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Relationships between Body Composition, Lipid Metabolism, and Platelet Fatty Acid Profiles in Women with Anorexia Nervosa: A cross-sectional study

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Abstract

Anorexia nervosa (AN) is associated with marked alterations in body composition and metabolism. However, the relationships between these changes, lipid metabolism, inflammation, and fatty acid (FA) profiles remain incompletely understood. This study aimed to investigate these associations in women with AN. In this cross-sectional case–control study 24 women with AN and 45 healthy controls were included. Body composition was assessed by dual-energy X-ray absorptiometry, and serum lipid profile, inflammatory, oxidative stress markers, and platelet membrane FA composition were analyzed. Women with AN showed significantly reduced total and regional lean and fat mass, with most (91.7%) presenting fat deficit. Total cholesterol and triglyceride levels were higher, whereas C-reactive protein levels were lower in women with AN, with no differences observed in oxidative stress markers. Platelet FA analysis revealed lower saturated and higher monounsaturated and polyunsaturated fatty acids. Particularly omega-6 fatty acids were elevated, and strongly positively correlated with malondialdehyde

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in women with AN. Study findings suggest that AN is associated with differences in body composition, lipid metabolism, and FA profiles, which may suggest changes linked to proinflammatory pathways. However, given the lack of differences in inflammatory and oxidative stress markers, these findings should be interpreted with caution.

Plain English summary

Anorexia nervosa is a severe eating disorder in which people, mostly young women, tend to have intensive fear of gaining weight and following restrictions of energy intake, which leads to long-term health problems. Dietary behavior causes changes in body composition and reduced fat and lean mass, which then impact further disturbances in metabolic and inflammatory changes in the human body. To explore the interactions between body composition, lipid and metabolic parameters and fatty acid composition, we examined a group of anorexia nervosa women. The results revealed that women with anorexia had lower body fat and lean mass, and their lipid profiles were different from those of healthy controls. Women with anorexia nervosa had higher unsaturated fatty acid contents and, in particular, higher omega-6 fatty acid contents. These findings indicate that there might be an increased proinflammatory state in anorexia nervosa patients, which may predict oxidative stress pathways.

Keywords: anorexia nervosa, body composition, lipids, cholesterol, oxidative stress, fatty acid

Background

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Anorexia nervosa (AN) is a severe psychiatric disorder that is more common in young women and is characterized by self-starvation-induced weight loss resulting in low body weight (1). Dietary behaviors driven by intensive fear of fat gain causes body composition changes, resulting in marked reductions in fat mass (FM) and lean mass (LM), reflecting the extensive catabolic state induced by chronic starvation (2,3). These alterations impact metabolic abnormalities, including lipid and lipoprotein alterations, increased inflammation and oxidative stress (4). However, the pathophysiology mechanisms of AN are still unknown. Lipid abnormalities in women with AN have been documented in several studies, with elevated levels of total cholesterol, triglycerides (TG), and low-density lipoproteins (LDL) and decreased high-density lipoproteins (HDL). These changes are thought to result from complex mechanisms, including increased triglycerides-rich lipoprotein synthesis and altered cholesterol absorption and synthesis (5,6). Chronic malnutrition from prolonged starvation, coupled with inadequate consumption of essential nutrients, including natural antioxidants, and increased physical and psychological stress cause women with AN to be particularly vulnerable to oxidative stress. Oxidized lipoproteins (oxLDL and oxHDL) play a central role in oxidative stress pathways, promoting inflammation, whereas elevated LDL and small LDL particles in AN are inherently more susceptible to oxidation, potentially leading to increased oxLDL levels. Several studies have revealed that AN is associated with increased markers of oxidative stress (7,8). The predominantly produced

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carbonyl compound during lipid peroxidation, malondialdehyde (MDA), which is widely used as a biomarker for oxidative stress, plays a significant role in promoting vascular damage and inflammation (9). Moreover, studies have shown that AN is associated with abnormal metabolism of fatty acids, which are crucial for brain function and neuropsychiatric health (10). Changes in the composition of FAs, mainly polyunsaturated fatty acids (PUFAs), are particularly susceptible to oxidative damage due to their double bonds, which increases free radical levels and creates an imbalance between systemic manifestations of reactive oxygen species, leading to deterioration of organ functions. Although data concerning the underlying pathophysiology of this eating disorder are inconsistent, these imbalances can have far-reaching implications for systemic inflammation in women with AN.

This single-center cross-sectional study aimed to assess the relationships between body composition, lipid metabolism, inflammatory parameters and platelet FA profiles in women with AN. By integrating anthropometric measurements with biochemical and FA analyses, this research seeks to provide a comprehensive understanding of the metabolic alterations associated with AN. These findings may offer valuable insights into the pathophysiology of this disorder and help inform strategies for its clinical management.

Materials and methods:

Study population

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This cross-sectional case–control study included women aged 18–49 years who attended the outpatient clinic at the National Osteoporosis Center, Vilnius, Lithuania, between 2023 May and 2024 June and who volunteered to participate in the study. The diagnosis of AN was established according to the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5™) (1). The diagnosis of AN was followed up by psychiatrist at Eating Disorder Center of Vilnius, Lithuania. Women with AN, referred by psychiatrist to National Osteoporosis Center for body composition evaluation, were invited to participate in the study. All women with AN had secondary amenorrhea (absence of menstruation for ≥3 months) and over the past 12 months have not been hospitalized. Healthy controls (HC) group consisted of women who attended National Osteoporosis Center seeking evaluation of their body mass and composition and were invited to participate in study. Inclusion criteria were 18 – 49 years women and, for HC group, normal weight. Exclusion criteria for all participants were acute or chronic cardiovascular disease, diabetes, thyroid or adrenal disease, or cancer and using medications, which could influence weight, endocrine or metabolic state. Lifestyle characteristics, including supplement use and alcohol consumption and smoking, were assessed during the survey. For all participants, body mass index (BMI) was evaluated by clinical examination, total and regional body composition and laboratory parameters were measured, and the platelet phospholipid membrane FA composition was calculated.

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The study was approved by the Vilnius Regional Biomedical Research Ethics Committee of Vilnius University (2021/2-1309-787). All participants provided informed consent regarding the study procedure and the anonymous publication of the findings. All procedures involving human participants were performed in accordance with the ethical standards of the institutional research committee and with the Declaration of Helsinki and its later amendments or comparable ethical standards (11).

Anthropometrics and body composition

BMI was calculated via the following formula: body mass (kg)/height (m^2). For the healthy control group, normal weight was defined according to the World Health Organization (WHO) criteria as a BMI of 18.5–24.9 kg/m^2 (12). Total body composition, including total and regional FM, LM, bone mass, and gynoid and android FM, was assessed using dual-energy X-ray absorptiometry (DXA) (GE Healthcare Lunar iDXA). The fat mass index (FMI) was calculated via the following formula: FM (kg)/height (m^2). Based on published guidelines for body composition assessment, specifically the recommendations of the International Society for Clinical Densitometry, the participants were categorized into three groups on the basis of FMI values: deficit fat (FMI < 5 kg/m^2), normal fat (FMI 5–9 kg/m^2) and excess fat (FMI > 9 kg/m^2) (13). The android-to-gynoid (A/G) ratio was calculated as the android FM (kg) divided by the gynoid FM (kg). The trunk-to-leg ratio (T/L) was calculated as total trunk fat (kg) divided by total leg fat (kg).

Laboratory measurements

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All blood samples were collected in the early morning (7–9 a.m.) after a 12-hour fast. The concentrations of total cholesterol, LDL-cholesterol, HDL-cholesterol, TG, C-reactive protein (CRP), glucose and insulin in the blood serum were determined via standardized enzymatic and electrochemiluminescence immunoassay methods (Roche Diagnostics, Germany). Reference biological values were as follows: total cholesterol < 5.2 mmol/L, LDL-cholesterol < 3.0 mmol/L, HDL-cholesterol > 1.2 mmol/L in women, TG < 3.7 mmol/L, CRP < 1.0 mg/L, glucose 3.5 -5.6 mmol/L, and insulin 2.6 - 24.9 mU/L. The homeostatic model assessment for insulin resistance (HOMA-IR) score was calculated via the following formula: glucose × insulin/22.5. These parameters were analysed immediately after blood collection. Serum and plasma aliquots for subsequent analyses were stored at -80 °C until analysis, and all assays were performed in batches within 3 months to minimise storage-related and inter-assay variability. MDA concentrations in the blood serum of the subjects were determined via high-performance liquid chromatography (the commercial kit “Chromsystems Diagnostics by HPLC&LC–MS/MS: Malondialdehyde in Plasma/Serum” (Chromsystems, Germany)) according to the manufacturer's protocol. The concentrations of oxidized high-density lipoprotein (OxHDL), oxidized low-density lipoprotein (OxLDL) and paraoxonase (PON1) in the serum were determined via enzyme-linked immunosorbent assay (ELISA) via the “Human OxHDL ELISA Kit”, “Human OxLDL ELISA Kit” (Abbexa, UK) and “Human PON1 ELISA Kit” (Thermo Fisher, USA).

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Lipids were extracted from platelet membranes using the Folch method (14). Briefly, samples were homogenized in chloroform–methanol (2:1, v/v; chloroform (Cat. No. 32211-2.5L) and methanol (Cat. No. 34860-2.5L), Honeywell, Germany), followed by phase separation with an aqueous solution. The organic phase was collected and evaporated under a stream of nitrogen. Phospholipids were isolated by thin-layer chromatography using silica gel plates (Sil G-25 UV254 (Cat. No. 809022), Macherey-Nagel, Germany) (15). The phospholipid fraction was collected and subjected to transmethylation according to a previously described protocol (14). FA methyl esters (FAMEs) were extracted into n-hexane (SupraSolv®, Cat. No. 1.04371.2500, Sigma-Aldrich, Germany), dried over anhydrous sodium sulfate (Cat. No. 1.06649.1000, Merck, Germany), and concentrated prior to analysis (14). FAME analysis was performed using gas chromatography–mass spectrometry (GC–MS; GCMS-QP2010 Ultra, Shimadzu, Japan) equipped with a capillary column (Rxi®-5ms, 30 m × 0.25 mm ID × 0.25 µm film thickness, Cat. No. 13423, Restek, USA). Helium (5.0 purity) was used as the carrier gas in linear velocity mode, with a column flow of 0.90 mL/min. Samples were injected in splitless mode with an injection temperature of 250 °C and a sampling time of 1.0 min. The oven temperature was initially set at 80 °C (held for 1 min), then increased to 310 °C at a rate of 6 °C/min and held for 5 min. The ion source and interface temperatures were set at 200 °C and 310 °C, respectively. Mass spectra were acquired in electron ionization mode (70 eV) with a scan range of m/z 29–500, a scan speed of 2500 amu/s, and an

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event time of 0.20 s. Identification of FAs was performed by comparing retention times and mass spectra with those of a certified reference standard mixture (Supelco 37 Component FAME Mix (Cat. No. CRM47885), Sigma-Aldrich, USA). Quantification was carried out based on peak area normalization, and FA composition was expressed as a percentage of total FA content.

Saturated fatty acids (SFAs) included myristic (C14:0), palmitic (C16:0), and stearic (C18:0) acids, while monounsaturated fatty acids (MUFAs) comprised palmitoleic (C16:1ω7), vaccenic (C18:1ω7), oleic (C18:1ω9; OA), and gondoic (C20:1ω9) acids. Polyunsaturated fatty acids (PUFAs) were classified as omega-3 (ω3) or omega-6 (ω6) fatty acids. The ω3 PUFAs included α-linolenic (C18:3ω3; ALA), eicosapentaenoic (C20:5ω3; EPA), docosapentaenoic (C22:5ω3; DPA), and docosahexaenoic (C22:6ω3; DHA), whereas the ω6 PUFAs included linoleic (C18:2ω6; LA) and arachidonic (C20:4ω6; ARA) acids. The PUFA-to-SFA and ω3/ω6 ratios were calculated as the ratios of total PUFAs to SFAs and total ω3 to ω6 fatty acids, respectively.

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Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 30.0 and Microsoft Excel. Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range, IQR), and categorical variables as numbers (percentages). Normality was assessed separately in each group using the Shapiro–Wilk test. In both HC and women with AN body

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composition parameters were normally distributed, except for android lean mass in AN group.

Metabolic and FA variables showed mixed distributions, with several deviating from normality, particularly in controls group. Accordingly, parametric tests were used for body composition and non-parametric tests were applied for metabolic and FA variables. Body composition variables were compared using the independent samples Student's *t*-test, with mean differences, 95% confidence intervals, and Cohen's d reported. Non-normally distributed variables were analyzed using the Mann–Whitney U test, with effect size calculated as $r = Z/\sqrt{N}$. Categorical variables were compared using the χ^2 test or Fisher's exact test. Spearman's correlation was used to assess associations between body composition and metabolic parameters, and for FAs and MDA. The strength of correlations was interpreted as very weak (< 0.20), weak (0.20 - 0.39), moderate (0.40 - 0.59), strong (0.60 - 0.79), and very strong (≥ 0.80). A two-sided $p < 0.05$ was considered statistically significant.

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Results

Among the 76 women invited to participate in our study, 69 were enrolled. Three women did not agree to participate, and four women were excluded from the present analysis because they were acutely ill, were using medications or did not complete full blood sampling. The AN group consisted of 24 women, and the HC group included 45 women.

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The mean age of the women with AN was 35.21 ± 5.38 years, which did not significantly differ from that of the HC group (32.83 ± 9.06 years, p = 0.246). Smoking was reported by 20.5% of healthy women and 20.8% of women with AN (p = 0.971). Regarding alcohol consumption, the frequency of strong alcoholic beverage intake did not differ significantly between groups (p = 0.123). Beer and low-alcohol beverage consumption were significantly lower among women with AN, with a higher proportion reporting no consumption compared to healthy women (beer: 91.7% vs. 45.5%, p = 0.003; low-alcohol beverages: 50% vs. 11.4%, p = 0.010). There was no significant difference in total alcohol consumption expressed as units per week between groups (median 0 (IQR 0 - 1) vs. 0 (IQR 0 – 0), p = 0.303) (Supplement 1).

The overall use of dietary supplements did not differ significantly between groups (p = 0.087), although a higher proportion of women with AN reported almost daily supplements use (62.5% vs. 43.2%). The frequency of vitamin D and ω3 supplements use was comparable between groups (p = 0.660). The proportion of participants using vitamin D and/or ω3 supplements did not differ significantly between HCs and women with AN (46.7% vs. 37.5%, p = 0.464) (Supplement 1).

The body composition parameters of the participants are presented in Table 1. Compared with the control group subjects, women with AN had significantly lower total body mass, bone mass, LM and FM. In the women with AN group, lean and fat mass were lower in all body regions, including the trunk, android, gynoid, and appendicular regions (legs and arms),

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compared to HC. However, the A/G ratio and T/L ratio did not differ between women with AN and HC.

Table 1 Body composition characteristics of women with AN and healthy controls

Body composition characteristic	Healthy controls	Women with AN	Mean difference (95% CI)	Effect size	p
BMI	21.40 ±	16.55 ± 1.88	4.86 (3.84 - 5.88)	2.40	**<0.001**
Total body mass (kg)	61.83 ±	46.64 ± 5.68	15.19 (11.40 -	2.02	**<0.001**
Total bone mass (kg)	2.45 ± 0.27	2.11 ± 0.35	0.34 (0.19 - 0.49)	1.12	**<0.001**
Total lean mass (kg)	40.72 ±	35.57 ± 3.53	5.16 (2.98 - 7.33)	1.20	**<0.001**
Total fat mass (kg)	18.65 ±	8.96 ± 4.05	9.69 (7.24 - 12.15)	1.99	**<0.001**
Trunk bone mass (kg)	0.63 ± 0.12	0.46 ± 0.12	0.17 (0.11 - 0.23)	1.40	**<0.001**
Trunk lean mass (kg)	17.66 ±	15.69 ± 1.60	1.97 (0.95 - 2.99)	0.97	**<0.001**
Trunk fat mass (kg)	6.78 ± 2.69	2.91 ± 1.75	3.87 (2.65 - 5.09)	1.60	**<0.001**
Android lean mass (kg)	2.42 ± 0.34	2.24 ± 0.30	0.18 (0.01 - 0.34)	0.55	**0.035**
Android fat mass (kg)	1.19 ± 0.53	0.45 ± 0.29	0.74 (0.55 - 0.94)	1.61	**<0.001**
Gynoid lean mass (kg)	5.34 ± 0.66	4.78 ± 0.74	0.56 (0.21 - 0.91)	0.82	**0.002**
Gynoid fat mass (kg)	4.20 ± 1.15	1.92 ± 0.95	2.28 (1.73 - 2.83)	2.10	**<0.001**
Appendicular bone mass (kg)	1.28 ± 0.15	1.13 ± 0.18	0.15 (0.07 - 0.23)	0.93	**<0.001**
Appendicular lean mass (kg)	19.86 ±	16.83 ± 2.16	3.03 (1.83 - 4.23)	1.27	**<0.001**
Appendicular fat mass (kg)	11.02 ±	5.30 ± 2.46	5.73 (4.36 - 7.09)	2.11	**<0.001**
Total fat %	30.99 ±	19.61 ± 7.29	11.38 (8.17 -	1.79	**<0.001**
Trunk fat %	27.01 ±	15.03 ± 7.46	11.98 (8.06 -	1.54	**<0.001**
Android fat %	31.83 ±	15.94 ± 8.87	15.89 (10.78 -	1.57	**<0.001**
Gynoid fat %	43.42 ±	27.65 ± 11.26	15.77 (10.70 -	1.89	**<0.001**
Appendicular fat %	35.30 ±	23.27 ± 8.94	12.03 (8.59 -	1.77	**<0.001**
A/G ratio	0.78 ± 0.09	0.80 ± 0.16	-0.02 (-0.09 - 0.05)	-0.16	0.600
T/L ratio	0.77 ± 0.23	0.70 ± 0.30	0.07 (-0.06 - 0.20)	0.26	0.303
FMI	6.42 ± 1.66	3.19 ± 1.47	3.24 (2.43 - 4.04)	2.03	**<0.001**
LMI	14.05 ±	12.61 ± 0.93	1.44 (0.92 - 1.96)	1.41	**<0.001**

Student's t test was used for calculations. Mean difference represents healthy controls minus AN. Effect size was calculated using Cohen's d. AN – anorexia nervosa; BMI – body mass index; FMI – fat mass index; LMI – lean mass index; A/G ratio – android-to-gynoid ratio; T/L ratio – trunk-to-leg ratio. Bold text indicates $p < 0.05$.

Distribution of FM in women with AN and HCs are presented in Table 2.

Table 2 Distribution of participants according to fat mass (13)

Fat mass category	Women with AN	Healthy controls
Deficit fat (FMI < 5 kg/m²)	22 (91.7%)	8 (17.8%)
Normal fat (FMI 5–9 kg/m²)	2 (8.3%)	34 (75.6%)
Excess fat (FMI > 9 kg/m²)	0	3 (6.7%)

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χ^2 test was used for calculations. FMI - fat mass index

In women with AN group, 22 subjects (91.7%) had fat deficit, and 2 women (8.3%) had normal fat levels. In the HC group, 8 women (17.8%) had a fat deficit, 34 (75.6%) had normal fat levels, and 3 (6.7%) had excess fat.

Analysis of metabolic parameters revealed that women with AN had significantly higher total cholesterol and TG levels compared to the HC group, with moderate effect sizes (Cohen's d = 0.68 and 0.73, respectively). Elevated total cholesterol level was observed more frequently in women with AN than in HCs (13 (54.2%) vs. 10 (22.2%), p = 0.004). LDL-cholesterol level showed a similar pattern (12 (50.0%) vs. 15 (33.3%)), but the group difference did not reach statistical significance. No differences were observed in glucose concentration, insulin level or HOMA-IR between the two groups. CRP level were significantly lower in women with AN than in HCs, with a moderate effect size (Cohen's d = 0.59). No significant differences were found in the oxHDL, oxLDL, MDA or PON1 concentrations between the two groups (Table 2).

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Table 3 Metabolic and inflammatory characteristics in women with AN and healthy controls

Metabolic and inflammatory	Healthy controls	Women with AN	Effect size	p
Total cholesterol	4.80 (4.41 - 5.19)	5.33 (4.46 - 6.28)	0.26	**0.038**
LDL cholesterol	2.73 (2.38 - 3.39)	3.26 (2.38 - 3.97)	0.19	0.132
HDL cholesterol	1.87 (1.72 - 2.12)	2.06 (1.74 - 2.45)	0.20	0.108
Triglycerides (mmol/L)	0.72 (0.55 - 1.02)	0.99 (0.70 - 1.30)	0.34	**0.006**
Glucose (mmol/L)	4.94 (4.72 - 5.37)	4.97 (4.67 - 5.36)	0.03	0.787
Insulin (mU/L)	6.31 (4.63 - 8.41)	5.78 (3.74 - 8.60)	0.07	0.551
HOMA-IR	1.34 (0.90 - 1.97)	1.27 (0.78 - 1.85)	0.09	0.462
C-reactive protein	0.46 (0.30 - 0.83)	0.30 (0.30 - 0.36)	0.26	**0.033**
Oxidized HDL (ng/mL)	22.94 (17.49 -	27.76 (19.67 -	0.21	0.115
Oxidized LDL (ng/mL)	220.61 (145.51 -	251.37 (183.37 -	0.10	0.457

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MDA (ng/mL)	95.58 (82.36 -	107.09 (78.69 -	0.12	0.357
PON1 (mcg/mL)	9.87 (7.97 - 12.10)	8.80 (8.00 - 12.83)	0.05	0.708

Mann–Whitney U test was used for calculations. Effect size was calculated using r. AN – anorexia nervosa; LDL – low-density lipoprotein; HDL – high-density lipoprotein; HOMA-IR - Homeostatic Model Assessment of Insulin Resistance; MDA – malondialdehyde; PON1 - paraoxonase 1; bold text – $p < 0,05$.

In women with AN, several statistically significant correlations were observed between body composition and metabolic parameters. Moderate negative correlations were found between total cholesterol level and LM measures (total, trunk, and gynoid) (ρ = -0.42 to -0.54, all $p < 0.05$), as well as between MTL-cholesterol level and total and gynoid LM (ρ = -0.53, all $p < 0.05$). TG level were negatively correlated with gynoid FM (ρ = -0.43, p = 0.047).

Glucose level was positively correlated with total FM, gynoid FM, and FMI (ρ = 0.43 to 0.48, all $p < 0.05$), while HOMA-IR was positively associated with FMI (ρ = 0.44, p = 0.043).

CRP concentration showed positive correlations with total mass, total bone mass, total LM, and trunk LM (ρ = 0.44 to 0.59, all $p < 0.05$). OxMTL concentration demonstrated moderate negative correlations with total, trunk, and gynoid LM, as well as with LMI (ρ = -0.53 to -0.59, all $p < 0.05$). PON1 concentration was positively correlated with total FM, gynoid FM, and FMI (ρ = 0.52 to 0.62), as well as with trunk bone mass (ρ = 0.63, p = 0.009), and negatively correlated with appendicular LM (ρ = -0.60, p = 0.015) (Supplement 2).

In the control group, positive correlations were observed between total cholesterol level and trunk and android FM (ρ = 0.31 to 0.35, $p < 0.05$), as

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well as between LDL-cholesterol level and trunk FM ($\rho = 0.34$, $p = 0.025$). Insulin concentration and HOMA-IR were positively correlated with total FM, gynoid FM, and FMI ($\rho = 0.31$ to 0.35, $p < 0.05$), while insulin concentration was additionally associated with android FM ($\rho = 0.30$, $p = 0.048$). CRP level was positively correlated with total FM, trunk FM, android FM and FMI ($\rho =$ 0.33 to 0.38, $p < 0.05$).

In terms of the platelet membrane FA composition, the largest proportion of total FAs constituted SFAs, but for women with AN, the total SFA content was lower compared to control group (67.99 (IQR 62.54 - 73.42) vs. 83.87 (IQR 73.83 - 92.44), $p < 0.001$), primarily due to a lower percentage of palmitic acid (C16:0) (44.17 (IQR 39.72 - 48.55) vs. 58.39 (IQR 51.62 - 64.89), $p < 0.001$). The proportions of MUFAs (14.59 (IQR 10.97 - 16.64) vs. 8.54 (IQR 3.62 - 13.45), $p = 0.002$) and PUFAs (18.03 (IQR 14.58 - 20.04) vs. 7.20 (IQR 4.14 - 11.47), $p < 0.001$) were significantly greater in women with AN than in HCs (Figure 1).

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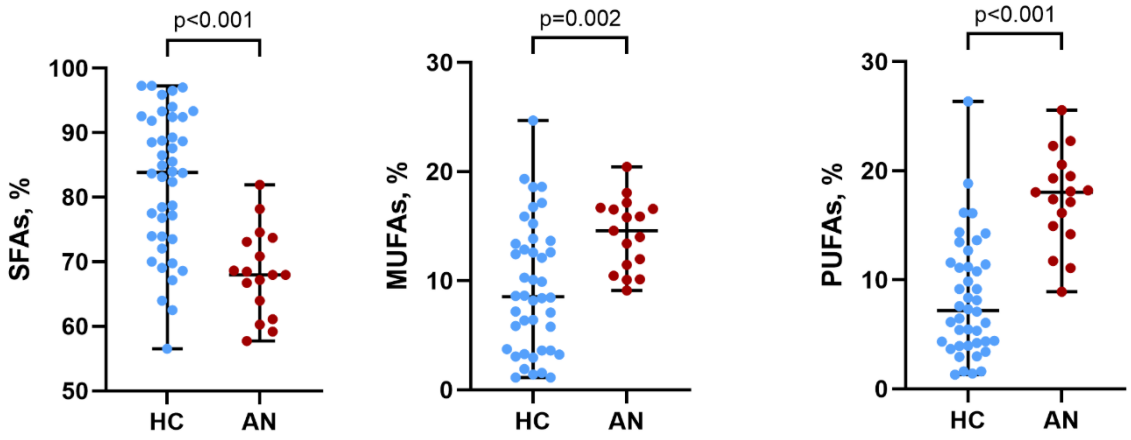

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Fig. 1 Saturated and unsaturated fatty acid compositions of healthy controls and women with AN. SFA – saturated fatty acids; MUFA – monounsaturated fatty acids; PUFA – polyunsaturated fatty acids; HC – healthy control; AN – anorexia nervosa.

Among the MUFAs, a greater percentage of vaccenic (C18:1ω7) and oleic (C18:1ω9) acids and a lower percentage of gondoic acid (C20:1ω9) were observed in women with AN compared to control group. Among the PUFAs, the percentages of LA (C18:2ω6), ALA (C18:3ω3), ARA (C20:4ω6), EPA (C20:5ω3), DPA (C22:5ω3), and DHA (C22:6ω3) were significantly greater in women with AN than in HCs (Table 4).

Table 4 Platelet membrane fatty acids in healthy controls and women with AN

Fatty acid %	Healthy women	Women with AN	Effect size	p
C14:0	3.45 (2.54 - 4.11)	2.72 (2.16 - 3.55)	0.23	0.073
C16:0	58.39 (51.62 - 64.89)	44.17 (39.72 - 48.55)	0.58	**<0.001**
C18:0	21.82 (17.80 - 24.52)	20.91 (19.13 - 22.56)	0.06	0.651
C16:1ω7	1.02 (0.46 - 2.64)	2.05 (0.49 - 2.97)	0.07	0.598
C18:1ω7	1.14 (0.51 - 1.87)	1.78 (1.39 - 2.11)	0.31	**0.018**
C18:1ω9	5.27 (2.24 - 9.43)	10.46 (8.70 - 12.37)	0.54	**<0.001**
C20:1ω9	0.37 (0.26 - 0.48)	0.20 (0.17 - 0.29)	0.39	**0.003**
C18:2ω6	5.25 (2.58 - 9.47)	13.18 (11.36 - 14.49)	0.64	**<0.001**
C18:3ω3	0.29 (0.17 - 0.58)	0.17 (0.09 - 0.23)	0.33	**0.012**
C20:4ω6	0.88 (0.56 - 1.84)	2.55 (2.04 - 3.82)	0.57	**<0.001**
C20:5ω3	0.25 (0.10 - 0.40)	0.53 (0.31 - 1.03)	0.41	**0.002**
C22:5ω3	0.07 (0.04 - 0.11)	0.43 (0.22 - 0.66)	0.62	**<0.001**
C22:6ω3	0.08 (0.05 - 0.11)	0.50 (0.23 - 0.88)	0.62	**<0.001**

Mann–Whitney U test was used for calculations. Effect size was calculated using r. AN – anorexia nervosa. Fatty acids: C14:0 myristic, C16:0 palmitic, C18:0 stearic, C16:1ω7 palmitoleic, C18:1ω7 vaccenic, C18:1 ω9 oleic (OA), C20:1 ω9 gondoic, C18:2ω6 linoleic (LA), C18:3ω3 α-linolenic (ALA), C20:4ω6 arachidonic (ARA), C20:5ω3 eicosapentaenoic acid (EPA), C22:5ω3 docosapentaenoic (DPA), and C22:6ω3 docosahexaenoic (DHA). Bold text – $p < 0,05$.

Compared with the control group, the women with AN presented significantly greater ω3 FA levels (1.52 (IQR 1.29 - 2.40) vs. 0.79 (IQR 0.54 - 1.15), $p < 0.001$) and ω6 FA levels (15.82 (IQR 13.52 - 18.10) vs. 6.15 (IQR 3.25 - 10.79),

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$p < 0.001$). However, the ω3 to ω6 ratio did not differ significantly between the groups (0.13 vs. 0.11, $p = 0.349$).

Correlations were determined between the oxidative stress marker MDA level and different fatty acids in the two groups, as presented in Figure 2.

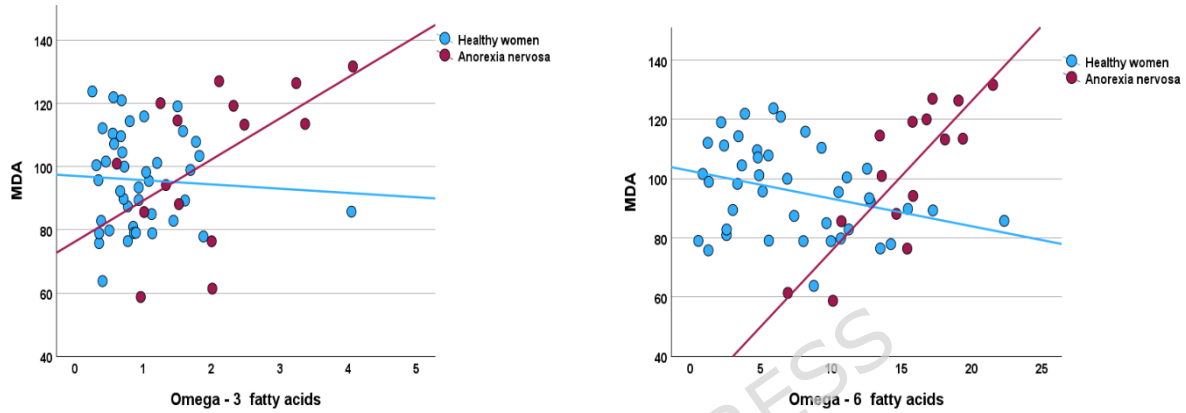

Fig. 2 Association between malondialdehyde (MDA) level and platelet membrane ω3 and ω6 fatty acids in women with AN and healthy women. Spearman's correlations of MDA with ω3 and ω6 fatty acids in women with AN (red) and controls (blue). The coloured dots and solid lines represent individual data points and the slopes of relationships, respectively. MDA – malondialdehyde, AN – anorexia nervosa

A moderate positive correlation was found between MDA level and ω3 PUFAs ($\rho = 0.55$, $p = 0.035$), and a strong positive correlation was detected between MDA level and ω6 PUFAs ($\rho = 0.76$, $p < 0.001$) in women with AN. In the control group no significant correlations were found between MDA level and ω3 or ω6 PUFAs.

Discussion

This study aimed to analyse the relationships among body composition, lipid metabolism, inflammatory parameters and platelet FA profiles in women with AN. Our findings indicate that AN is linked to distinct alterations across these

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domains. Despite existing research, the pathophysiology of AN, particularly the links between anthropometric and metabolic changes, remains incompletely understood.

The results of our study demonstrate that women with AN have significantly lower total body mass (bone mass, LM and FM) than control group subjects. Both LM and FM are lower across all body regions. Body composition assessment plays an important role in evaluating nutritional status in women with AN, as body composition restoration is one of the most important goals in AN treatment (16). Previous studies (2,17–20) on women with AN have shown that FM is markedly decreased; however, findings regarding LM depletion have been inconsistent. A study by Kerruish K.P. et al. reported comparable LM between women with AN and healthy controls (17), although a meta-analysis on body composition in women with AN demonstrated, as our study results also revealed, that LM is significantly lower in women with AN than in healthy controls (2). Low LM in AN is influenced by hormonal and metabolic disturbances. Starvation has a lowering effect on the hormones needed for muscle growth (testosterone, IGF-1, thyroid hormones) while increasing cortisol, which increases muscle breakdown and blocks muscle building (18). Nutrient deprivation impairs mitochondrial efficiency, leading to increased production of reactive oxygen species (ROS). This elevated oxidative stress contributes to muscle cell damage and further exacerbates muscle atrophy (21). Furthermore, we evaluated metabolic and inflammatory parameters and found that women with AN had significantly higher total

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cholesterol and TG levels than did the controls. LDL- and HDL- cholesterol levels did not differ between the groups. These findings partially align with results reported by other studies (6,22,23), demonstrating that elevated total cholesterol and TG levels persist even after partial weight restoration (24). A shortage of energy can likely decrease the body's own cholesterol production, which in turn impairs both cholesterol clearance and the synthesis of steroid hormones. Interestingly, other researchers, while not identifying significant differences in routinely measured plasma lipids, reported that AN is associated with markedly altered LDL subclasses, from large LDL (LDL1) to medium (LDL2) and small LDL subclasses (LDL3–LDL7). Their study results suggested a transition toward lipoprotein profiles with increased atherogenic potential, although no changes in HDL subclass distribution, HDL function or PON1 activity were observed in women with AN (5). Consistent with this observation, our study also did not detect significant differences in PON1 activity. Our findings do not provide evidence of an imbalance in oxidative status, as there was no difference in oxLDL, oxHDL, or MDA levels between the two groups; however, lower CRP level were detected in women with AN. Lower CRP level were also reported in previous studies, possibly due to malnutrition-related physiological changes (body fat reduction, which can affect liver function) and specific dietary influences (low-energy, fat-restricted diets), as well as hormonal changes (lower leptin levels and alterations in the hypothalamic–pituitary–adrenal axis), as these changes

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may not precisely reflect the ongoing inflammatory state in women with AN (25).

The results of our study revealed that the platelet membrane FA profile differed between the two groups: women with AN and presented significantly lower SFA contents and higher proportions of MUFAs and PUFAs, comparing to HC. Authors of some previous studies have also reported alterations in FA composition in women with AN. Swenne I. et al. reported an elevated ratio of MUFAs to their corresponding SFAs in the erythrocyte membranes of women with eating disorders. They proposed that the upregulation of stearoyl-CoA desaturase (SCD), an enzyme that catalyzes the conversion of SFAs to MUFAs, acts as an adaptive response to starvation by promoting lipid remodeling and maintaining membrane fluidity under conditions of limited dietary fat availability (26,27). In our study, lower level of saturated palmitic acid and higher level of unsaturated oleic acid were observed in women with AN. These findings support the notion that, during energy depletion, SCD activity (particularly that of SCD-18) increases, causing the conversion of saturated to unsaturated FAs, reflecting *de novo* lipogenesis in adipose tissue, which plays a crucial role in lipid metabolism and energy storage (28). The results of our study revealed a greater proportion of PUFAs in women with AN. Similar results were shown in a meta-analysis by Satugami K. et al., who reported abnormal levels of PUFAs in peripheral blood tissue in women with eating disorders (29). Compared with HC, women with AN presented elevated concentrations of plasma ω3 fatty acids (ALA, stearidonic acid, EPA,

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and DHA), and their study subjects were acutely ill and recovered AN or restrictive AN subtypes (23). We also found that ω3 DPA and DHA were significantly greater in women with AN than in the HC group, although our women with AN were stable, and we did not divide AN according to subtype. Although elevated PUFA levels in the AN may initially appear paradoxical given their characteristically low dietary fat intake, emerging evidence suggests that essential FAs, particularly ω3 PUFAs, may be preferentially conserved or even enriched during caloric restriction due to altered enzymatic activity—increased delta-6 desaturase and decreased elongase 5 (23,30–32). These enzymatic alterations may contribute to the selective retention of ω3 FAs and may increase the affinity for unsaturated FAs during starvation in individuals with eating disorders. Moreover, PUFAs serve as precursors to bioactive lipid mediators, eicosanoids, including prostaglandins, thromboxanes, and leukotrienes, which regulate inflammation and blood clotting. Compared with their ω3 PUFA counterparts, eicosanoids derived from ω6 PUFAs, particularly ARA, are significantly more potent at promoting inflammation and thrombosis (33,34). In addition, studies by Shih P.B. et al. demonstrated that dysregulation of PUFA-derived eicosanoids was associated with AN risk (23) and comorbid psychopathology (35).

The findings of our study demonstrated a disproportionate increase in ω6 levels, particularly LA and ARA in women with AN. Similar patterns have been reported in some previous publications, with the results of studies

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examining individuals with AN. Caspar-Bauguil S. et al. reported the amount of PUFA reduced specifically in the ω3 family (EPA and DHA), but not in the ω6 family in the red blood cell membranes of women with AN than in those of HC (36). Nguyen N. et al reported a disproportionate increase in ω6 levels relative to ω3 levels in acutely ill women with AN compared with HCs and in women who recovered from AN (30). This imbalance may suggest to subtle proinflammatory shifts (37), despite low systemic CRP level and PON1 activity. Moreover, this FA differences may affect oxidative stress pathways in AN (7), as evidenced by our study results, which revealed strong positive correlations between PUFA and MDA concentration. Although, the strong correlations observed in the AN group should be interpreted with caution due to the relatively small sample size.

The primary strength of this study lies in its comprehensive evaluation of FA profiles, integrating platelet phospholipid membrane composition with detailed assessments of body composition and metabolic parameters. The use of GC-MS for FA quantification ensures high analytical specificity and sensitivity, enabling the precise detection of individual FA species. Additionally, the use of the DXA method to assess regional and total body composition provides robust, reproducible, and objective measurements of FM, LM, and their distribution, thereby supporting meaningful correlations with FA data.

Our study had several limitations. Women with AN group sample size was relatively small. We did not collect detailed information on the clinical status

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of AN (e.g., acutely ill vs. in remission, duration of illness) or AN subtype (e.g., restricting vs. binge eating/purging), both of which may influence metabolic, inflammatory, and FA profiles. Although participants' dietary and supplement intake was recorded, it was not controlled, which is an important consideration given the significant impact of dietary fat composition on plasma and platelet membrane FA levels. Moreover, although platelet membranes are a valid matrix for evaluating FA status, their FA composition may not fully represent other biologically relevant compartments of the body. Therefore, extrapolations to systemic lipid metabolism should be performed with caution. Besides, future studies including men are warranted.

Despite these limitations, this study could provide useful insights into the associations between anthropometric and metabolic differences in women with AN, which could provide a deeper understanding of systemic inflammatory changes in this eating disorder. Furthermore, these findings highlight the potential clinical relevance of comprehensive body composition and FA profiling in women with AN, as they may provide additional insight into metabolic and inflammatory alterations beyond conventional markers. Future studies should include larger cohorts and consider stratification by AN subtype, disease stage, hormonal status, and controlled dietary intake to better elucidate the underlying mechanisms for both men and women with AN. Longitudinal investigations are also warranted to determine whether these alterations persist after nutritional rehabilitation and to assess their potential role as biomarkers for disease progression or treatment response.

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Conclusion

Women with AN exhibited significant differences in body composition, metabolic markers, and platelet membrane fatty acid profiles. Reduced fat and lean mass, increased total cholesterol and triglyceride levels, and lower CRP concentrations were observed. In addition, women with AN showed lower saturated and higher monounsaturated and polyunsaturated fatty acids, particularly omega-6. Elevated omega-6 levels and their positive correlation with malondialdehyde levels may suggest changes in fatty acid metabolism that could be linked to proinflammatory pathways; however, in the absence of differences in inflammatory and oxidative stress markers, these findings should be interpreted with caution.

List of abbreviations

AN anorexia nervosa
HC healthy controls
FA fatty acid
CRP C-reactive protein
HDL high-density lipoprotein
LDL low-density lipoprotein
TG triglycerides
OxHDL oxidized HDL
OxLDL oxidized LDL
MDA malondialdehyde
PON1 paraoxanase 1
SFA saturated fatty acid
MUFA monounsaturated fatty acid
PUFA polyunsaturated fatty acids
BMI body mass index

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DXA dual-energy X-ray absorptiometry
FM fat mass
FMI fat mass index
LM lean mass
A/G android to gynoid ratio
T/L trunk-to-leg ratio
HOMA-IR: Homeostatic Model Assessment for Insulin Resistance
ELISA enzyme-linked immunosorbent assay
ALA α-linolenic acid
EPA eicosapentaenoic acid
DPA docosapentaenoic acid
DHA docosahexaenoic acid
OA oleic acid
LA linoleic acid
ARA arachidonic acid
SD standard deviation
IGF-1 insulin-like growth factor
ROS reactive oxygen species
SCD stearoyl-CoA desaturase
GC-MS gas chromatography–mass spectrometry
DSM-5 Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
FAME FA methyl esters
ω3 omega-3
ω6 omega-6

Declarations

Ethics approval and consent to participate

This study was approved by the Vilnius Regional Biomedical Research Ethics Committee, Vilnius University, Lithuania (2021/2-1309-787). All participants, before inclusion, provided written informed consent regarding the study procedure and the anonymous publication of the findings.

Consent for publication

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Not applicable

Availability of data and materials

The dataset generated and/or analysed during the current study is available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

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Author contributions

IF, IB, DK and VS designed the study; IF, BB, IB, and DK collected the data; JU conducted the statistical analyses; IF, JU and IB analysed and interpreted the data and wrote the main manuscript; and IF and MT substantively revised the work and prepared the final version for submission. All the authors have read and approved the final manuscript before submission.

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