG and EG1 was confirmed ($p = 0.03$) (Table 4, Figure 2).

**Table 3.** Concentrations of homeostatic model assessment—adiponectin (HOMA-(AD) and homeostatic model assessment—triglycerides (HOMA-TG) in the participants' blood in the aerobic group (EG1), aerobic–resistance group (EG2) and control group (CG).

| | Group | Week 1 Baseline | Week 6 Intervention | Week 12 Intervention | Week 16 Follow-Up | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\overline{X} \pm SD$ | $\overline{X} \pm SD$ | $\overline{X} \pm SD$ | $\overline{X} \pm SD$ | Test ANOVA (ES) | d 6-1 (ES) | d 12-1 (ES) | d 16-1 (ES) |
| HOMA-AD | EG1 | 624.63 ± 733.61 | 548.62 ± 840.29 | 676.14 ± 899.51 | 487.19 ± 740.30 | 0.78 (0.00) | 0.87 (0.05) | 0.83 (0.07) | 0.52 (0.21) |
| | EG2 | 509.01 ± 425.69 | 669.88 ± 534.83 | 403.09 ± 353.73 | 277.22 ± 199.89 | 0.02 (0.30) | 0.03 (0.71) | 0.43 (0.30) | 0.57 (0.22) |
| | CG | 748.10 ± 789.61 | 572.24 ± 443.26 | 1085.25 ± 1362.91 | 704.11 ± 802.73 | 0.26 (0.11) | 0.83 (0.07) | 0.20 (−0.46) | 0.81 (−0.08) |
| | *p*-value | 0.61 | 0.85 | 0.19 | 0.36 | | | | |
| HOMA-TG | EG1 | 2.80 ± 1.43 | 2.33 ± 1.73 | 2.41 ± 1.27 | 2.26 ± 1.23 | 0.04 (0.04) | 0.11 (0.55) | 0.05 (1.15) | 0.07 (0.66) |
| | EG2 | 2.27 ± 1.18 | 2.78 ± 2.16 | 1.53 ± 0.48 | 1.38 ± 0.49 | 0.03 (0.17) | 0.77 (−0.13) | 0.06 (0.70) | 0.04 (0.73) |
| | CG | 2.99 ± 2.53 | 2.91 ± 2.12 | 2.59 ± 1.47 | 3.09 ± 2.77 | 0.97 (0.00) | 0.78 (0.10) | 0.91 (−0.04) | 0.96 (−0.02) |
| | *p*-value | 0.52 | 0.75 | 0.05 | 0.10 | | | | |

EG1—aerobic group, EG2—aerobic–resistance group, CG—control group, d 6-1, d 12-1, d 16-1—differences in results obtained after 6 and 12 weeks of interventions, respectively, and after 4 weeks of follow-up in relation to measurements taken before interventions, $\overline{X}$—mean, SD—standard deviation, $p < 0.05$—statistically significant difference, ES—effect size.

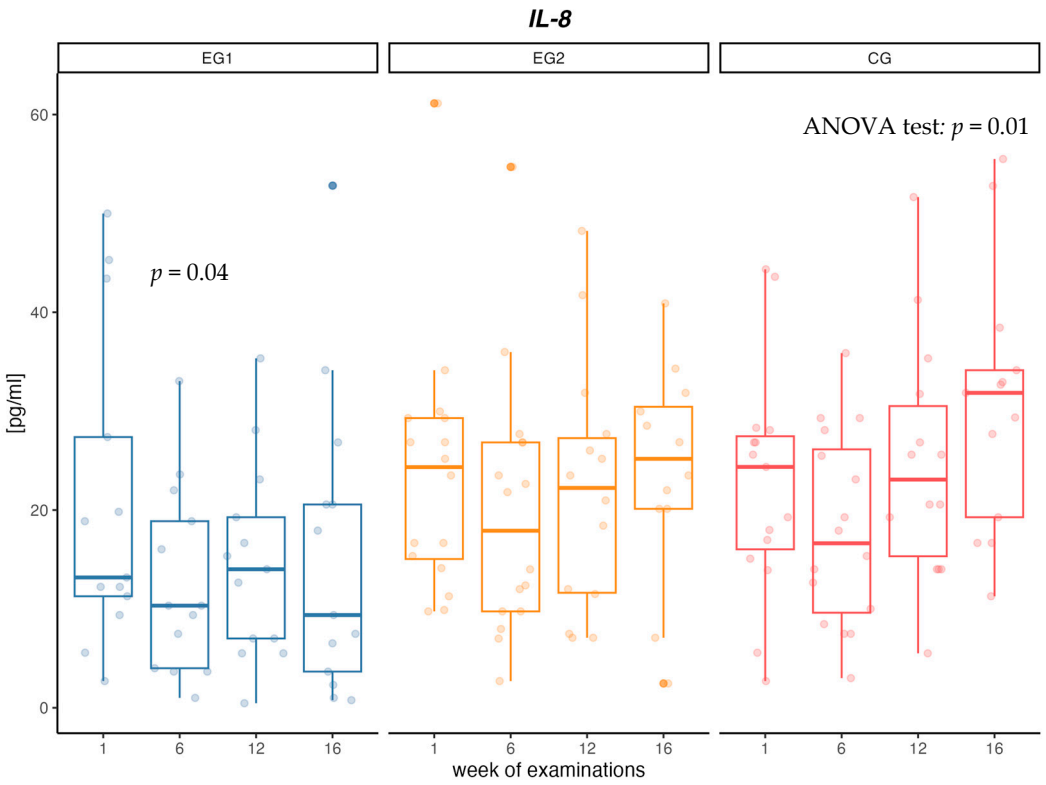


**Figure 2.** Changes in interleukin-8 (IL-8) concentration [pg/mL] in aerobic group (EG1), aerobic–resistance group (EG2) and control group (CG) during weeks of examinations.

**Table 4.** Concentrations of adiponectin (ADIPO), leptin-to-adiponectin ratio (ADIPO/LEP ratio) and interleukin-8 (IL-8) in participants' blood plasma in the aerobic group (EG1), aerobic–resistance group (EG2) and control group (CG).

| | Group | Week 1 Baseline | Week 6 Intervention | Week 12 Intervention | Week 16 Follow-Up | *p*-Value | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\overline{X} \pm SD$ | $\overline{X} \pm SD$ | $\overline{X} \pm SD$ | $\overline{X} \pm SD$ | Test ANOVA (ES) | d 6-1 (ES) | d 12-1 (ES) | d 16-1 (ES) |
| ADIPO [ng/mL] | EG1 | 4.61 ± 2.01 | 4.04 ± 1.84 | 4.29 ± 1.67 | 4.39 ± 2.01 | 0.32 (0.01) | 0.08 (0.51) | 0.32 (0.28) | 0.52 (0.18) |
| | EG2 | 4.57 ± 2.82 | 3.98 ± 2.26 | 3.85 ± 2.13 | 4.00 ± 1.95 | 0.32 (0.02) | 0.14 (0.47) | 0.32 (0.30) | 0.53 (0.20) |
| | CG | 4.36 ± 1.87 | 4.83 ± 2.29 | 3.77 ± 2.24 | 4.43 ± 2.19 | 0.30 0.03 | 0.09 (−0.54) | 0.51 (0.20) | 0.23 (−0.37) |
| | *p*-value | 0.95 | 0.47 | 0.77 | 0.85 | | | | |
| ADIPO/ LEP ratio | EG1 | 2.77 ± 4.86 | 0.71 ± 0.79 | 4.08 ± 7.60 | 0.68 ± 0.87 | <0.001 (0.45) | 0.01 (0.70) | 0.95 (0.03) | <0.001 (0.73) |
| | EG2 | 0.73 ± 0.76 | 0.70 ± 0.71 | 0.68 ± 0.55 | 0.93 ± 0.86 | 0.40 (0.01) | 0.87 (0.05) | 0.40 (0.26) | 0.43 (−0.25) |
| | CG | 3.21 ± 6.79 | 0.52 ± 0.47 | 0.77 ± 0.83 | 0.73 ± 0.47 | 0.16 (0.13) | 0.15 (0.43) | 0.20 (0.39) | 0.38 (0.27) |
| | *p*-value | 0.31 | 0.66 | 0.08 | 0.71 | | | | |
| IL-8 [pg/mL] | EG1 | 20.87 ± 15.80 | 13.64 ± 9.34 | 15.79 ± 9.43 | 16.91 ± 15.42 | 0.37 (0.06) | 0.04 (0.63) | 0.13 (0.45) | 0.46 (0.21) |
| | EG2 | 23.75 ± 12.74 | 21.73 ± 13.87 | 22.83 ± 12.93 | 24.15 ± 11.39 | 0.39 (0.03) | 0.45 (0.22) | 0.54 (0.19) | 0.34 (−0.29) |
| | CG | 22.63 ± 11.67 | 17.92 ± 9.70 | 24.71 ± 12.23 | 30.71 ± 13.22 | 0.01 (0.14) | 0.08 (0.56) | 0.61 (−0.15) | 0.10 (−0.52) |
| | *p*-value | 0.85 | 0.22 | 0.08 | 0.02 * | | | | |

* post hoc EG1-CG: $p = 0.02$; EG1—aerobic group, EG2—aerobic–resistance group, CG—control group, d 6-1, d 12-1, d 16-1—differences in results obtained after 6 and 12 weeks of interventions, respectively, and after 4 weeks of follow-up in relation to measurements taken before interventions, $\overline{X}$—mean, SD—standard deviation, $p < 0.05$—statistically significant difference, ES—effect size.

Significant correlations (Table S3, Supplement) were confirmed in EG1 between ADIPO and dietary carbohydrate (r = −0.27), dietary fat (r = −0.35), GYNOID (r = 0.33) and insulin resistance indices HOMA-AD (r = −0.63) and HOMA-TG (r = −0.48). No significant correlations were observed for IL-8. There were significant correlations between HOMA-AD and the level of carbohydrates (r = 0.37), fats (r = 0.34), WC (r = 0.36) and HOMA-TG (r = 0.81), and negative significant correlations for HOMA-AD and ADIPO (r = −0.63). Analyzing the correlations in the EG2 group, significant correlations between ADIPO and carbohydrates (r = 0.43), GYNOID (r = 0.42), HOMA-AD (r = −0.56) and ADIPO/LEP ratio (r = 0.68) were confirmed. For IL-8, one significant correlation with HOMA-AD was observed (r = −0.28). In the case of HOMA-AD, there were significant correlations with GYNOID (r = −0.27), WC (r = 0.39), HOMA-TG (r = 0.55), ADIPO (r = −0.56), ADIPO/LEP ratio (r = −0.50) and IL-8 (r = −0.28). In CG, significant correlations were observed between ADIPO and TEE (r = 0.26), HOMA-AD (r = −0.59) and HOMA-TG (r = −0.29). In the case of IL-8, the correlation with TEE was confirmed (r = 0.43). HOMA-AD had a significant linear relationship with HOMA-TG (r = 0.53) and ADIPO (r = −0.59).

The applied multiple regression model demonstrated that both HOMA-AD and GYNOID were significantly connected with the concentration of ADIPO ($p < 0.001$). The variability of ADIPO was explained by the analyzed variables in 36% (value of $R^2$ model = 0.36) (Table 5).

**Table 5.** Parameters of multiple regression model of the adiponectin (ADIPO) dependent variable.

| Dependent Variable | Parameter Assessment | Standard Error | t Value | *p*-Value |
|---|---|---|---|---|
| Free parameter | 1.47 | 0.87 | 1.69 | 0.09 |
| HOMA-AD | −0.002 | 0.0002 | −8.43 | <0.001 |
| GYNOID | 0.10 | 0.02 | 4.41 | <0.001 |

Free parameter—intercept, HOMA-AD—homeostatic model assessment—adiponectin, GYNOID—gynoid body fat.

## 4. Discussion

The aim of the study was to compare the 12-week effect of two types of physical training on ADIPO and IL-8 concentrations and carbohydrate metabolism indices in men with MetS compared to men with MetS not undertaking physical activity, and to evaluate changes in these parameters after 4 weeks of observation without scheduled training. Training interventions over 12 weeks did not change the concentration of ADIPO, but significant correlations were observed between ADIPO and HOMA-AD and GYNOID. The applied multiple regression model showed that both variables explained 36% of ADIPO variability. Aerobic exercise was associated with a decrease in IL-8 concentration after 6 weeks of intervention in men with MetS. The use of a combined resistance and aerobic training led to a significant increase in FFM, a decrease in GYNOID and WC and a reduction in the level of insulin resistance in the group of men with MetS.

In a meta-analysis of studies on people with pre-diabetes or diabetes, in which the participants were overweight or obese and often had MetS, it was observed that physical exercise increased the concentration of ADIPO. Furthermore, it was emphasized that the results in improving the concentration of ADIPO were observed in studies using aerobic exercise, whereas other forms of physical exercise did not bring such results [55]. Similar results were presented in earlier meta-analyses [39,56]. Additionally, Balducci et al. [15] showed that aerobic exercise, but also a combination of resistance and aerobic exercise, bring beneficial changes in the concentration of ADIPO (increase by 36% and 38%) and in the level of insulin resistance in patients with MetS, despite the lack of changes in body mass and the level of adipose tissue. In our study, however, no changes in ADIPO concentration were observed in any of the analyzed groups. The authors suggest that significant changes in the concentration of ADIPO are influenced by a higher negative energy balance caused by aerobic exercise compared to other types of activity [57]. There are also reports in which the interventions did not have a significant effect on the concentration of ADIPO. In five clinical trials evaluating the effect of a 10% reduction in body mass on the concentration and expression of ADIPO in plasma, no significant changes were observed [58–62]. The authors noticed that in a short time (up to 12 weeks), the concentration of the hormone increased—hence, favorable changes in the level of ADIPO were observed, after which the fluctuations usually stabilized. Moreover, one study has shown that a reduction of 5 to 10% of body mass has little or no effect on the concentration of ADIPO [63].

Our study confirmed changes in the level of GYNOID, achieving a significant reduction after 6 weeks in both intervention groups. We also observed a correlation between ADIPO and GYNOID in the intervention groups, which may suggest that while achieving greater beneficial changes in body composition, the concentration of ADIPO could increase to obtain significant differences. Moreover, there have been reports that ADIPO is negatively correlated with the level of android and total adipose tissue and positively correlated with insulin sensitivity [64].

Our study confirmed significant correlations between ADIPO and two indices of insulin resistance: HOMA-AD and HOMA-TG. Khan et al. [45] proposed HOMA-TG as a good indicator for the diagnosis of MetS, indicating that HOMA-TG may provide better diagnostic performance in the diagnosis of MetS than HOMA-IR, HOMA2 and QUICKI. Matsuhisa et al. [44] noted that HOMA-AD showed a greater correlation with the level of insulin resistance than HOMA-IR. However, the concentration of ADIPO is used to calculate HOMA-AD, which in turn increases the correlation between the described hormone and

the index of insulin resistance. Our research also showed that both indicators were strongly correlated with each other and that the values of both indicators changed significantly after the aerobic–resistance intervention: after 16 weeks, the decrease in HOMA-AD was 46%, while HOMA-TG was 39%. Such beneficial changes in carbohydrate metabolism, resulting from the use of a combination of resistance and aerobic training, may offer perspectives in the treatment of people with MetS, insulin resistance and type 2 diabetes.

The processes that can occur under the influence of training sessions should be analyzed in detail in order to properly understand the relation between ADIPO, insulin resistance and physical activity in males with MetS and obesity. Skeletal muscles are the main area of carbohydrate metabolism in the human body; moreover, they are also the main area of insulin resistance development [65]. Chronic positive energy balance of the body, leading to obesity, results not only in disorders at adipokine levels but also in accumulation of adipose tissue in the liver and skeletal muscles, and subsequently in improper metabolic response, including mainly insulin resistance. ADIPO, after connecting to its receptor in muscles (ADIPO R1) through An Adaptor Protein 1 (APPL1), affects the activation of many signaling pathways, including the insulin receptor substrate (IRS) pathway, AMP-activated protein kinase (AMPK) and p38 mitogen-activated protein kinase (p38 MAPK), leading to the regulation of blood glucose. The main insulin-regulating mechanism affected by ADIPO is the IRS, whose functioning is impaired in obesity [66].

In obesity, transcription factors such as SERBP1c may lead to the development of lipotoxicity in skeletal muscles through the deposition of triglycerides, acyl-CoA, phosphatides, diacylglycerols (DAG) and ceramides [67]. In our research, in the EG2 group, there was a significant increase in FFM in the first 6 weeks of the intervention, amounting to 4.1%, and in the same period the level of GYNOID decreased. However, HOMA-AD and HOMA-TG insulin resistance indicators increased by 31.6% and 22.5%. The main component affecting the increase in insulin resistance was the increase in insulin concentration in the analyzed period, which was shown in our former work [41]. The increase in insulin concentration may have resulted from a limited ability to respond to insulin at its receptor, caused by lipotoxicity related to the insulin receptor substrate (IRS) or a limitation in the function of glucose transporter type 4 (GLUT4) [68,69]. Insulin resistance could also be associated with the occurrence of muscle microdamages, caused mainly by eccentric contractions, the prolonged phase of which is characteristic of resistance training, affecting the reduction of GLUT4 levels and partial inability to resynthesis of glycogen [70]. The probability of occurrence of muscle microdamage was higher in this group due to the initial adaptation processes as a result of increasing the volume and intensity of training.

Our results showed that the ADIPO/LEP ratio decreased significantly after 6 weeks of aerobic intervention. The occurring relation resulted from a significant increase of LEP level, presented in our previous work [42] and the lack of significant changes in the level of ADIPO during the analyzed period. LEP can react to the changes taking place in the population of people with MetS faster than ADIPO. Such biological fluctuations of the described hormones were also confirmed [63]. Frühbeck et al. [27] indicated that the ADIPO/LEP ratio is characterized by a higher level of correlation with insulin resistance than either ADIPO or LEP alone; however, such a relationship was not confirmed in our research.

In our study, a significant 35% decrease in IL-8 concentration was observed after the first 6 weeks of intervention in the group using aerobic training. Decreased concentration of IL-8, in relation to the initial concentration, was observed until the end of the research project in the group with aerobic training, but no such dependencies were found in the group with aerobic–resistance training. The results presented in the meta-analysis show that the physical activity of people with MetS leads to a decrease in the concentration of IL-8 [71]. However, the results are still conflicting, since same studies did not observe changes in serum concentrations of IL-8. In a large population study of 489 MetS people, men and women over 55 years of age who engaged in moderate or intense exercise of a minimum of 150 min per week, no significant changes in IL-8 levels were observed during

one year of follow-up [72]. In their paper, Guo et al. showed that increased plasma cytokine levels (TNF-α, IL-6 and IL-8) were associated with reduced strength gain during resistance training [73].

In our study, in the group without physical activity, a gradual increase in IL-8 concentration between measurements was observed and the cytokine level was 45% higher in the control group compared to the group with aerobic intervention. According to paper Bruun et al., [74] high levels of IL-8 are secreted from human adipose tissue, and the accumulation of IL-8 in this tissue may be partly responsible for the increase in circulating concentrations of IL-8 seen in obese individuals. Elevated levels of IL-8 secreted from myotubes in diabetes create a muscle microenvironment that stimulates reduced capillarity in diabetes, ultimately limiting the availability of substrates including glucose, exacerbating impaired muscle glucose clearance and contributing to the diabetes phenotype [75]. Failure to treat obesity and metabolic disorders leads to a further increase in inflammation in the body and numerous health complications [76].

Currently, the physiological function of IL-8 in skeletal muscle is still unknown; thus, further research is needed to identify the potential of IL-8 as a diagnostic biomarker.

The current study has some limitations. The participants of the project increased their nutrient intake despite recommendations to maintain their current diet. Determination of specialized biochemical indicators, e.g., the level of glycated hemoglobin (HbA1c) could allow for a better determination of the level of insulin resistance and give the possibility of a more precise description of the correlation and assessment of modified HOMA indices.

In conclusion, undertaking a 12-week aerobic–resistance training program, despite the lack of significant changes in the level of ADIPO, led to a decrease in insulin resistance expressed as HOMA-AD and HOMA-TG. In the aerobic training group, no significant changes were observed in the ADIPO concentration, but a decrease in insulin resistance expressed in HOMA-TG was confirmed. The level of ADIPO was significantly related to the level of GYNOID and HOMA-AD. Under the influence of aerobic–resistance training, there was a significant increase in FFM and a decrease in GYNOID and WC. Aerobic training led to a decrease in IL-8 after 6 weeks of intervention. The use of aerobic training, as well as a combination of aerobic and resistance training, brought health benefits to men with MetS. In our study, a combination of aerobic and resistance training resulted in more benefits. More tests are recommended in order to select the correct training method in the treatment of MetS.

**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/biom13050852/s1, Figure S1: A comprehensive strategy for the aerobic program intended for a group engaged in aerobic activities (EG1); Table S1: A comprehensive strategy for a combined aerobic and resistance training program intended for a group engaged in aerobic–resistance activities (EG2); Table S2: The progressions of loads [kg] in selected resistance exercises during the intervention and follow-up in comparison to baseline in the aerobic–resistance group EG2; Table S3: The value of the Pearson correlation for variables in the aerobic group (EG1), aerobic–resistance group (EG2), and control group (CG).

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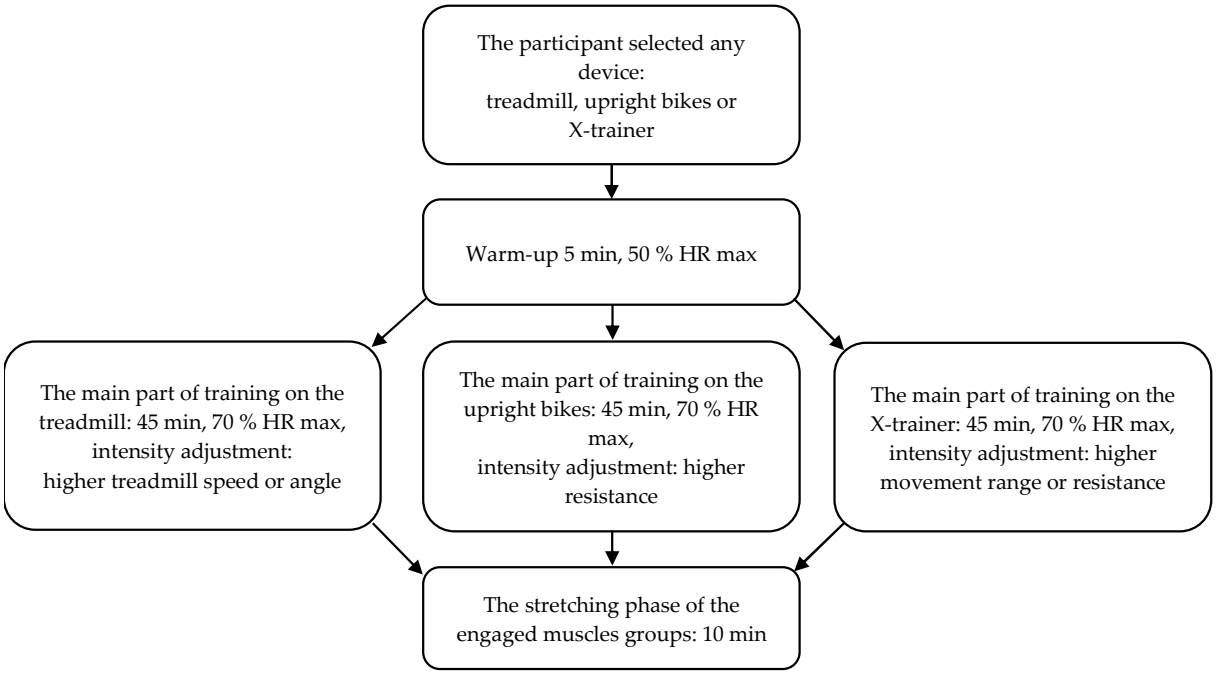
## References

1. Tan, M.C.; Ng, O.C.; Wong, T.W.; Joseph, A.; Yoke, M.C.; Hejar, A.R. Prevalence of metabolic syndrome in type 2 diabetic patients: A comparative study using WHO, NCEP ATP III, IDF and Harmonized definitions. *Health* **2013**, *5*, 1689–1696. [CrossRef]
2. Thottam, G.E.; Krasnokutsky, S.; Pillinger, M.H. Gout and metabolic syndrome: A tangled web. *Curr. Rheumatol. Rep.* **2017**, *19*, 60. [CrossRef]
3. Uzunlulu, M.; Telci Caklili, O.; Oguz, A. Association between metabolic syndrome and cancer. *Ann. Nutr. Metab.* **2016**, *68*, 173–179. [CrossRef] [PubMed]
4. Kostoglou-Athanassiou, I.; Athanassiou, P. Metabolic syndrome and sleep apnea. *Hippokratia* **2008**, *2*, 81–86. Available online: http://www.ncbi.nlm.nih.gov/pmc/articles/pmc2464309/ (accessed on 13 February 2023).
5. Moreira, G.C.; Cipullo, J.P.; Ciorlia, L.A.S.; Cesarino, C.B.; Vilela-Martinet, J.F. Prevalence of metabolic syndrome: Association with risk factors and ardiovascular complications in an urban population. *PLoS ONE* **2014**, *9*, 105056. [CrossRef] [PubMed]
6. Furukawa, S.; Fujita, T.; Shimabukuro, M.; Iwaki, M.; Yamada, Y.; Nakajima, Y.; Nakayama, O.; Makishima, M.; Matsuda, M.; Shimomura, I. Increased oxidative stress in obesity and its impact on metabolic syndrome. *J. Clin. Investig.* **2004**, *114*, 1752–1761. [CrossRef] [PubMed]
7. Lee, I.M.; Manson, J.E.; Hennekens, C.H.; Paffenbarger, R.S., Jr. Body weight and mortality. A 27-year follow-up of middle-aged men. *JAMA* **1993**, *270*, 2823–2828. [CrossRef]
8. Attarzadeh Hosseini, S.R.; Mohammad Rahimi, G.R.; Ghaemi, J. Compare waist circumference, waist-to-hip ratio and waist-to-stature ratio in predicting overweight/obese male students. *Razi J. Med. Sci.* **2017**, *24*, 67–76.
9. Sang, H.; Yao, S.; Zhang, L.; Li, X.; Yang, N.; Zhao, J.; Zhao, L.; Si, Y.; Zhang, Y.; Lv, X. Walk-run training improves the antiinflammation properties of high-density lipoprotein in patients with metabolic syndrome. *J. Clin. Endocrinol. Metab.* **2015**, *100*, 870–879. [CrossRef]
10. Suder, A. Body fatness and its social and lifestyle determinants in young working males from Cracow, Poland. *J. Biosoc. Sci.* **2009**, *41*, 139–154. [CrossRef]
11. Suder, A. Socioeconomic and lifestyle determinants of body fat distribution in young working males from Cracow, Poland. *Am. J. Hum. Biol.* **2008**, *20*, 100–109. [CrossRef]
12. Steckhan, N.; Hohmann, C.D.; Kessler, C.; Dobos, G.; Michalsen, A.; Cramer, H. Effects of different dietary approaches on inflammatory markers in patients with metabolic syndrome: A systematic review and meta-analysis. *Nutrition* **2016**, *32*, 338–348. [CrossRef]
13. He, D.; Xi, B.; Xue, J.; Huai, P.; Zhang, M.; Liet, J. Association between leisure time physical activity and metabolic syndrome: A meta-analysis of prospective cohort studies. *Endocrine* **2014**, *46*, 231–240. [CrossRef]
14. Edwardson, C.L.; Gorely, T.; Davies, M.J.; Gray, L.J.; Khunti, K.; Wilmot, E.G.; Yates, T.; Biddle, S.J.H. Association of sedentary behaviour with metabolic syndrome: A metaanalysis. *PLoS ONE* **2012**, *7*, 34916. [CrossRef]
15. Balducci, S.; Zanuso, S.; Nicolucci, A.; Fernando, F.; Cavallo, S.; Cardelli, P.; Fallucca, S.; Alessi, E.; Letizia, C.; Jimenez, A.; et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. *Nutr. Metab. Cardiovasc. Dis.* **2010**, *20*, 608–617. [CrossRef]
16. Nicholson, T.; Church, C.; Baker, D.J.; Jones, S.W. The role of adipokines in skeletal muscle inflammation and insulin sensitivity. *J. Inflamm.* **2018**, *15*, 9. [CrossRef] [PubMed]
17. Rome, S. Muscle and Adipose Tissue Communicate with Extracellular Vesicles. *Int. J. Mol. Sci.* **2022**, *23*, 7052. [CrossRef] [PubMed]
18. Coelho-Junior, H.J.; Picca, A.; Calvani, R.; Uchida, M.C.; Marzetti, E. If my muscle could talk: Myokines as a biomarker of frailty. *Exp. Gerontol.* **2019**, *127*, 110715. [CrossRef]
19. Nelke, C.; Dziewas, R.; Minnerup, J.; Meuth, S.G.; Ruck, T. Skeletal muscleas potential central link between sarcopenia and immune senescence. *eBioMedicine.* **2019**, *49*, 381–388. [CrossRef] [PubMed]

20. Tsao, T.S.; Burcelin, R.; Katz, E.B.; Huang, L.; Charron, M.J. Enhanced insulin action due to targeted GLUT4 overexpression exclusively in muscle. *Diabetes* **1996**, *45*, 28–36. [CrossRef] [PubMed]
21. Tsao, T.S.; Li, J.; Chang, K.S.; Stenbit, A.E.; Galuska, D.; Anderson, J.E.; Zierath, J.R.; McCarter, R.J.; Charron, M.J. Metabolic adaptations in skeletal muscle overexpressing GLUT4: Effects on muscle and physical activity. *FASEB J.* **2001**, *15*, 958–969. [CrossRef]
22. Yamauchi, T.; Kamon, J.; Ito, Y.; Tsuchida, A.; Yokomizo, T.; Kita, S.; Sugiyama, T.; Miyagishi, M.; Hara, K.; Tsunoda, M.; et al. Cloning of adiponectin receptors that mediate antidiabetic metabolic effects. *Nature* **2003**, *423*, 762–769. [CrossRef]
23. Fang, H.; Judd, R.L. Adiponectin Regulation and Function. *Society. Compr. Physiol.* **2018**, *8*, 1031–1063. [CrossRef]
24. Supriya, R.; Tam, B.T.; Yu, A.P.; Lee, P.H.; Lai, C.W.; Cheng, K.K.; Yau, S.Y.; Chan, L.W.; Yung, B.Y.; Sheridan, S.; et al. Adipokines demonstrate the interacting influence of central obesity with other cardiometabolic risk factors of metabolic syndrome in Hong Kong Chinese adults. *PLoS ONE* **2018**, *13*, 0201585. [CrossRef] [PubMed]
25. Arita, Y.; Kihara, S.; Ouchi, N.; Maeda, K.; Kuriyama, H.; Okamoto, Y.; Kumada, M.; Hotta, K.; Nishida, M.; Takahashi, M.; et al. Adipocyte-derived plasma protein adiponectin acts as a platelet-derived growth factor- BB-binding protein and regulates growth factor-induced common postreceptor signal in vascular smooth muscle cell. *Circulation* **2002**, *105*, 2893–2898. [CrossRef]
26. Yamauchi, T.; Kamon, J.; Waki, H.; Terauchi, Y.; Kubota, N.; Hara, K.; Mori, Y.; Ide, T.; Murakami, K.; Tsuboyama-Kasaoka, N.; et al. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. *Nat. Med.* **2001**, *7*, 941–946. [CrossRef]
27. Frühbeck, G.; Catalán, V.; Rodríguez, A.; Gómez-Ambrosi, J. Adiponectin-leptin ratio: A promising index to estimate adipose tissue dysfunction. Relation with obesity-associated cardiometabolic risk. *Adipocyte* **2018**, *7*, 57–62. [CrossRef]
28. Suder, A.; Płonka, M.; Jagielski, P.; Piórecka, B.; Głodzik, J. Physiological and environmental factors associated with central fat distribution in pubertal girls. *J. Physiol. Pharmacol.* **2015**, *66*, 463–470.
29. Blüher, M.; Mantzoros, C.S. From leptin to other adipokines in health and disease: Facts and expectations at the beginning of the 21st century. *Metabolism* **2015**, *64*, 131–145. [CrossRef] [PubMed]
30. Vega, G.L.; Grundy, S.M. Metabolic risk susceptibility in men is partially related to adiponectin/leptin ratio. *J. Obes.* **2013**, *2013*, 409679. [CrossRef] [PubMed]
31. Meniailo, M.E.; Malashchenko, V.V.; Shmarov, V.A.; Gazatova, N.D.; Melashchenko, O.B.; Goncharov, A.G.; Seledtsova, G.V.; Seledtsov, V.I. Interleukin-8 favors pro-inflammatory activity of human monocytes/macrophages. *Int. Immunopharmacol.* **2018**, *56*, 217–221. [CrossRef]
32. Bruun, J.M.; Pedersen, S.B.; Richelsen, B. Interleukin-8 production in human adipose tissue. Inhibitory effects of anti-diabetic compounds, the thiazolidinedione ciglitazone and the biguanide metformin. *Horm. Metab. Res.* **2000**, *32*, 537–541. [CrossRef] [PubMed]
33. Fain, J.N. Release of inflammatory mediators by human adipose tissue is enhanced in obesity and primarily by the nonfat cells: A review. *Mediat. Inflamm.* **2010**, *2010*, 513948. [CrossRef] [PubMed]
34. Bruun, J.M.; Pedersen, S.B.; Richelsen, B. Regulation of interleukin 8 production and gene expression in human adipose tissue in vitro. *J. Clin. Endocrinol. Metab.* **2001**, *86*, 1267–1273. [CrossRef] [PubMed]
35. Marques, P.; Collado, A.; Martinez-Hervás, S.; Domingo, E.; Benito, E.; Piqueras, L.; Real, J.T.; Ascaso, J.F.; Sanz, M.J. Systemic Inflammation in Metabolic Syndrome: Increased Platelet and Leukocyte Activation, and Key Role of CX3CL1/CX3CR1 and CCL2/CCR2 Axes in Arterial Platelet-Proinflammatory Monocyte Adhesion. *J. Clin. Med.* **2019**, *8*, 708. [CrossRef]
36. Mirhafez, S.R.; Tajfard, M.; Zarifian, A.; Movahedi, A.; Amiri, N.; Ghazizadeh, H.; Avan, A.; Ferns, G.A.; Ghayour-Mobarhan, M. Association between the serum concentrations of 12 cytokines and growth factors and metabolic syndrome in patients undergoing angiography. *Growth Factors* **2019**, *37*, 238–246. [CrossRef] [PubMed]
37. Moldoveanu, A.I.; Shephard, R.J.; Shek, P.N. The cytokine response to physical activity and training. *Sports Med.* **2001**, *31*, 115–144. [CrossRef]
38. Frydelund-Larsen, L.; Penkowa, M.; Akerstrom, T.; Zankari, A.; Nielsen, S.; Pedersen, B.K. Exercise induces interleukin-8 receptor (CXCR2) expression in human skeletal muscle. *Exp. Physiol.* **2007**, *92*, 233–240. [CrossRef]
39. Yu, N.; Ruan, Y.; Gao, X.; Sun, J. Systematic Review and Meta-Analysis of Randomized, Controlled Trials on the Effect of Exercise on Serum Leptin and Adiponectin in Overweight and Obese Individuals. *Horm. Metab. Res.* **2017**, *49*, 164–173. [CrossRef]
40. Blair, S.N.; Cheng, Y.; Holder, J.S. Is physical activity or physical fitness more important in defining health benefits? *Med. Sci. Sports Exerc.* **2001**, *33*, 379–399. [CrossRef] [PubMed]
41. Makiel, K.; Suder, A.; Targosz, A.; Maciejczyk, M.; Haim, A. Effect of exercise interventions on irisin and interleukin 6 concentrations and indicators of carbohydrate metabolism in males with metabolic syndrome. *J. Clin. Med.* **2023**, *12*, 369. [CrossRef] [PubMed]
42. Makiel, K.; Suder, A.; Targosz, A.; Maciejczyk, M.; Kozioł-Kozakowska, A.; Haim, A. Impact of Two Types of Exercise. Interventions on Leptin and Omentin Concentrations and Indicators of Lipid and Carbohydrate Metabolism in Males with Metabolic Syndrome. *J. Clin. Med.* **2023**, *12*, 2822. [CrossRef] [PubMed]
43. Alberti, K.G.; Zimmet, P.; Shaw, J. Metabolic syndrome–a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabet. Med.* **2006**, *23*, 469–480. [CrossRef] [PubMed]

44. Matsuhisa, M.; Yamasaki, Y.; Emoto, M.; Shimabukuro, M.; Ueda, S.; Funahashi, T.; Matsuzawa, Y. A novel index of insulin resistance determined from the homeostasis model assessment index and adiponectin levels in Japanese subjects. *Diabetes Res. Clin. Pract.* **2007**, *77*, 151–154. [CrossRef]
45. Khan, S.H.; Khan, A.N.; Chaudhry, N.; Anwar, R.; Fazal, N.; Tariq, M. Comparison of various steady state surrogate insulin resistance indices in diagnosing metabolic syndrome. *Diabetol. Metab. Syndr.* **2019**, *14*, 11–44. [CrossRef] [PubMed]
46. Craig, C.L.; Marshall, A.J.; Sjöström, M.; Bauman, A.E.; Booth, M.L.; Ainsworth, B.E.; Pratt, M.; Ekelund, U.; Yngve, A.; Sallis, J.F.; et al. International Physical Activity Questionnaire: 12-country reliability and validity. *Med. Sci. Sport. Exerci.* **2003**, *35*, 1381–1395. [CrossRef]
47. Garber, C.E.; Blissmer, B.; Deschenes, M.R.; Franklin, B.A.; Lamonte, M.J.; Lee, I.M.; Nieman, D.C.; Swain, D.P. American College of Sports Medicine. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: Guidance for prescribing exercise. *Med. Sci. Sport. Exerc.* **2011**, *43*, 1334–1359. [CrossRef]
48. Brzycki, M. Strength Testing—Predicting a One-Rep Max from Reps-to-Fatigue. *J. Phys. Educ. Recreat. Dance* **1993**, *64*, 88–90. [CrossRef]
49. Grgic, J.; Lazinica, B.; Schoenfeld, B.J.; Pedisic, Z. Test-Retest Reliability of the One-Repetition Maximum (1RM) Strength Assessment: A Systematic Review. *Sport. Med. Open.* **2020**, *6*, 31. [CrossRef]
50. Ainsworth, B.E.; Haskell, W.L.; Herrmann, S.D.; Meckes, N.; Bassett, D.R., Jr.; Tudor-Locke, C.; Greer, J.L.; Vezina, J.; Whitt-Glover, M.C.; Leon, A.S. 2011 Compendium of Physical Activities: A second update of codes and MET values. *Med. Sci. Sport. Exerc.* **2011**, *43*, 1575–1581. [CrossRef]
51. Tanaka, H.; Monahan, K.D.; Seals, D.R. Age-predicted maximal heart rate revisited. *J. Am. Coll. Cardiol.* **2001**, *37*, 153–156. [CrossRef]
52. Levinger, I.; Goodman, C.; Hare, D.L.; Jerums, G.; Toia, D.; Selig, S. The reliability of the 1RM strength test for untrained middle-aged individuals. *J. Sci. Med. Sport.* **2009**, *12*, 310–316. [CrossRef] [PubMed]
53. Fritz, C.O.; Morris, P.E.; Richler, J.J. Effect size estimates: Current use, calculations, and interpretation. *J. Exp. Psychol. Gen.* **2012**, *141*, 2–18. [CrossRef]
54. Pripp, A.H. Pearsons eller Spearmans korrelasjonskoeffisienter [Pearson's or Spearman's correlation coefficients]. *Tidsskr. Nor. Laegeforen.* **2018**, *8*, 138. [CrossRef]
55. Becic, T.; Studenik, C.; Hoffmann, G. Exercise Increases Adiponectin and Reduces Leptin Levels in Prediabetic and Diabetic Individuals: Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Med. Sci.* **2018**, *30*, 97. [CrossRef]
56. Hayashino, Y.; Jackson, J.L.; Hirata, T.; Fukumori, N.; Nakamura, F.; Fukuhara, S.; Tsujii, S.; Ishii, H. Effects of exercise on C-reactive protein, inflammatory cytokine and adipokine in patients with type 2 diabetes: A meta-analysis of randomized controlled trials. *Metabolism* **2014**, *63*, 431–440. [CrossRef] [PubMed]
57. Evans, R.A.; Dolmage, T.E.; Robles, P.G.; Brooks, D.; Goldberg, R.S. The effects of exercise modality and intensity on energy expenditure and cardiorespiratory response in adults with obesity and treated obstructive sleep apnoea. *Chron. Respir. Dis.* **2017**, *14*, 342–351. [CrossRef] [PubMed]
58. Esposito, K.; Pontillo, A.; Di Palo, C.; Giugliano, G.; Masella, M.; Marfella, R.; Giugliano, D. Effect ofweight loss and lifestyle changes on vascular inflammatory markers in obese women: A randomized trial. *JAMA* **2003**, *289*, 1799–1804. [CrossRef] [PubMed]
59. Belza, A.; Toubro, S.; Stender, S.; Astrup, A. Effect of diet-induced energy deficit and body fat reduction on high-sensitive CRP and other inflammatory markers in obese subjects. *Int. J. Obes.* **2009**, *33*, 456–464. [CrossRef]
60. Chan, D.C.; Watts, G.F.; Ng, T.W.; Yamashita, S.; Barrett, P.H. Effect of weight loss on markers of triglyceride-rich lipoprotein metabolism in the metabolic syndrome. *Eur. J. Clin. Investig.* **2008**, *38*, 743–751. [CrossRef]
61. Larrouy, D.; Barbe, P.; Valle, C.; Déjean, S.; Pelloux, V.; Thalamas, C.; Bastard, J.P.; Le Bouil, A.; Diquet, B.; Clément, K.; et al. Gene expression profiling of human skeletal muscle in response to stabilized weight loss. *Am. J. Clin. Nutr.* **2008**, *88*, 125–132. [CrossRef]
62. Claessens, M.; van Baak, M.A.; Monsheimer, S.; Saris, W.H. The effect of a low-fat, high-protein or high-carbohydrate ad libitum diet on weight loss maintenance and metabolic risk factors. *Int. J. Obes.* **2009**, *33*, 296–304. [CrossRef]
63. Klempel, M.C.; Varady, K.A. Reliability of leptin, but not adiponectin, as a biomarker for diet-induced weight loss in humans. *Nutr. Rev.* **2011**, *69*, 145–154. [CrossRef] [PubMed]
64. Cnop, M.; Havel, P.J.; Utzschneider, K.M.; Carr, D.B.; Sinha, M.K.; Boyko, E.J.; Retzlaff, B.M.; Knopp, R.H.; Brunzell, J.D.; Kahn, S.E. Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: Evidence for independent roles of age and sex. *Diabetologia* **2003**, *46*, 459–469. [CrossRef] [PubMed]
65. Zierath, J.R.; Krook, A.; Wallberg-Henriksson, H. Insulin action and insulin resistance in human skeletal muscle. *Diabetologia* **2000**, *43*, 821–835. [CrossRef] [PubMed]
66. Achari, A.E.; Jain, S.K. Adiponectin, a Therapeutic Target for Obesity, Diabetes, and Endothelial Dysfunction. *Int. J. Mol. Sci.* **2017**, *18*, 1321. [CrossRef] [PubMed]
67. Sethi, J.K.; Vidal-Puig, A.J. Thematic review series: Adipocyte biology. Adipose tissue function and plasticity orchestrate nutritional adaptation. *J. Lipid Res.* **2007**, *48*, 1253–1262. [CrossRef]

68. Paz, K.; Hemi, R.; LeRoith, D.; Karasik, A.; Elhanany, E.; Kanety, H.; Zick, Y. A molecular basis for insulin resistance. Elevated serine/threonine phosphorylation of IRS-1 and IRS-2 inhibits their binding to the juxtamembrane region of the insulin receptor and impairs their ability to undergo insulin-induced tyrosine phosphorylation. *J. Biol. Chem.* **1997**, *272*, 29911–29918. [CrossRef]
69. Shulman, G.I. Cellular mechanisms of insulin resistance. *J. Clin. Investig.* **2000**, *106*, 171–176. [CrossRef]
70. Clarkson, P.M. Eccentric exercise and muscle damage. *Int. J. Sport. Med.* **1997**, *4*, 314–317. [CrossRef]
71. Alizaei Yousefabadi, H.; Niyazi, A.; Alaee, S.; Fathi, M.; Mohammad Rahimi, G.R. Anti-Inflammatory Effects of Exercise on Metabolic Syndrome Patients: A Systematic Review and Meta-Analysis. *Biol. Res. Nurs.* **2021**, *23*, 280–292. [CrossRef] [PubMed]
72. Fuentes, G.C.; Castañer, O.; Warnberg, J.; Subirana, I.; Buil-Cosiales, P.; Salas-Salvadó, J.; Corella, D.; Serra-Majem, L.; Romaguera, D.; Estruch, R.; et al. Prospective association of physical activity and inflammatory biomarkers in older adults from the PREDIMED-Plus study with overweight or obesity and metabolic syndrome. *Clin. Nutr.* **2020**, *39*, 3092–3098. [CrossRef] [PubMed]
73. Guo, A.; Li, K.; Xiao, Q. Sarcopenic Obesity: Myokines as Potential Diagnostic Biomarkers and Therapeutic Targets? *Exp. Gerontol.* **2020**, *139*, 111022. [CrossRef] [PubMed]
74. Bruun, J.M.; Lihn, A.S.; Madan, A.K.; Pedersen, S.B.; Schiott, K.M.; Fain, J.N.; Richelsen, B. Higher production of IL-8 in visceral vs. subcutaneous adipose tissue. Implication of nonadipose cells in adipose tissue. *Am. J. Physiol. Endocrinol. Metab.* **2004**, *286*, 8–13. [CrossRef] [PubMed]
75. Amir, L.Y.; Ciaraldi, T.P.; Mudaliar, S.R.; Phillips, S.A.; Henry, R.R. Excessive secretion of IL-8 by skeletal muscle in type 2 diabetes impairs tube growth: Potential role of PI3K and the Tie2 receptor. *Am. J. Physiol. Endocrinol. Metab.* **2015**, *309*, 22–34. [CrossRef]
76. Yang, M.; Liu, S.; Zhang, C. The Related Metabolic Diseases and Treatments of Obesity. *Healthcare* **2022**, *10*, 1616. [CrossRef]




HR max – maximal heart rate

**Figure S1.** A comprehensive strategy for the aerobic program intended for a group engaged in aerobic activities (EG1).

**Table S1.** A comprehensive strategy for a combined aerobic and resistance training program intended for a group engaged in aerobic–resistance activities (EG2).

| | **Training Sessions 1 - 3** | **Training Sessions 4 - 6** | **Training Sessions 6 <** |
|---|---|---|---|
| Type of training | Whole-body training | Training of antagonistic parts | Training of antagonistic parts |
| Volume of resistance training [exercises x series x repetitions] | 3 x 4 x 15 | 6 x 3 x 12 | 9 x 3 x 12 |
| Intensity of resistance training [% 1 RM] | 50 | 70 | 70 |
| Breaks between series [min] | 2 | 1.5 | 1 |
| Duration of resistance training [min] | 30 | 35 | 40 |
| Duration of aerobic training [min] | 20 | 15 | 10 |
| Intensity of aerobic training [% HR max] | 50 | 70 | 70 |
| Specialised exercises | One-arm row with dumbbell<br>Supported push-ups (Smith machine)<br>Supported sit-ups (with bar)<br>Front support (plank) | Standing dumbbell press<br>Barbell bench press<br>Reverse grip lat pulldown<br>Hip thrust lying<br>Bent dumbbell row | Dumbbell deadlift<br>Cable tricep extension<br>Standing dumbbell curl |

HR max—maximal heart rate, 1RM—one repetition maximum.

**Table S2.** The progressions of loads [kg] in selected resistance exercises during the intervention and follow-up in comparison to baseline in the aerobic–resistance group EG2.

| Time of observation | Barbell Bench press [kg] | Lat Pull Down [kg] | Dumbbell Squat [kg] |
|---|---|---|---|
| Baseline | 63.36 ± 12.92 | 11.58 ± 2.56 | 44.51 ± 8.26 |
| After 6 weeks of intervention | 72.78 ± 14.77 | 13.15 ± 2.84 | 51.77 ± 9.84 |
| After 12 weeks of intervention | 76.65 ± 15.04 | 14.89 ± 2.64 | 56.78 ± 9.77 |
| After 16 weeks, follow-up period | 79.32 ± 17.29 | 14.91 ± 2.02 | 57.74 ± 10.78 |
| *p*- value | 0.00 | 0.00 | 0.00 |

*p*-value—ANOVA test.

**Table S3.** The value of the Pearson correlation for variables in the aerobic group (EG1), aerobic–resistance group (EG2), and control group (CG).

| | TEE[1] [kcal/day] | Proteins[1] [g] | Carbohydrates[1] [g] | Fats[1] [g] | FFM[1] [%] | GYNOID[1] [%] | WC[1] [cm] | HOMA-AD[1] | HOMA-TG[1] | ADIPO[1] [ng/ml] | ADIPO/LEP ratio[1] | IL-8[1] [pg/ml] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ADIPO EG1 [ng/ml] | −0.23 | −0.14 | −0.27* | −0.35* | −0.24 | 0.33* | 0.03 | −0.63* | −0.48* | 1.00 | 0.23 | 0.03 |
| ADIPO EG2 [ng/ml] | 0.14 | −0.08 | −0.43* | 0.06 | −0.13 | 0.42* | −0.16 | −0.56* | −0.04 | 1.00 | 0.68* | 0.12 |
| ADIPO CG [ng/ml] | 0.26* | 0.17 | 0.05 | −0.04 | −0.06 | 0.23 | −0.02 | −0.59* | −0.29* | 1.00 | 0.00 | 0.11 |
| IL-8 EG1 [ng/ml] | −0.16 | 0.11 | −0.07 | −0.01 | −0.23 | 0.20 | 0.19 | −0.19 | −0.22 | 0.03 | 0.02 | 1.00 |
| IL−8 EG2 [ng/ml] | −0.26 | 0.18 | −0.07 | −0.01 | 0.04 | 0.24 | −0.12 | −0.28* | −0.09 | 0.12 | −0.06 | 1.00 |
| IL-8 CG [ng/ml] | 0.43* | −0.10 | 0.01 | −0.05 | 0.23 | −0.25 | −0.19 | −0.02 | 0.14 | 0.11 | −0.08 | 1.00 |
| HOMA-AD EG1 | 0.26 | 0.04 | 0.37* | 0.34* | −0.19 | 0.02 | 0.36* | 1.00 | 0.81* | −0.63* | −0.19 | −0.19 |
| HOMA-AD EG2 | −0.05 | 0.05 | 0.21 | 0.14 | −0.14 | −0.27* | 0.39* | 1.00 | 0.55* | −0.56* | −0.50* | −0.28* |
| HOMA-AD CG | 0.04 | −0.20 | −0.09 | −0.02 | 0.08 | −0.11 | 0.11 | 1.00 | 0.53* | −0.59* | −0.08 | −0.02 |

*—statistically significant $p < 0.05$; ADIPO EG1—concentrations of adiponectin in EG1 taken from the four timepoints; ADIPO EG2—concentrations of adiponectin in EG2 taken from the four timepoints; ADIPO CG—concentrations of adiponectin in CG taken from the four timepoints; IL-8 EG1—concentrations of interleukin-8 in EG1 taken from the four timepoints; IL-8 EG2—concentrations of interleukin-8 in EG2 taken from the four timepoints; IL-8 CG—concentrations of interleukin-8 CG taken from the four timepoints, total energy expenditure (TEE), fat-free mass (FFM), gynoid body fat (GYNOID), waist circumference (WC), homeostatic model assessment—adiponectin (HOMA-AD), homeostatic model assessment—triglycerides (HOMA-TG), adiponectin (ADIPO), adiponectin-to-leptin ratio (ADIPO/LEP ratio), interleukin-8 (IL-8), 1—taken from the four timepoints, corresponding to the group and measurement week in column 1.

The course of 1RM:

The examined participants underwent the 1 RM test before the examination, and after 6, 12 and 16 weeks.

The personal coach carried out the warm-up on the treadmill (Technogym New Excite Run Now 500, Cesena, Italy) for 5 min at 60% HR. The subjects warmed up in 2 series of 10 repetitions using about 50% of their 1 RM estimated load before the beginning of the test protocol.

After a 5 min break, the subjects were instructed to perform the selected test exercise until unable to continue the exercise series while maintaining the proper technique (failure).

For the 1RM bench press test, the subjects were instructed to maintain 5-point body contact (i.e., head, back and hips with the bench, and both feet with the floor) during the test; the barbell had to touch the chest when lowered.

In the 1RM squat test, subjects were instructed to move from a standing position to a position of 90 degrees of flexion at the knee joints.

The pull-down test was performed on a training atlas. The repetition was passed when the subject made a full extension of the arms during the eccentric phase and touching the bar to the chest during the concentric phase.

A qualified personal coach controlled the range of motion to verify the correctness of the test.

The last repetition of a series occurred when the participant could not continue the exercise while maintaining the proper technique.

The obtained load and number of repetitions were converted into 1 RM based on the 1 RM calculator [49], applying the Brzycki formula [48].

## References

48. Brzycki, M. Strength Testing—Predicting a One-Rep Max from Reps-to-Fatigue. J. Phys. Educ. Recreat. Dance 1993, 64, 88–90. https://doi.org/10.01080/07303084.1993.10606684.

49. Grgic, J.; Lazinica, B.; Schoenfeld, B.J.; Pedisic, Z. Test-Retest Reliability of the One-Repetition Maximum (1RM) Strength Assessment: A Systematic Review. Sport. Med. Open. 2020, 6, 31. https://doi.org/10.1186/s40798-020-00260-z.

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Mój udział w przygotowaniu publikacji pod tytułem: "Effect of exercise interventions on irisin and interleukin-6 concentrations and indicators of carbohydrate metabolism in males with metabolic syndrome", Journal of Clinical Medicine, 2023, 12(1), 369; DOI: https://doi.org/10.3390/jcm12010369 obejmował:

- ✓ Przygotowanie koncepcji badań,
- ✓ Opracowanie metodologii badań,
- ✓ Przeprowadzenie badań,
- ✓ Analiza i interpretacja wyników,
- ✓ Opracowanie statystyki,
- ✓ Pisanie wszystkich rozdziałów pracy,
- ✓ Opracowanie piśmiennictwa,
- ✓ Pozyskanie funduszy i administracja projektu.

Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 56 %.

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- ✓ Pomoc w przeprowadzeniu badań,
- ✓ Pomoc przy analizie i interpretacji wyników,
- ✓ Recenzja i redakcja ostatecznej wersji artykułu,
- ✓ Pozyskanie funduszy i administracja projektu.

Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 33 %.

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- ✓ Przeprowadzenie oznaczeń hormonalnych,
- ✓ Konsultacje przy przygotowaniu artykułu i zaakceptowanie jego ostatecznej wersji.

Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 5 %.

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Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 3 %.

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- ✓ methodological consultations of the project;
- ✓ consultations in the preparation of the article and approval of its final version.

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- ✓ Przygotowanie koncepcji badań,
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- ✓ Pisanie wszystkich rozdziałów pracy,
- ✓ Opracowanie piśmiennictwa,
- ✓ Pozyskanie funduszy i administracja projektu.

Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 56 %.

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- ✓ Recenzja i redakcja ostatecznej wersji artykułu,
- ✓ Pozyskanie funduszy i administracja projektu.

Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 32 %.

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- ✓ Konsultacje przy przygotowaniu artykułu i zaakceptowanie jego ostatecznej wersji.

Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 5 %.

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Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 3 %.

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- ✓ Konsultacje przy przygotowaniu artykułu i zaakceptowanie jego ostatecznej wersji.

Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 2 %.

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Mój udział w przygotowaniu publikacji pod tytułem: "Exercise-induced alternations of adiponectin, interleukin-8 and indicators of carbohydrate metabolism in males with metabolic syndrome", Biomolecules, 2023, 13(5), 852; https://doi.org/10.3390/biom13050852 obejmował:

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Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 56 %.

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Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 5 %.

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Potwierdzenie promotora

Podpis

Kraków, 17. 05. 2023

prof. dr hab. Marcin Maciejczyk
Zakład Fizjologii i Biochemii
Wydział Wychowania Fizycznego i Sportu
Akademia Wychowania Fizycznego
im. Bronisława Czecha w Krakowie

**Oświadczenie współautora**

Mój udział w przygotowaniu publikacji pod tytułem: "Exercise-induced alternations of adiponectin, interleukin-8 and indicators of carbohydrate metabolism in males with metabolic syndrome", Biomolecules, 2023, 13(5), 852; https://doi.org/10.3390/biom13050852 obejmował:

- ✓ Konsultacje metodologiczne przed przygotowaniem projektu,
- ✓ Konsultacje przy przygotowaniu artykułu i zaakceptowanie jego ostatecznej wersji.

Oświadczam, że mój udział wkładu pracy w powstanie artykułu wyniósł 3 %.

Agnieszka Zuwer
Potwierdzenie promotora

Marcin Maciejczyk
Podpis

17. 05. 2023

dr Alon Haim
Department of Pediatrics Endocrinology and Diabetes,
Faculty of Health Sciences,
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Soroka University Medical Center, Israel

**Co-authors' contribution statement**

I confirm that my participation in preparing the article entitled: "Exercise-induced alternations of adiponectin, interleukin-8 and indicators of carbohydrate metabolism in males with metabolic syndrome", Biomolecules, 2023, 13(5), 852; https://doi.org/10.3390/biom13050852 included:

- ✓ methodological consultations of the project;
- ✓ consultations in the preparation of the article and approval of its final version.

My participation on the preparation of the manuscript could be estimated as 3 % of all the work.

Agnieszka Cuder

Promoter confirmation

Signature

Komisja Bioetyczna
przy Okręgowej Izbie Lekarskiej
w Krakowie

**Opinia**

**Nr 90/KBL/OIL/2020 z dnia 5 czerwca 2020 r.**

Na posiedzeniu w dniu 5 czerwca 2020 r. Komisja zapoznała się z wnioskiem (dokumentacja w załączeniu) złożonym przez :

**Koordynator Badania: mgr Karol Makiel**
**Akademia Wychowania Fizycznego, Wydział Rehabilitacji Ruchowej, Al. Jana Pawła II 78, 31-571 Kraków**

**Tytuł Protokołu: „Wpływ dwunastotygodniowego treningu zdrowotnego na wskaźniki morfologiczne oraz poziom wybranych adiopkin tkanki tłuszczowej u mężczyzn z otyłością brzuszną".**

Do wniosku dołączono:
Protokół badania
Streszczenie protokołu
Życiorys Głównego Badacza
Informacja dla Pacjenta
Formularz Świadomej Zgody Pacjenta
Formularz „Ochrony Danych Osobowych"
Polisa Ubezpieczenia Lekarza
Oświadczenie Lekarza o objęciu opieką uczestników badania
Polisa Ubezpieczenia Ośrodka
Lista ośrodków biorących udział w badaniu

**Komisja wyraża zgodę na przeprowadzenia badania na warunkach przedstawionych we wniosku.**

Zgoda Komisji dla Ośrodka jest ważna do dnia ważności Polisy Ubezpieczeniowej
Skład i działanie Komisji zgodne z zasadami Dobrej Praktyki Klinicznej (GCP) oraz wymogami lokalnymi
Lista członków Komisji biorących udział w posiedzeniu stanowi załącznik do niniejszego dokumentu.
Pouczenie: W ciągu 14 dni od otrzymania niniejszej opinii Wnioskodawcy przysługuje prawo odwołania do Komisji Odwoławczej za pośrednictwem Komisji Bioetycznej przy OIL w Krakowie

**Kraków, dnia 17.06.2020 r.**

**Przewodniczący Komisji Bioetycznej**
**przy OIL w Krakowie**

**Dr Mariusz Janikowski**

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Komisja Bioetyczna
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w Krakowie

***Lista obecności członków Komisji Bioetycznej przy Okręgowej Izbie Lekarskiej w Krakowie na posiedzeniu w dniu 5 czerwca 2020r.***

**dr Mariusz Janikowski** .....
lekarz– specjalista chorób wewnętrznych,
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I Klinika Chorób Wewnętrznych i Gerontologii
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**mgr Jerzy Bilek** .....
mgr farmacji

**ks. dr hab. Jerzy Brusiło** .....
Uniwersytet Papieski Jana Pawła II
duchowny, etyk

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dr hab. medycyny
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**dr med. Jerzy Friediger** .....
dr medycyny – specjalista chirurgii ogólnej
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**mgr Zbigniew Grochowski** .....
mgr psychologii
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**prof. dr hab. med. Zbigniew Kojs** .....
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**dr Lech Kucharski** .....
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Kraków, 31. 05. 2023

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**Oświadczenie**

Zapoznałam się z niniejszą rozprawą doktorską Pana mgr Karola Makiela pt.: „Wpływ treningu fizycznego na skład ciała i stan zdrowia mężczyzn z zespołem metabolicznym" i akceptuję jej treść w obecnej formie.

z poważaniem

dr Aneta Targosz
Promotor pomocniczy

**Streszczenie**

**Temat: Wpływ treningu fizycznego na skład ciała i stan zdrowia mężczyzn z zespołem metabolicznym**

**Wstęp:** Zespół metaboliczny (MetS) to współwystępowanie czynników ryzyka rozwoju chorób sercowo-naczyniowych i cukrzycy, takich jak: otyłość brzuszna, insulinooporność, nadciśnienie tętnicze oraz hiperlipidemia. Głównym czynnikiem predysponującym do wystąpienia zespołu metabolicznego jest otyłość, szczególnie z centralną dystrybucją tkanki tłuszczowej. W populacji osób otyłych, zagrożonych zespołem metabolicznym, zaburzona produkcja adipokin może prowadzić do insulinooporności oraz zwiększenia poziomu stanu zapalnego w organizmie. Proces leczenia otyłości oraz zespołu metabolicznego rozpoczyna się od modyfikacji stylu życia, głownie poprzez wprowadzenie systematycznej aktywności fizycznej. Zarówno trening aerobowy, jak i trening oporowy, poprzez wpływ na tkankę tłuszczową, mięśnie szkieletowe oraz ich produkcję wewnętrzną, są głównymi narzędziami stosowanymi w poprawie parametrów metabolicznych u pacjentów z otyłością.

**Cel:** Celem badań była ocena wpływu dwóch typów dwunastotygodniowego treningu fizycznego (trening o charakterze aerobowym *vs* trening o charakterze aerobowo-oporowym) na skład ciała, poziom wskaźników insulinooporności, profil lipidowy oraz stężenie wybranych adipokin u mężczyzn z MetS, w odniesieniu do mężczyzn z MetS nie poddawanych treningowi (grupa kontrolna). Następnie badani ze wszystkich trzech grup zostali poddani czterotygodniowej obserwacji bez zaplanowanej interwencji (follow-up).

**Materiał i metody:** W badaniu udział wzięło 62 mężczyzn (BMI = 34 ± 4 kg/m$^2$), w wieku 30–45 lat (37 ± 7 lat) z podwyższonym obwodem talii (WC ≥ 94 cm) i ze stwierdzonymi dwoma z czterech kryteriów zespołu metabolicznego. Badani zostali losowo przydzieleni do trzech grup: grupa EG1 (n = 21), realizująca treningi aerobowe, grupa EG2 (n = 21), realizująca treningi aerobowo-oporowe, grupa kontrolna CG (n = 20), nie podejmująca treningów.

Bezpośrednie pomiary antropometryczne, skład ciała (podwójna absorpcjometria rentgenowska DEXA), wskaźniki gospodarki węglowodanowo-lipidowej (glukoza, insulina, profil lipidowy, HOMA-AD, HOMA-TG, QUICKI) oraz stężenie adipokin (iryzyna, interleukina-6, leptyna, omentyna, interleukina-8, adiponektyna, adiponektyna/leptyna)

oszacowano czterokrotnie: przed rozpoczęciem interwencji, po 6 i 12 tygodniach treningów oraz 4 tygodnie po zakończeniu sesji treningowych (obserwacja).

Interwencje treningiem fizycznym o charakterze aerobowym (3 x 6 MET) oraz aerobowo-oporowych (3 x 5,5 MET) obejmowały trzy sesje tygodniowo i były zaplanowane indywidualnie. Całkowite wydatki energetyczne w grupie EG1 wyniosły 823,37 ± 175,76 kcal/dzień po 6 tygodniach oraz 835,18 ± 234,05 kcal/dzień po 12 tygodniach interwencji. Natomiast w grupie EG2 wyniosły 735,17 ± 119,64 kcal/dzień po 6 tygodniach oraz 797,89 ± 383,25 kcal/dzień po 12 tygodniach interwencji.

Zmiany międzygrupowe (między badanymi grupami) i wewnątrzgrupowe (w obrębie każdej grupy) poddano analizie statystycznej.

**Wyniki:** W grupie EG1 potwierdzono istotną redukcję masy ciała, tkanki tłuszczowej oraz jej frakcji trzewnej. W grupie EG2 wykazano zwiększenie beztłuszczowej masy ciała oraz redukcję tkanki tłuszczowej, gynoidalnej tkanki tłuszczowej i obwodu talii. W przypadku wskaźników insulinooporności w grupie EG1 zaobserwowano spadek HOMA-TG oraz wzrost QUICKI. W grupie EG2 wykazano istotne obniżenie HOMA-TG, HOMA-AD oraz zwiększenie QUICKI. W żadnej z grup nie potwierdzono istotnych zmian w nieHDL-C oraz HDL. Podczas interwencji zaobserwowano natomiast zmiany w poziomie adipokin. W grupie EG1 potwierdzono wzrost stężenia iryzyny oraz spadek IL-8 (po 6 tygodniach interwencji), a także obniżenia stężenia IL-6 i leptyny po 12 tygodniach interwencji. W grupie EG2 potwierdzono obniżenie stężenia IL-6 oraz leptyny na każdym etapie interwencji. W żadnej z grup biorących udział w badaniu nie potwierdzono istotnych zmian w stężeniu adiponektyny oraz omentyny.

**Wnioski:** Połączenie treningów aerobowych z oporowymi związane było z wyraźnymi korzyściami w poprawie składu ciała oraz wrażliwości na insulinę u mężczyzn z zespołem metabolicznym.

Zastosowanie treningów aerobowych wywołało zmiany w poziomie wybranych adipocytokin we krwi mężczyzn z zespołem metabolicznym. W grupie stosującej trening aerobowy w połączeniu z oporowym przez 12 tygodni potwierdzono obniżenie stężenia IL-6 oraz leptyny na każdym etapie interwencji, wyraźnie wskazując na działanie przeciwzapalne.

W okresie obserwacji, w którym nie prowadzono zorganizowanych treningów, w obu grupach interwencyjnych efekt redukcji tkanki tłuszczowej oraz jej trzewnej kumulacji został podtrzymany. W obu grupach potwierdzono także dalsze korzystne zmiany we wskaźnikach

insulinooporności. W grupie aerobowo-oporowej wykazano dalsze obniżenie stężenia IL-6, wskazując na redukcję stanu zapalnego. Poddani badaniom mężczyźni poprzez podejmowanie systematycznych treningów fizycznych w okresie obserwacji, utrzymali korzystne rezultaty zdrowotne.

**Abstract**

**Title: The effect of physical training on body composition and health in men with metabolic syndrome**

**Background:** Metabolic syndrome (MetS) is the co-occurrence of risk factors for cardiovascular disease and diabetes, such as abdominal obesity, insulin resistance, hypertension, and hyperlipidemia. The main predisposing factor for MetS is obesity, especially with central fat distribution. In obese individuals at risk for MetS, disrupted adipokine production can lead to insulin resistance and increased inflammation in the body. The treatment process for obesity and metabolic syndrome begins with lifestyle modifications, primarily through the introduction of regular physical activity. Both aerobic and resistance training, by affecting adipose tissue, skeletal muscles, and their internal production, are the main tools used to improve metabolic parameters in patients with obesity.

**Aim:** The aim of this study was to assess the impact of two types of twelve-week physical training (aerobic training vs. aerobic-resistance training) on body composition, insulin resistance markers, lipid profile, and selected adipokine concentrations in men with MetS, compared to men with MetS not undergoing training (control group). Subsequently, participants from all three groups were observed for four weeks without any planned intervention (follow-up).

**Material and methods:** The study involved 62 men (BMI = 34 ± 4 kg/m$^2$), aged 30-45 years (37 ± 7 years), with increased waist circumference (WC ≥ 94 cm) and two out of four diagnosed MetS criteria. The participants were randomly assigned to three groups: group EG1 (n = 21) performing aerobic training, group EG2 (n = 21) performing aerobic-resistance training, and control group CG (n = 20) not engaging in any training.

Direct anthropometric measurements, body composition (dual-energy X-ray absorptiometry - DEXA), carbohydrate-lipid metabolism markers (glucose, insulin, lipid profile, HOMA-AD, HOMA-TG, QUICKI), and adipokine concentrations (irisin, interleukin-6, leptin, omentin, interleukin-8, adiponectin, adiponectin/leptin) were assessed four times: before the intervention, after 6 and 12 weeks of training, and 4 weeks after the end of the training sessions (observation).

The physical training interventions, aerobic (3 x 6 MET) and aerobic-resistance (3 x 5.5 MET), involved three sessions per week and were individually planned. The total energy expenditures in group EG1 were 823.37 ± 175.76 kcal/day after 6 weeks and 835.18 ± 234.05 kcal/day after 12 weeks of intervention. In group EG2, they were 735.17 ± 119.64 kcal/day after 6 weeks and 797.89 ± 383.25 kcal/day after 12 weeks of intervention.

Inter-group (between the examined groups) and intra-group (within each group) changes were subjected to statistical analysis.

**Results:** In group EG1, a significant reduction in body weight, adipose tissue, and visceral adipose tissue fraction was confirmed. In group EG2, an increase in fat free mass and a reduction in adipose tissue, gynoid adipose tissue, and waist circumference were observed. As for insulin resistance markers, group EG1 showed a decrease in HOMA-TG and an increase in QUICKI. In group EG2, a significant decrease in HOMA-TG, HOMA-AD, and an increase in QUICKI were observed. No significant changes in non-HDL cholesterol and HDL were confirmed in any of the groups. However, changes in adipokine levels were observed during the intervention. In group EG1, an increase in irisin and IL-8 concentrations (after 6 weeks of intervention) and a decrease in IL-6 and leptin concentrations after 12 weeks of intervention were confirmed. In group EG2, a decrease in IL-6 and leptin concentrations was observed at every stage of the intervention. No significant changes in adiponectin and omentin levels were found in any of the participating groups.

**Conclusions:** Combining aerobic and resistance training is associated with clear benefits in improving body composition and insulin sensitivity in men with metabolic syndrome.

The implementation of aerobic training leads to changes in the levels of selected adipokines in the blood of men with metabolic syndrome. In the group performing aerobic-resistance training for 12 weeks, a decrease in IL-6 and leptin concentrations at every stage of the intervention was confirmed, indicating anti-inflammatory effects.

During the observation period without organized training in both intervention groups, the effects of reducing adipose tissue and its visceral accumulation were maintained. Both intervention groups also confirmed further favorable changes in insulin resistance markers. In the aerobic-resistance group, a further decrease in IL-6 concentration was observed, indicating a reduction in inflammation. Male participants maintained favorable health outcomes by engaging in regular physical training during the observation period.