Lipids in Health and Disease

RESEARCH

Open Access

Fat mass index is associated with altered platelet fatty acid composition, oxidative stress, and inflammation

Inga Fomčenko[1*], Inga Bikulčienė[2], Arvydas Kaminskas[3], Emilis Gabrielis Byčius[3], Aušra Linkevičiūtė-Dumčė[2], Virginijus Šapoka[1] and Dovilė Karčiauskaitė[2]

Abstract

Background Obesity and excessive body fat lead to metabolic and inflammatory disturbances. The fat mass index (FMI) has recently been recognized as a more sensitive measure of obesity than body mass index (BMI). Therefore, we investigated the relationship between higher FMI and alterations in platelet phospholipid fatty acid (FA) composition, oxidative stress, and inflammation.

Methods Cross-sectional study of adults aged 18–49 years attended an outpatient clinic National Osteoporosis Center from May 2023 till June 2024, who agreed to participate in the study. Exclusions: major chronic diseases, active cancer, pregnancy, weight-affecting medications, thyroid/adrenal disorders, and diabetes. The total body composition was assessed via DXA; FMI (kg/m^2) was categorized as fat deficit, normal, excess fat, or obesity. Fasting blood was analysed for glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, CRP, and insulin; serum malondialdehyde (MDA) by HPLC; platelet phospholipid FA profile by GC/MS. FMI group differences were tested with Kruskal–Wallis and Mann–Whitney. The Spearman coefficient was used to evaluate the associations.

Results The study included 169 participants (36.3 ± 6.25 years; 64.5% female). Across ascending FMI groups (fat-deficit to obesity), adverse metabolic shifts were observed: HDL-cholesterol declined from 1.8 to 1.3 mmol/L ($p < 0.001$), whereas triglycerides rose from 0.7 to 1.4 mmol/L ($p < 0.001$) and CRP from 0.3 to 2.4 mg/L ($p < 0.001$). In platelet phospholipid membrane, the proportion of polyunsaturated FAs increased with FMI (from 2.5% to 4.8%; $p = 0.002$), including ω3 (from 1.1% to 2.0%; $p = 0.003$) and ω6 (from 7.5% to 11.4%; $p = 0.016$). The ω6/ω3 ratio showed a weak positive association with LDL-cholesterol ($\rho = 0.166$; $p = 0.040$). Serum MDA increased across FMI groups (from 95.5 to 104.3 µg/L; $p = 0.019$) and correlated with the polyunsaturated FAs ($\rho = 0.178$, $p = 0.027$).

Conclusions An elevated FMI is associated with altered platelet FA composition and increased OS. These changes may be early markers for metabolic and inflammatory dysregulations that underlie the pathogenesis of cardiometabolic risk. Moreover, platelet FA profiling could provide additional value for risk stratification in overweight individuals.

Keywords Adiposity, Membrane lipids, Malondialdehyde, C-reactive protein

*Correspondence:
Inga Fomčenko
inga.aleknaite@gmail.com
[1]Faculty of Medicine, Vilnius University, Vilnius, Lithuania
[2]Translational Health Research Institute, Faculty of Medicine, Vilnius University, Vilnius, Lithuania
[3]Department of Physiology, Biochemistry, Microbiology and Laboratory Medicine, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

Background

Obesity is a chronic condition characterized by excessive accumulation of body fat, which can substantially increase the risk of developing metabolic syndrome, cardiovascular diseases, and certain cancers [1]. Excess adiposity, lipid metabolism, and oxidative stress (OS) are involved in the pathogenesis of this condition. The fat mass index (FMI), which standardizes fat mass in relation to height, provides a qualitative assessment of adiposity and its metabolic implications, unlike the commonly used body mass index (BMI), which does not distinguish between fat mass and lean mass [2]. FMI offers several advantages over traditional body adiposity measures like BMI and percent body fat, making it a superior and valuable tool in scientific research for assessing and understanding body fat and its health implications. FMI provides an absolute fat mass normalized to height, offering a clearer quantification [3]. Studies show FMI correlates more strongly with metabolic syndrome components, insulin resistance, and cardiovascular risk factors than BMI [4, 5]. By adjusting fat mass for height, FMI facilitates comparisons across individuals and populations of different sizes, ages, and sexes more accurately than fat mass or percent body fat alone [3]. Percent body fat can be misleading in very lean or obese individuals due to variations in lean mass [6]. Recent data indicate that platelet membranes are targets of oxidation because of their high polyunsaturated fatty acid (PUFA) content. These structural lipids are substrates to produce bioactive lipid mediators of inflammation and thrombosis. Platelet activation in the presence of enhanced OS can lead to membrane lipid peroxidation, changes in fatty acids (FAs) associated with membrane structure, and increased generation of activated platelet-leukocyte aggregates, all of which may contribute to vascular injury, inflammation, and the growth of atherosclerotic lesions [7, 8]. However, studies confirming the effects of oxidative processes on platelets are lacking.

OS is defined by the excessive production of reactive oxygen species (ROS), which can induce damage to cells by attacking biomolecules, such as lipids and proteins. This process can result in cellular malfunction, apoptosis, and increased inflammation. These studies underscore the existence of a bidirectional relationship between body fat content, OS, and platelet FA changes. Individuals with higher FMI tend to have greater systemic OS and altered FA distribution in the platelet membrane, which may impact platelet reactivity and be associated with disease risk [9–14]. These processes highlight the importance of the fat mass–OS–platelet axis in health and disease. Therefore, in this study, we sought to test the hypothesis that increased FMI is related to significant changes in platelet phospholipid membrane FA composition and elevated OS, both of which are metabolic and inflammatory conditions that may eventually contribute to increased cardiometabolic risk.

Methods

Study design

This cross-sectional study included adults aged 18–49 years who attended the outpatient clinic National Osteoporosis Center, Vilnius, Lithuania, between May 2023 and June 2024 and who volunteered to participate in the study. The exclusion criteria were chronic noninflammatory diseases, active cancer, pregnancy, the use of medications altering body mass, a history of previous diagnosis and/or treatment of thyroid and adrenal pathologies, and diabetes mellitus. Written consent was obtained from all volunteers after they were informed about the study. The study protocol was approved by the Vilnius Regional Biomedical Research Ethics Committee (No. 2021/2–1309–787), and all national regulations of biomedical research ethics were followed correctly.

For all participants, medical history was evaluated and clinical examination was performed. Weight (kg) was measured using electronic medical scales (Radwag, Poland), with an accuracy of 50 g. Participants were weighed wearing only underwear, without shoes. A standard vertical height meter (Harpenden Stadiometer, "Holtain limited", UK) was used to measure height (mm). Height was measured without shoes, standing with feet together and leaning against a wall with heels, buttocks and back, and the head held horizontally. BMI was calculated via the following formula: body mass (kg)/height (m^2). Body composition was assessed using dual-energy X-ray absorptiometry (DXA) (GE Healthcare Lunar iDXA) [3, 15]. The duration of the total body scan was 5–15 min, the radiation dose – less than 3 μG. The data were processed using the enCore software. The results of the body component measurements (total and regional fat mass, lean mass, bone mineral mass) were expressed in absolute numbers or percentages (kg, g/cm2, %) [15]. The FMI was calculated via the following formula: fat mass (kg)/height (m^2), followed by classification according to The Official Positions of the International Society for Clinical Densitometry into one of four groups based on FMI values: fat deficit (FMI < 5 kg/m^2 for females, FMI < 3 kg/m^2 for males), normal (FMI 5–9 kg/m^2 for females, FMI 3–6 kg/m^2 for males), excess fat (FMI 9–13 kg/m^2 for females, FMI 6–9 kg/m^2 for males), and obesity (FMI > 13 kg/m^2 for females, FMI > 9 kg/m^2 for males) [15].

Blood sample collection and preparation

Venous blood samples were collected from individuals via standard phlebotomy procedure. Blood was drawn into serum-separating tubes with polymer gel and clot activator (3.5 ml, BD Vacutainer® SST II Advance Tube,

BD Biosciences, USA) for the determination of HDL-cholesterol, LDL-cholesterol, total cholesterol, triglycerides, insulin, CRP, and malondialdehyde. For glucose measurement, an additional sodium fluoride-containing tube (4 ml, BD Vacutainer® Fluoride Tube, BD Biosciences, USA) was used to inhibit glycolysis.

Following collection, the blood samples were allowed to clot for 30 min at room temperature and then centrifuged at 2500 × g for 10–15 min at 4 °C to obtain clear supernatants, which were processed immediately.

For the preparation of platelet-rich plasma, blood was drawn into the following tube: sodium heparin vacutainer (4 ml/BD Vacutainer® Heparin Tubes, BD Biosciences, USA) and spun immediately at 3000 × g for 10 min at 4 °C.

All samples were visually scrutinized for haemolysis, lipemia, or icterus to ensure maximum analytical integrity, and those with marked interference were not further elaborated.

Determination of routine clinical laboratory parameters

HDL-cholesterol (HDL-Cholesterol Gen.4), LDL-cholesterol (LDL-Cholesterol Gen.3), total blood cholesterol (Cholesterol Gen.2), and triglycerides (Triglycerides Gen.3), as well as glucose (Glucose HK Gen. 3), insulin (Elecsys Insulin), and CRP (CRP4), were quantitatively measured via enzymatic, electrochemiluminescence immunoassay, and immunoturbidimetric methods employing Cobas® pro and Cobas® e 402 analyser systems. All reagents were purchased from Roche Diagnostics GmbH (Mannheim, Germany).

Total blood cholesterol, triglyceride, and glucose assays were calibrated with a calibrator f.a.s. (Roche Diagnostics GmbH). A calibrator f.a.s. Proteins (Roche Diagnostics GmbH) were used for CRP calibration. Lipids (Roche Diagnostics GmbH) and Insulin CalSet (Roche Diagnostics GmbH) were used for HDL cholesterol, LDL cholesterol, and insulin, respectively. Quality controls were performed with PreciControl ClinChem Multi 1 and 2 (Roche Diagnostics GmbH) for total blood cholesterol, triglycerides, glucose, HDL-cholesterol, LDL-cholesterol, and PreciControl Multimarkers 1 and 2 (Roche Diagnostics GmbH) for insulin assays. CRP T Control N (Roche Diagnostics GmbH) internal quality control was used for CRP evaluation.

All tests were validated according to the Clinical and Laboratory Standards Institute EP05-A3 guidelines. Precision was determined in human sera and controls, and the coefficient of variation for reproducibility was between 0.30 and 1.4%, and for intermediate precision, it was 0.5 and 2.1%. Moreover, the assays correlated well with the reference methods ($r = 0.999–1.000$), indicating good accuracy. The results are expressed in mmol/L for HDL cholesterol, LDL cholesterol, total blood cholesterol, triglycerides, and glucose; mU/L for insulin; and mg/L for CRP.

Platelet isolation and fatty acid determination

Following centrifugation, three-quarters of the plasma was removed without disturbing the cells or the buffy coat. The remaining quarter of the plasma, enriched in thrombocytes, was extracted and mixed with freezing medium (NutriFreez® D10, Biological Industries, Israel Beit Haemek Ltd.) at a 2:1 ratio. This mixture was stored at −80 °C for subsequent analysis [16].

Lipid extraction was performed via the Folch method [17]. The dried lipid extract was resuspended for further analysis via thin-layer chromatography on Sil G-25 UV254 glass plates (MACHEREY-NAGEL GmbH & Co. KG, Germany) [18]. FA methyl esters of platelet membrane phospholipids were analysed via gas chromatography/mass spectrometry (GC−MS/QP2010 Ultra, Shimadzu, Japan). Data processing and analysis were conducted via LabSolutions software (Shimadzu, Japan).

The FA content was expressed as a percentage of the total amount of FAs (100%). It was calculated as the percentage of total monounsaturated FAs (C16:1ω7, C18:1ω9, C18:1ω7, and C20:1ω9), polyunsaturated FAs (C18:2ω6, C18:3ω3, C20:4ω6, C20:5ω3, C22:5ω3, and C22:6ω3), and saturated FAs (C14:0, C16:0 and C18:0). Furthermore, specific ratios between omega-3 (ω3) (C18:3ω3/C20:5ω3), omega-6 (ω6) (C18:2ω6/C20:4ω6), omega-9 (ω9) (C18:0/C18:1ω9) and ω6/ω3 FA were calculated.

Blood serum malondialdehyde determination

The determination of blood serum MDA was based on the scientific article published by Khoschsorur G.A. et al. [19] with slight modifications. The sample preparation is used for sample clean-up and derivatization of the analyte with thiobarbituric acid (TBA) in a detectable form, i.e., the MDA-TBA adduct. Malondialdehyde levels were analysed via a Shimadzu Nexera X2 UHPLC system (Shimadzu). Chromatographic separation was performed on an Agilent Poroshell 120 EC–C18 (2.7 µm, 3.0 × 100 mm, Agilent Technologies) reversed-phase column with a mobile phase consisting of 40:60 (v/v) 50 mM phosphate buffer (pH 6.8) and methanol. The flow rate was 1.0 mL min^{-1}. Fluorometric detection was performed with excitation at 515 nm and emission at 553 nm. LabSolutions software (Shimadzu) was used to process the measurement data. The MDA results are expressed in µg/L.

Statistical analysis

Statistical analyses were performed using SPSS software (IBM Corp., Armonk, NY, USA). Normality of variables was assessed with the Shapiro–Wilk test, and homogeneity of variances with Levene's test. Using one-way

ANOVA, normally distributed variables (laboratory measurements, fatty acids, anthropometric, and body composition data) were compared across FMI groups. Tukey's HSD was applied when variances were equal (Levene's $p \geq 0.05$), and Welch's ANOVA with Games–Howell post hoc test was used when variances were unequal (Levene's $p < 0.05$). Non-normally distributed variables were compared using the Kruskal–Wallis test and Mann–Whitney U tests for post hoc pairwise comparisons. Results are reported as means ± standard deviations, or for non-normally distributed variables as medians [Q1, Q3] with adjusted *p*-values. Bonferroni correction was applied to non-parametric analyses to account for multiple comparisons; thus, the adjusted significance level was $p < 0.0083$. K-means clustering (k = 2) was applied to z-standardized features to partition participants into clusters. Cluster characteristics were then compared: an independent-samples t-test was used when data were normally distributed and variances were equal, a Welch's t-test when variances were unequal, and a Mann–Whitney U test when distributions were non-normal. Spearman's correlation (ρ) was used to examine associations between fatty acids and laboratory measurements. Correlation strength was classified as negligible (0.0–0.1), poor (0.1–0.3), fair (0.4–0.6), moderate (0.6–0.8), and very strong (0.8–1.0) [20]. Statistical significance was defined as a two-sided *p* value of < 0.05.

Results

Study population characteristics and body composition

Of the 180 subjects invited to participate, 169 were successfully enrolled in the study. Seven individuals were excluded because they were acutely ill, were using medications that could influence weight, or did not complete full blood sampling, and four individuals did not agree to participate. The study population comprised 35.5% males ($n = 60$) and 64.5% females ($n = 109$). The mean age of the participants was 36.3 ± 6.25 years. The mean FMI was 9.4 ± 4.41. Eleven (6.5%) participants had a fat deficit, 59 (34.9%) had normal fat, 51 (30.2%) had excess fat, and 48 (28.4%) subjects were obese. Patient age and weight were not distributed normally, whilst BMI, FMI, and total fat mass were. The clinical data and anthropometrics of the participants are presented in Table 1.

A significant positive correlation ($\rho = 0.831$, $p < 0.001$) between FMI and BMI was observed. Total bone mass and total lean mass did not differ significantly across FMI groups.

Routine clinical laboratory parameters in blood serum

When evaluating the normality of the variables, it was found that glucose concentration, total blood cholesterol, HDL-cholesterol, and LDL-cholesterol levels were normally distributed across all FMI groups, whereas other laboratory measurements showed skewness. Glucose also had heterogeneous variances (Levene's test showed F (3, 159) = 3.23, $p = 0.24$), whilst other normally distributed variables had homogenous variances. Therefore, normally distributed measurements were compared using a One-way ANOVA test with Tukey HSD for homogeneous variables and Games-Howell for heterogeneous glucose post hoc tests, whilst the nonparametric Kruskal–Wallis and Mann–Whitney U post hoc tests were used to compare not normally distributed measurements among the FMI groups. For a more detailed analysis, glucose, total blood cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, CRP, and insulin levels were specifically selected for comparison (Table 2).

All tests, apart from total blood cholesterol, revealed significant differences across the FMI groups. While

Table 1 Anthropometric and body composition in different fat mass index (FMI) groups

Characteristic	Fat mass index group				*p*
	Fat deficit (*n* = 11)	Normal (*n* = 59)	Excess fat (*n* = 51)	Obesity (*n* = 48)	
Gender, *n* (%)					
Male	3 (27.3)	22 (37.3)	20 (39.2)	15 (31.3)	-
Female	8 (72.7)	37 (62.7)	31 (60.8)	33 (68.8)	
Age (years)	32.0 [29.6, 36.2][c]	36.0 [31.1, 40.1]	36.9 [31.4, 41.5]	39.8 [34.0, 42.7][c]	**0.010**
Height (m)	1.7 ± 0.12	1.8 ± 0.09	1.74 ± 0.09	1.7 ± 0.08	0.652
Weight (kg)	55.9 [48.3, 68.8][b, c]	69.0 [61.9, 78.8][d, e]	83.0 [75.0, 89.6][b, d,f]	102.5 [85.4, 111.8][c, e,f]	**< 0.001**
BMI	19.1 ± 3.62[a, b,c]	23.2 ± 2.70[a, d,e]	27.6 ± 2.58[b, d,f]	35.2 ± 5.19[c, e,f]	**< 0.001**
FMI	3.5 ± 0.90[a, b,c]	6.1 ± 1.43[a, d,e]	9.5 ± 2.09[b, d,f]	14.8 ± 3.35[c, e,f]	**< 0.001**
Total bone mass (kg)	2.6 ± 0.66	2.9 ± 0.59	2.9 ± 0.44	2.8 ± 0.44	0.140
Total fat mass (kg)	10.5 ± 2.44[a, b,c]	18.5 ± 3.48[a, d,e]	28.7 ± 4.98[b, d,f]	43.5 ± 8.06[c, e,f]	**< 0.001**
Total lean mass (kg)	48.2 ± 17.60	49.7 ± 12.88	52.0 ± 10.62	53.4 ± 8.51	0.283

Continuous, normally distributed data is presented as mean ± standard deviation, whilst not normally distributed data is presented as the median [Quartile 1, Quartile 3]. Gender is shown as a count (percentage). Significance for non-normally distributed variables was determined via a nonparametric Kruskal–Wallis test, whilst the significance of normally distributed variables was assessed using One-way ANOVA. Different superscript letters indicate statistically significant differences between FMI groups after post-hoc testing: a - fat deficit vs normal; b - fat deficit vs excess fat; c - fat deficit vs obese; d - normal vs excess fat; e - normal vs obese; f - excess fat vs obese. Bold text – $p < 0.05$

Table 2 Comparison of selected laboratory test results between the fat mass index (FMI) groups

Characteristic	Fat mass index group				*p*
	Fat deficit (*n* = 11)	Normal (*n* = 59)	Excess fat (*n* = 51)	Obesity (*n* = 48)	
Glucose (mmol/L)	5.0 ± 0.41[b, c]	5.1 ± 0.48[d, e]	5.5 ± 0.31[b, d]	5.6 ± 0.52[c, e]	**< 0.001**
Total blood cholesterol (mmol/L)	4.7 ± 0.88	4.8 ± 0.72	5.1 ± 1.06	5.0 ± 0.80	0.231
LDL-cholesterol (mmol/L)	2.9 ± 0.91	2.9 ± 0.65[d, e]	3.3 ± 0.65[d]	3.3 ± 0.71[e]	**0.004**
HDL-cholesterol (mmol/L)	1.8 ± 0.15[c]	1.8 ± 0.44[d, e]	1.5 ± 0.33[d]	1.3 ± 0.28[c, e]	**< 0.001**
Triglycerides (mmol/L)	0.7 [0.6, 0.9][c]	0.8 [0.6, 1.1][e]	1.0 [0.8, 1.2][f]	1.4 [1.0, 1.7][c, e,f]	**< 0.001**
CRP (mg/L)	0.3 [0.3, 0.5][c]	0.5 [0.3, 0.8][d, e]	0.9 [0.5, 2.3][d, f]	2.4 [1.1, 6.2][c, e,f]	**< 0.001**
Insulin (mU/L)	5.4 [3.3, 6.1][b, c]	6.3 [4.7, 8.6][d, e]	8.9 [6.4, 14.0][b, d,f]	14.0 [10.8, 21.4][c, e,f]	**< 0.001**

The normally distributed data is presented as mean ± standard deviation, whilst non-normally distributed data is presented as the median [Quartile 1, Quartile 3]. The Significance of non-normally distributed variables was determined via a nonparametric Kruskal–Wallis test, while the significance of normally distributed variables was assessed using One-way ANOVA. Different superscript letters indicate statistically significant differences between FMI groups after post-hoc testing: a - fat deficit vs normal; b - fat deficit vs excess fat; c - fat deficit vs obese; d - normal vs excess fat; e - normal vs obese; f - excess fat vs obese. *LDL-cholesterol* low-density lipoprotein cholesterol, *HDL-cholesterol* high-density lipoprotein cholesterol, *CRP* C-reactive protein. Bold text – $p < 0.05$

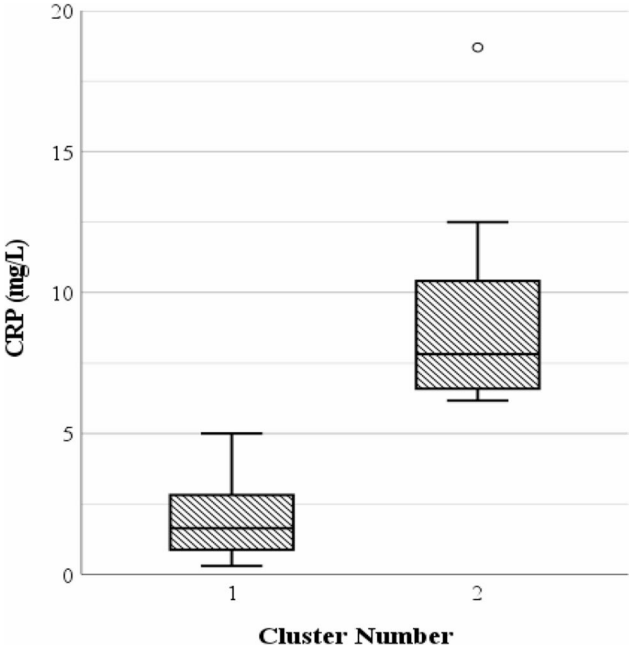

Fig. 1 Diagram depicting the formation of distinct CRP result clusters within the study population. CRP – C reactive protein

all tests indicated an increase, HDL-cholesterol levels decreased. Post hoc analyses for individual groups demonstrated that no measurements differed significantly between the fat deficit and normal fat groups. Comparing fat deficit and excess fat revealed significant differences in glucose ($p = 0.009$) and insulin ($p < 0.001$) levels. When fat deficit was compared with obesity, significant differences were found in glucose ($p = 0.001$), HDL-cholesterol ($p = 0.003$), triglyceride ($p < 0.001$), CRP ($p < 0.001$), and insulin ($p < 0.001$) levels. The glucose ($p < 0.001$), LDL-cholesterol ($p = 0.015$), HDL-cholesterol ($p < 0.001$), CRP ($p < 0.001$), and insulin ($p < 0.001$) levels significantly differed between the normal and excess fat groups. A comparison of normal fat levels with obesity revealed significant differences in glucose ($p < 0.001$), LDL-cholesterol ($p = 0.023$), HDL-cholesterol ($p < 0.001$), triglyceride ($p < 0.001$), CRP ($p < 0.001$), and insulin ($p < 0.001$) levels. The comparison between excess fat and obesity groups revealed significant differences in triglyceride ($p = 0.001$), CRP ($p < 0.001$), and insulin ($p < 0.001$) levels.

Table 3 Characterisation of CRP cluster groups

Characteristic	Low CRP (*n* = 35)	High CRP (*n* = 12)
Gender, *n* (%)		
Male	13 (37.1)	2 (16.7)
Female	22 (62.9)	10 (83.3)
Age (years)	41.1 [34.4, 44.1]	33.8 [26.9, 40.5]
Height (m)	1.7 ± 0.08	1.7 ± 0.09
Weight (kg)	101.0 [92.6, 110.4]	106.7 [99.7, 119.1]
BMI	33.8 ± 4.26	38.7 ± 5.98
FMI	13.9 ± 3.18	17.0 ± 2.62

Continuous, normally distributed data is presented as mean ± standard deviation, whilst non-normally distributed data is presented as the median [Quartile 1, Quartile 3]. Gender is shown as a count (percentage)

BMI body mass index, *FMI* fat mass index, *CRP* C reactive protein

Another observation was made concerning CRP levels in the obesity group (Fig. 1). Two separate clusters emerged. The clinical data and anthropometrics of two CRP clusters are presented in Table 3. The first cluster (low CRP) had an average CRP level of 1.96 mg/L with 35 participants, whereas the second cluster (high CRP) had an average CRP level of 9.12 mg/L with 12 participants. Independent-samples t-test revealed a significant difference between CRP levels of these clusters ($p = 0.003$). Comparison of the CRP clusters revealed no significant differences in the levels of different fatty acid types or MDA concentrations.

Continuous, normally distributed data is presented as mean ± standard deviation, whilst non-normally distributed data is presented as the median [Quartile 1, Quartile 3]. Gender is shown as a count (percentage). BMI – body mass index; FMI – fat mass index; CRP – C reactive protein.

Table 4 Comparison of total amounts of fatty acids and malondialdehyde between the fat mass index (FMI) groups

Characteristic	Fat mass index group				*p*
	Fat deficit (*n* = 11)	Normal (*n* = 59)	Excess fat (*n* = 51)	Obesity (*n* = 48)	
Total SFAs (%)	78.0 ± 14.86	81.8 ± 11.05[a]	75.4 ± 12.97	74.1 ± 13.17[a]	**0.012**
Total MUFAs (%)	18.7 ± 12.49	15.8 ± 9.62[a]	20.8 ± 10.44	21.1 ± 10.39[a]	**0.035**
Total PUFAs (%)	3.3 ± 2.78	2.5 ± 1.93[a]	3.8 ± 2.99	4.8 ± 3.67[a]	**0.002**
Total w3 (%)	1.3 ± 0.82	1.1 ± 0.84[a]	1.5 ± 1.16	2.0 ± 1.35[a]	**0.003**
Total w6 (%)	9.4 ± 7.20	7.5 ± 5.11[a]	10.7 ± 6.57	11.4 ± 7.90[a]	**0.016**
w6/w3 ratio	7.6 ± 9.55	6.8 ± 10.89	8.5 ± 10.36	11.0 ± 16.13	0.447
C18:3ω3/ C20:5ω3 ratio	2.4 ± 3.03	2.4 ± 2.47	1.7 ± 2.31	1.3 ± 1.64	0.147
C18:2ω6/C20:4ω6 ratio	4.3 ± 2.24	6.3 ± 5.93[a]	5.2 ± 2.64	3.8 ± 2.71[a]	**0.033**
C18:0/ C18:1ω9 ratio	10.0 ± 16.02	8.0 ± 12.31	5.1 ± 8.21	4.3 ± 5.17	0.149
Malondialdehyde (mg/L)	95.5 [89.3, 101.6]	95.7 [80.9, 120.2][a]	100.2 [89.6, 116.8]	104.3 [94.8, 124.2][a]	**0.019**

The normally distributed data is presented as mean ± standard deviation, whilst non-normally distributed data is presented as the median [Quartile 1, Quartile 3]. Significance for non-normally distributed variables was determined via a nonparametric Kruskal–Wallis test, whilst normally distributed variable significance was assessed using One-way ANOVA. Different superscript letters indicate statistically significant differences between FMI groups after post-hoc testing: a - normal vs obese. *SFAs* saturated fatty acids, *MUFAs* monounsaturated fatty acids, *PUFAs* polyunsaturated fatty acids, ω – omega. Bold text – $p < 0.05$

Fatty acids in the platelet membrane and malondialdehyde in blood serum

The findings revealed significant differences in FAs among the FMI groups (Table 4). All the variables shown in Table 4, apart from the concentration of MDA, were distributed normally, as well as all, apart from PUFA and ω9 ratio, had homogenous variances. No distinct linear relationships were observed. Individual post hoc analyses revealed no significant differences in the total FA content between the fat deficit group, excess fat group and other groups. Significant differences were observed comparing the normal fat and obesity groups, where the total amounts of SFAs ($p = 0.012$), PUFAs ($p = 0.003$), MUFA ($p = 0.035$), ω3 FAs ($p = 0.001$), and ω6 FAs ($p = 0.014$) differed. Analysis of the ω3, ω6, and ω9 ratios revealed no significant differences between all the FMI groups, with exception of the ratio of ω6 ($p = 0.033$) FAs. Individual post hoc analysis revealed a significant difference in ω6 FA ratio ($p = 0.022$) between the normal and obese groups. In addition, the MDA concentration increased significantly ($p = 0.019$) alongside increasing FMI and showed a significant ($p = 0.003$) difference between the normal and obese groups.

The normally distributed data is presented as mean ± standard deviation, whilst non-normally distributed data is presented as the median [Quartile 1, Quartile 3]. Significance for non-normally distributed variables was determined via a nonparametric Kruskal–Wallis test, whilst normally distributed variable significance was assessed using One-way ANOVA. Different superscript letters indicate statistically significant differences between FMI groups after post-hoc testing: a - normal vs. obese. SFAs – saturated fatty acids, MUFAs – monounsaturated fatty acids, PUFAs – polyunsaturated fatty acids, ω – omega. Bold text – $p < 0.05$.

Relationships between fatty acids and serum lipids

Correlations between ω3, ω6, and ω9 ratios and laboratory measurements revealed that the ω3 ratio was significantly correlated with total blood cholesterol ($\rho = -0.175$, $p = 0.030$), LDL-cholesterol ($\rho = -0.189$, $p = 0.019$), and CRP ($\rho = -0.216$, $p = 0.007$). The ω6 ratio was significantly correlated with HDL cholesterol ($\rho = 0.176$, $p = 0.029$), the triglyceride concentration ($\rho = -0.316$, $p < 0.001$), and the CRP level ($\rho = -0.188$, $p = 0.020$). The ω9 ratio did not yield any significant results. The correlations between ω6/ω3 ratio and laboratory measurements revealed only a weak, statistically significant positive correlation with the LDL-cholesterol concentration ($\rho = 0.166$, $p = 0.040$).

The concentration of HDL cholesterol in the blood serum was significantly associated with the total amounts of SFAs ($\rho = 0.194$, $p = 0.016$), MUFAs ($\rho = -0.172$, $p = 0.033$), PUFAs ($\rho = -0.262$, $p = 0.001$), and ω3 ($\rho = -0.279$, $p < 0.001$). Additionally, the triglyceride concentration was significantly correlated with the total amount of ω3 FAs ($\rho = 0.182$, $p = 0.025$). CRP levels were also significantly associated with total SFAs ($\rho = -0.158$, $p = 0.050$) and PUFAs ($\rho = 0.202$, $p = 0.012$). In contrast, the concentrations of glucose, total blood cholesterol, LDL-cholesterol, and insulin were not significantly correlated with the total amount of FAs. Spearman's correlation test was also performed between the MDA concentration and total amount of FAs, which revealed a significant positive ($\rho = 0.178$, $p = 0.027$) correlation with PUFAs, whereas correlations with other FAs were not significant.

Discussion

In the present study, fat mass increased across FMI categories (from 10.5 to 43.5 kg; $p < 0.001$), whereas total lean mass showed only a modest, non-significant rise (from

48.2 to 53.4 kg; $p = 0.283$), and bone mass did not differ. These findings indicate that higher FMI primarily reflects greater adiposity without proportional gains in lean mass [21, 22]. We also found that the platelet FA composition is significantly associated with fat mass, especially when moving from the normal to the excess fat and obese groups. Interestingly, the total FA content was similar among the fat deficit and other FMI groups, suggesting that a mild reduction in fat mass may not markedly influence the lipid composition of platelets. Additionally, obesity was significantly related to increased MUFAs, PUFAs, ω3 and ω6 FAs. These changes are likely the result of altered lipid metabolism secondary to increased adipose tissue turnover as well as to increased lipogenesis, along with increase in desaturase enzyme activity, especially stearoyl-CoA desaturase 1 (SCD1), as was found by E. Warensjo et al. [23]. High levels of ω6 FAs, including C20:4 ω6 fatty acids, may also indicate increases in the proinflammatory state associated with excess fat, since these FAs are precursors of eicosanoids involved in inflammatory processes [24]. Dietary obesity-related adjustments could additionally influence the observed FA profiles [25].

Compared with those in the normal fat group, the obese individuals in our study presented lower SFA levels and higher MUFA, PUFA, ω3, and ω6 FA levels. Owing to the anti-inflammatory and metabolic effects of ω3 FAs, this increase could compensate for adiposity. These observations indicate a threshold effect, such as an increase in fat mass and systemic inflammation, which could favour the incorporation of higher amounts of ω3 in platelet membranes. Considering the anti-inflammatory properties and cardiovascular protective role of ω3 FAs, their deficiency in obese individuals might aggravate metabolic problems and increase the risk for cardiovascular diseases [24, 26]. Thus, these profound changes observed in platelet FA profiles, especially elevated levels of the ω6 and ω3 FA classes, usually occur when a critical fat mass threshold is exceeded, indicating further deterioration in metabolism and inflammation [7, 8]. Strikingly, individuals with obesity demonstrated significant alterations in ω6 FA ratio, further supporting the concept of a metabolic threshold beyond which lipid handling and inflammatory processes become markedly dysregulated. The constant decrease in the ω6 ratio, is consistent with the progressive inflammatory state associated with obesity. High ω6 FAs, especially C20:4ω6, are the precursors of proinflammatory eicosanoids, which contribute to systemic inflammation [24, 27].

We also investigated the differences in the ω6/ω3 FA ratio among FMI groups and examined whether body fat content affected essential FA composition. The analysis revealed no statistically significant differences in the ω6/ω3 ratio between the FMI groups (combined and separately). These results indicate that adiposity does not significantly influence the balance between ω6 and ω3 FAs. This finding agrees with data from earlier studies, demonstrating that dietary consumption is correlated more with the circulating ω6/ω3 ratio than with the body fat content [25, 28].

The correlation of the ω6/ω3 FA ratio with selected laboratory biomarkers was also investigated. A direct but weak correlation was detected between the ω6/ω3 ratio and LDL-cholesterol. While the strength of this association is modest, this finding is consistent with previous research that revealed that an increased ω6/ω3 ratio is a potential mediator of proinflammatory and atherogenic lipid profiles [27, 29]. The biological mechanisms for this association are plausible on the basis of the opposite effects of ω6 and ω3 FAs on lipid metabolism. Although ω6 FAs (i.e., C18:2ω6) might affect cholesterol transport, ω3 FAs (i.e., C20:5ω3 and C22:6ω3) have been shown to decrease serum triglyceride levels and seem to have anti-inflammatory effects [24]. Nevertheless, we emphasize that the clinical significance of this weak association should be interpreted with caution. In addition, other factors, including dietary intake, physical activity, or genetic background, could affect the ω6/ω3 ratio and lipid profiles. Thus, these results indicate that the FMI is not a significant predictor of the ω6/ω3 FA and requires future research.

The correlations between FA ratios and laboratory parameters also suggested that FA metabolism is associated with cardiometabolic health and inflammation. The negative correlations of the ω3 ratio (C18:3ω3/C20:5ω3) with both total cholesterol and LDL-cholesterol and CRP support the protective role of ω3 FAs, specifically C20:5ω3. Low ω3 ratios are related to increased levels of atherogenic lipids and systemic inflammation, which is consistent with the proven anti-inflammatory and lipid-lowering effects of ω3 FAs [24, 26]. These data indicate that a decrease in ω3 availability could contribute to an unfavourable lipid profile and a greater inflammatory profile in overweight/obese individuals.

The ratio of ω6 fatty acids (C18:2ω6/C20:4ω6) was positively associated with HDL cholesterol and inversely associated with triglyceride and CRP concentration. The underlying complexity may be due to opposing effects of individual ω6 subtypes. The negative correlation of the ω6 ratio with CRP indicates its relationship with systemic inflammation, which is consistent with previous findings that lower C18:2ω6/C20:4ω6 ratio, particularly the C20:4ω6 increase, is a source for stimulating the inflammatory response or compensatory alterations in lipid metabolism [25]. Interestingly, the ω9 ratio did not correlate with laboratory parameters. There is a possibility that endogenous MUFAs, especially C18:1ω9, are less directly involved in systemic lipid profiles or inflammatory factors

and act as markers reflecting changes in lipid synthesis rather than active players in metabolic disturbances. The effects of C18:1ω9 are frequently observed when it substitutes SFAs in the diet. These outcomes are likely due to the partial removal of the biological impact of SFAs rather than any specific molecular or cellular action of C18:1ω9 [24].

Prospective studies clearly show an increased risk of obesity due to increased ω6 FAs and an increased ω6/ω3 ratio in red blood cell (RBC) membranes [25]. In contrast, high ω3 RBC membrane phospholipid levels reduce the risk of obesity [25]. Our study revealed that this ratio, albeit insignificantly, increases with increasing FMI. Given the low correlation coefficient observed between the ratio of ω6/ω3 FAs and LDL-cholesterol, the clinical significance of this relationship should be interpreted with caution. In addition, the cross-sectional nature of this study limits the possibility of concluding a causal link. Furthermore, longitudinal studies and controlled nutritional interventions are needed to elucidate the mechanisms underlying this observation. Consequently, our results demonstrate that platelet FA ratios—particularly ω3 and ω6—are significantly associated with key cardiometabolic and inflammatory markers. Reduced ω3 ratios correlate with increased cholesterol levels and inflammation, reinforcing the need for dietary strategies to increase ω3 status in individuals with excess adiposity. Moreover, the negative correlation between ω6 ratios and CRP indicates a possible association the influence of the proinflammatory capacity of ω6 FAs in obesity-associated metabolic disturbances. The observation of FA ratios and routine laboratory parameters can provide further information about an individual's cardiometabolic risk and contribute to tailored nutritional recommendations.

The significant positive correlation between the MDA level and increasing FMI suggests that OS progressively increases with increasing fat mass. MDA, an important lipid peroxidation product, is widely used as a biomarker of oxidative damage, and its higher levels in individuals with higher FMI reflect a concomitant increase in OS. This is consistent with findings that increased adiposity leads to increased OS and thereby to a degree of metabolic impairment and increased risk for insulin resistance and cardiovascular disease [10, 30–32]. Interestingly, PUFAs were positively correlated with the MDA concentration, indicating that a high level of PUFAs might increase oxidative damage to excess fat. Even though PUFAs are essential FAs for normal cellular function and inflammation resolution, they are also prone to lipid peroxidation. The oxidation of PUFAs, especially in individuals with excess fat, might increase MDA levels by enhancing the proinflammatory and prooxidative environments typically observed in individuals with metabolic dysfunction [25]. However, the MDA levels did not correlate with other FAs (e.g., SFAs or MUFAs). This could be attributed to the stability of SFAs and MUFAs, which are less susceptible to oxidation than are PUFAs. Thus, FA profiling and MDA determination could improve the monitoring of cardiometabolic risk and the selection of nutritional approaches targeting the improvement of ω3 status, the PUFA balance, and the reduction of OS in individuals with excess adiposity.

Among individuals with obesity, clustering by CRP levels revealed marked heterogeneity in systemic inflammation. One subgroup exhibited markedly elevated CRP values despite similar anthropometric measures, indicating that obesity alone does not fully account for inflammatory variability. Additional factors, including genetic predisposition, adipose tissue distribution, or comorbidities, may contribute to this heightened inflammatory state [33, 34]. The predominance of women in the high-CRP cluster further suggests sex-related modulation of inflammatory pathways [35]. Interestingly, fatty acid composition and malondialdehyde concentrations did not differ between CRP clusters, implying that inflammatory heterogeneity in obesity is not directly linked to lipid metabolism or oxidative stress, though the small cluster size may have limited statistical power. Across FMI-defined groups, however, obesity was associated with significant alterations in SFA, PUFA, ω3, and ω6 levels, as well as increased malondialdehyde concentrations, reinforcing the role of adiposity in both lipid remodeling and oxidative stress [36–38].

While our study has certain limitations, it also possesses notable strengths. The present study evaluated FMI, platelet FA composition, and OS markers to provide a holistic perspective of cardiometabolic risk. The combination of DXA for body composition and GC–MS for FA profiling guaranteed accurate and reliable performance. In addition, the potential functional relevance of these findings might serve as a premise for early recognition of lipid-related biomarkers in individuals with excess adiposity. Nonetheless, this study is cross-sectional, and we cannot determine whether FMI causes the observed biochemical abnormalities. In addition, the missing information on dietary intake for patients is a limitation for interpretation of the observed FA changes, and single-time-point measurements may not indicate the long-term changes that occur in lipid metabolism or OS.

Conclusions

Our findings demonstrate that higher fat mass index (FMI) alters platelet phospholipid fatty acid (FA) composition and promotes oxidative stress, as indicated by elevated malondialdehyde (MDA) levels. These early changes in metabolic and inflammatory balance may contribute to cardiometabolic risk development. Notably, shifts in ω3/ω6 FA ratios alongside increased

monounsaturated (MUFA) and polyunsaturated fatty acids (PUFA) point to disrupted lipid metabolism and enhanced inflammatory signaling in obesity. These results highlight the potential of platelet FA profiling and oxidative stress markers as early indicators for identifying individuals at elevated risk of metabolic disorders, offering opportunities for timely intervention.

Abbreviations

BMI	Body mass index
CRP	C-reactive protein
DXA	Dual-energy X-ray absorptiometry
FAs	Fatty acids
FMI	Fat mass index
HDL Cholesterol	High-density lipoprotein cholesterol
LDL Cholesterol	Low-density lipoprotein cholesterol
PUFAs	Polyunsaturated fatty acids
MDA	Malondialdehyde
MUFAs	Monounsaturated fatty acids
OS	Oxidative stress
RBC	Red blood cell
ROS	Reactive oxygen species
SFAs	Saturated fatty acids
Ω	Omega

Acknowledgements
We would like to thank everyone who participated in this study.

Authors' contributions
IF, IB, DK and VS designed the study; IF, IB and AD collected the data; EB conducted the statistical analyses; IF, IB, AK and DK analysed and interpreted the data; IF, IB, AK and DK wrote the main manuscript; IB, AK, VS and DK substantively revised the work and prepared the final version for submission. All the authors have read and approved the final manuscript before submission.

Funding
The authors declare that no funding was received for this study.

Data availability
The datasets used and analysed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Vilnius Regional Biomedical Research Ethics Committee (No. 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
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 1 August 2025 / Accepted: 30 September 2025
Published online: 04 November 2025

References

1. World Health Organization. WHO European Regional Obesity Report 2022. Copenhagen: WHO Regional Office for Europe; 2022. p. 1–220. https://www.who.int/europe/publications/i/item/9789289057738.
2. Wu Y, Li D, Vermund SH. Advantages and limitations of the body mass index (BMI) to assess adult obesity. Int J Environ Res Public Health. 2024;21:757. https://doi.org/10.3390/ijerph21060757.
3. Kelly TL, Wilson KE, Heymsfield SB. Dual energy X-ray absorptiometry body composition reference values from NHANES. PLoS ONE. 2009;4(9):2–9.
4. Snijder MB, van Dam RM, Visser M, Seidell JC. What aspects of body fat are particularly hazardous and how do we measure them? Int J Epidemiol. 2006;35(1):83–92.
5. Bouchi R, Nakano Y, Ohara N, Takeuchi T, Murakami M, Asakawa M, et al. Clinical relevance of dual-energy X-ray absorptiometry (DXA) as a simultaneous evaluation of fatty liver disease and atherosclerosis in patients with type 2 diabetes. Cardiovasc Diabetol. 2016;15(1):1–9.
6. Wang ZM, Deurenberg P, Wang W, Pietrobelli A, Baumgartner RN, Heymsfield SB. Hydration of fat-free body mass: review and critique of a classic body-composition constant. Am J Clin Nutr. 1999;69(5):833–41. https://doi.org/10.1093/ajcn/69.5.833.
7. Bikulčienė I, Garjonytė N, Žėkas V, Matuzevičienė R, Žymantienė Ž, Baublytė A, et al. Relationship between composition of fatty acid in platelet phospholipid membrane and markers of oxidative stress in healthy men and men after a myocardial infarction. Med Sci Monit Basic Res. 2021;27:e929634.
8. Bikulčienė I, Golubevaitė O, Žėkas V, Radzevičius M, Karčiauskaitė D, Matuzevičienė R, et al. Association of platelet membrane fatty acid composition with markers of oxidative stress in healthy men. Med Sci Monit. 2019;25:6405–16.
9. Wu B, Fukuo K, Suzuki K, Yoshino G, Kazumi T. Relationships of systemic oxidative stress to body fat distribution, adipokines and inflammatory markers in healthy middle-aged women. Endocr J. 2009;56(6):773–82.
10. Colak E, Pap D. The role of oxidative stress in the development of obesity and obesity-related metabolic disorders. J Med Biochem. 2021;40(1):1–9.
11. Dandona P, Ghanim H, Chaudhuri A, Dhindsa S, Kim SS. Macronutrient intake induces oxidative and inflammatory stress: potential relevance to atherosclerosis and insulin resistance. Exp Mol Med. 2010;42(4):245–53.
12. Marseglia L, Manti S, D'Angelo G, Nicotera A, Parisi E, Di Rosa G, et al. Oxidative Stress in Obesity: A Critical Component in Human Diseases. Int J Mol Sci. 2014;16(1):378–400 http://www.mdpi.com/1422-0067/16/1/378.
13. Monnard CR, Dulloo AG. Polyunsaturated fatty acids as modulators of fat mass and lean mass in human body composition regulation and cardiometabolic health. Obes Rev. 2021;22 Suppl 2:e13197. https://doi.org/10.1111/obr.13197.
14. Solar I, Ribeiro FB, Barbosa MG, de Oliveira Nascimento Freitas RGB, Hanada AS, de Oliveira Ramos C, et al. Short-chain fatty acids are associated with adiposity, energy and glucose homeostasis among different metabolic phenotypes in the nutritionists' health study. Endocrine. 2023;80(3):529–40.
15. Petak S, Barbu CG, Yu EW, Fielding R, Mulligan K, Sabowitz B, et al. The official positions of the International Society for Clinical Densitometry: body composition analysis reporting. J Clin Densitom. 2013;16(4):508–19. https://doi.org/10.1016/j.jocd.2013.08.018.
16. Dhurat R, Sukesh M. Principles and methods of preparation of platelet-rich plasma: a review and author's perspective. J Cutan Aesthet Surg. 2014;7(4):189.
17. Folch J, Lees M, Sloane Stanley GH. A simple method for the isolation and purification of total lipides from animal tissues. J Biol Chem. 1957;226(1):497–509.
18. Fuchs B, Süß R, Teuber K, Eibisch M, Schiller J. Lipid analysis by thin-layer chromatography-a review of the current state. J Chromatogr A. 2011;1218(19):2754–74. https://doi.org/10.1016/j.chroma.2010.11.066.
19. Khoschsorur GA, Winklhofer-Roob B. Evaluation of a sensitive HPLC method for the determination of Malondialdehyde, and application of the method to different biological materials. Chromatographia. 2000;53(3):181–4.
20. Akoglu H. User's guide to correlation coefficients. Turk J Emerg Med. 2018;18(3):91–3.
21. AlMasud AA, Alothman S, Benajiba N, et al. Relationship of fat mass index and fat free mass index with body mass index and association with sleeping patterns and physical activity in Saudi young adults women. J Health Popul Nutr. 2025;44:64. https://doi.org/10.1186/s41043-025-00795-5.
22. Wong JC, O'Neill S, Beck BR, Forwood MR, Khoo SK. Comparison of obesity and metabolic syndrome prevalence using fat mass index, body mass index and percentage body fat. PLoS One. 2021;16(1 January):1–11. https://doi.org/10.1371/journal.pone.0245436.
23. Warensjö E, Rosell M, Hellenius ML, Vessby B, De Faire U, Risérus U. Associations between estimated fatty acid desaturase activities in serum lipids and

adipose tissue in humans: links to obesity and insulin resistance. Lipids Health Dis. 2009;8:6–11.
24. Calder PC. Omega-3 fatty acids and inflammatory processes: from molecules to man. Biochem Soc Trans. 2017;45(5):1105–15.
25. Simopoulos AP. An increase in the omega-6/omega-3 fatty acid ratio increases the risk for obesity. Nutrients. 2016;8(3):1–17.
26. Mozaffarian D, Wu JHY. Omega-3 fatty acids and cardiovascular disease: effects on risk factors, molecular pathways, and clinical events. J Am Coll Cardiol. 2011;58(20):2047–67.
27. Harris WS, Mozaffarian D, Rimm E, Kris-Etherton P, Rudel LL, Appel LJ, et al. Omega-6 fatty acids and risk for cardiovascular disease: A science advisory from the American heart association nutrition subcommittee of the Council on nutrition, physical activity, and metabolism; Council on cardiovascular nursing; and Council on epidem. Circulation. 2009;119(6):902–7.
28. Burdge GC, Calder PC. Conversion of α-linolenic acid to longer-chain polyunsaturated fatty acids in human adults. Reprod Nutr Dev. 2005;45(5):581–97.
29. Simopoulos AP. The importance of the omega-6/omega-3 fatty acid ratio in cardiovascular disease and other chronic diseases. Exp Biol Med. 2008;233(6):674–88.
30. Le Lay S, Simard G, Martinez MC, Andriantsitohaina R. Oxidative stress and metabolic pathologies: from an adipocentric point of view. Oxid Med Cell Longev. 2014;2014:908539. https://doi.org/10.1155/2014/908539.
31. Manna P, Jain SK. Obesity. Oxidative stress, adipose tissue dysfunction, and the associated health risks: causes and therapeutic strategies. Metab Syndr Relat Disord. 2015;13(10):423–44.
32. Świątkiewicz I, Wróblewski M, Nuszkiewicz J, Sutkowy P, Wróblewska J, Woźniak A. The Role of Oxidative Stress Enhanced by Adiposity in Cardiometabolic Diseases. Int J Mol Sci. 2023;24(7):6382. https://doi.org/10.3390/ijms24076382.
33. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006;444:860–7.
34. Ridker PM. From C-reactive protein to Interleukin-6 to Interleukin-1: moving upstream to identify novel targets for atheroprotection. Circ Res. 2016;118(1):145–56.
35. Casimir GJ, Lefèvre N, Corazza F, Duchateau J. Sex and inflammation in respiratory diseases: a clinical viewpoint. Biol Sex Differ. 2013;4(1):16.
36. Kawano Y, Cohen DE. Mechanisms of hepatic triglyceride accumulation in non-alcoholic fatty liver disease. J Gastroenterol. 2013;48(4):434–41.
37. Vincent H, Taylor A. Biomarkers and potential mechanisms of obesity-induced oxidant stress in humans. Int J Obes. 2006;30:400–18.
38. Keaney JF, Larson MG, Vasan RS, Wilson PWF, Lipinska I, Corey D, et al. Obesity and systemic oxidative stress: clinical correlates of oxidative stress in the Framingham study. Arterioscler Thromb Vasc Biol. 2003;23(3):434–9.

Publisher's Note