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Circulating free fatty acid signatures discriminate myocardial infarction and systemic arterial hypertension

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ABSTRACT

Background: Gut microbiome (GM) dysbiosis and altered circulating free fatty acid (FFA) profiles have been implicated in cardiovascular diseases (CVDs), including systemic arterial hypertension (SAH) and ST-segment elevation myocardial infarction (STEMI). This study evaluated serum short-, medium-, and long-chain fatty acids (SCFAs, MCFAs, and LCFAs) in patients with SAH and STEMI compared with healthy controls (HCs), aiming to identify candidate biomarkers and potential mechanistic links between FFAs, the GM, and cardiovascular health.

Methods: Serum samples from 47 STEMI patients, 17 SAH patients, and 28 HCs were analysed using gas chromatography–mass spectrometry.

Results: Principal coordinates analyses (PCoA) showed significant group separation based on FFA profiles. Both STEMI and SAH patients exhibited increased total SCFA levels, with higher acetic, propionic, 2-methylbutyric, and isovaleric acids compared with HCs. Conversely, STEMI patients showed reduced isobutyric and valeric acids versus both HCs and SAH, and lower 2-methylbutyric acid relative to SAH. STEMI patients also had lower total MCFA levels, mainly due to reduced octanoic acid, while both patient groups showed increased hexanoic acid versus HCs. Additionally, STEMI patients showed elevated hexadecanoic acid and reduced octadecanoic acid compared with the other groups.

Sparse partial least squares discriminant analysis (sPLS-DA) confirmed distinct FFA signatures: STEMI was characterised by increased propionic, hexadecanoic, and tetradecanoic acids, whereas SAH showed reduced isovaleric, 2-methylbutyric, hexanoic, and isobutyric acids.

Conclusions: These findings indicate disease-specific circulating FFA patterns that may reflect metabolic alterations and underlying pathophysiological mechanisms.

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Cardiovascular diseases; free fatty acids; gut-hearth axis; myocardial infarction; short-chain fatty acids; systemic arterial hypertension

1. Introduction

Free fatty acids (FFAs) are non-esterified fatty acids that serve as an important energy source for cells and tissues. They are classified as saturated or unsaturated depending on the presence of double bonds and are further categorised by carbon-chain length into short-chain fatty acids (SCFAs, C2–C5), medium-chain fatty acids (MCFAs, C6–C12), and long-chain fatty acids (LCFAs, C13–C20) [1]. SCFAs are primarily produced by the gut microbiome (GM) and are largely metabolised by enterocytes; however, a small fraction reaches the circulation, where SCFAs exert well-documented anti-inflammatory effects that support systemic health [2]. By contrast, MCFAs and LCFAs are mainly diet-derived, particularly from certain plant oils and daily products, and act as regulators of energy metabolism, gene expression, ion channels and pumps, membrane trafficking, and immune processes [3–5]. Recent evidence links imbalances in GM composition

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and function to the onset and progression of various disorders, including cardiovascular diseases (CVDs). Through the gut-hearth axis, GM-derived metabolites such as trimethylamine-N-oxide, bile acids and SCFAs can influence cardiovascular physiology [6]. Notably, dietary fibre intake and shifts in GM composition are major determinants of SCFA levels and, consequently, of inflammation-related CVD risk [7]. For instance, both SCFA concentrations and the abundance of SCFA-producing bacteria are reduced in patients with systemic arterial hypertension (SAH), a condition often associated with low dietary fibre intake [8]. Conversely, interventions that increase circulating SCFA levels have been shown to improve arterial compliance [9]. In the context of myocardial infarction, SCFAs may help prevent atherosclerosis by promoting regulatory T cell expansion, inhibiting histone deacetylases, and modulating lipid metabolism [10].

MCFAs have therapeutic applications in malabsorption syndromes owing to their favourable metabolic properties. In animal models, MCFA supplementation reduces fat deposition and improves glucose tolerance, demonstrating antidiabetic effects [11]. MCFAs have also been reported to improve systolic function and attenuate hypertrophy in type 2 diabetes mellitus (T2DM), suggesting potential cardiovascular benefits [12].

In contrast, many LCFAs are associated with adverse metabolic effects, including reduced insulin sensitivity and dysregulated lipid metabolism. Certain LCFAs can promote vascular dysfunction and insulin resistance *via* increased inflammation, activation of stress-related signalling pathways, and ectopic lipid accumulation [13].

Given that FFAs are promising candidate biomarkers of metabolic and cardiovascular health, this study aims to characterise circulating FFA profiles in patients with SAH and ST-segment elevation myocardial infarction (STEMI), compared with healthy controls (HC).

2. Materials and methods

2.1. Study participants

Adult patients with a confirmed diagnosis of primary SAH or STEMI within 24 h of symptom onset were recruited from the Coronary Care Unit of the Instituto Nacional de Cardiologia 'Ignacio Chávez' (Mexico City, Mexico). Exclusion criteria for STEMI patients included prior reperfusion or thrombolytic therapy, while secondary hypertension was an exclusion criterion for SAH patients. Additional exclusion criteria applicable to all participants included chronic heart failure, active infections, neoplastic, autoimmune, or other chronic disorders; pregnancy or the puerperium; use of prebiotics, probiotics, or antibiotics within the 3 months prior to enrolment; and treatment with immunosuppressants or glucocorticoids within the preceding 30 days. All patients were excluded if they had chronic heart failure, active infections, neoplastic, autoimmune or other chronic disorders; if they were pregnant or in the puerperium; is they assumed prebiotics, probiotics or antibiotics during the 3 months before enrolment, or if they had used immunosuppressants or glucocorticoids within the previous 30 days. In addition, adult volunteers aged ≥18 years residing in Mexico City or its metropolitan area were enrolled as healthy controls (HC). Inclusion criteria for HCs included the absence of any diagnosed medical condition and a body mass index (BMI) <25 kg/m^2. After providing written informed consent, all candidates underwent screening to confirm stable vital signs, a normal electrocardiogram, and normal capillary glucose, total cholesterol, and triglyceride levels.

The study was approved by the Ethics and Scientific Committees of the Instituto Nacional de Cardiología 'Ignacio Chávez' (protocol number 2018-41) and the Faculty of Medicine of the Universidad Nacional Autónoma de México (FM/DI/030/SR/2019) and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

2.2. Circulating short, medium and long chain fatty acids evaluation by GC-MS analysis

FFAs, namely circulating SCFAs (acetic, propionic, butyric, isobutyric, 2-methylbutyric, isovaleric and valeric acids), MCFAs (hexanoic, isohexanoic, octanoic, decanoic and dodecanoic acids) and LCFAs (tetradecanoic, hexadecanoic and octadecanoic acids), were analysed using an Agilent gas chromatography-mass spectrometry (GC– MS) system composed of an HP 5971 single quadrupole mass spectrometer, an HP 5890 gas chromatograph, and an HP 7673 autosampler, following previously described protocols [14,15]. Briefly, each sample was thawed and FFAs were extracted as follows: 200 µl of serum sample was mixed with 10 µl of internal standard mixture, 100 µl of tert–butyl methyl ether, and 20 µl of 6 M HCl + 0.5 M NaCl solution in a 0.5 mL centrifuge tube. Tubes were vortexed for 2 min and centrifuged at 10,000 rpm for 5 min; the solvent layer was then transferred to a GC-MS vial fitted with a microvolume insert for analysis.

2.3. Statistical analysis

All statistical analyses were performed in R 4.2 using the packages stats (v.4.2.2), vegan (v.2.6.2), MixOmics

(v.6.20.0) and other packages satisfying their dependencies. Data visualisation was carried out using ggplot2 (v.3.4.0). Differences in FFA levels between STEMI, SAH and HC groups were assessed using the Kruskal-Wallis test. Principal coordinates analysis (PCoA) was performed on Bray-Curtis dissimilarities of proportional abundances, and group differences were evaluated using permutation tests (PERMANOVA and Betadisper).

3. Results

3.1. Enrolled patients

A total of 92 participants, 63 males and 29 females aged 23–70 years, were enrolled and classified into three study groups: HC ($n=28$), STEMI ($n=47$), and SAH ($n=17$).

All participants underwent clinical evaluation, and comorbidities such as overweight/obesity, T2DM, dyslipidemia, smoking, and alcohol consumption, were recorded. Regarding lipid profiles, patients with SAH exhibited borderline elevations in total cholesterol and triglyceride levels. In addition, both STEMI and SAH patients had low c-HDL and elevated c-LDL concentrations, according to the 2019 ESC/EAS guidelines [16]. Detailed clinical characteristics of each study group are presented in Table 1.

3.2. Evaluation of serum FFAs profiles

Exploratory descriptive analyses were first performed on the marginal distributions of circulating FFAs (Table S1). Because absolute FFA concentrations can bias comparisons, subsequent analyses were conducted using the percentage composition of FFAs. PCoAs based on the Bray-Curtis dissimilarity index revealed significant differences (Table S2) among HC, STEMI and SAH groups for SCFA (Figure 1A), MCFA (Figure 1B) and LCFA (Figure 1C) profiles.

Focusing on individual FFAs, both STEMI and SAH patients exhibited increased total SCFAs and higher relative abundances of acetic, propionic, 2-methylbutyric and isovaleric acids compared with HC. In addition, STEMI patients showed reduced isobutyric and valeric acids relative to both HC and SAH patients, and lower 2-methylbutyric acid levels than SAH patients (Figure 2A, Table S3).

Regarding MCFAs, STEMI patients displayed significantly lower total MCFA levels and reduced octanoic acid concentrations compared with both HC and SAH groups. HC exhibited higher isohexanoic acid levels than STEMI patients and higher decanoic and dodecanoic acids than SAH patients. Both STEMI and SAH patients had significantly higher hexanoic acid levels than HC (Figure 2B, Table S3).

For LCFAs, HC exhibited higher total LCFA levels and increased octadecanoic acid concentrations compared with STEMI and SAH groups. Conversely, STEMI patients showed elevated hexadecanoic acid and decreased octadecanoic acid levels relative to both HC and SAH groups (Figure 2C, Table S3).

To assess group separation and identify discriminant features, a sparse partial least squares discriminant analysis (sPLS-DA) was performed using FFA data from STEMI and SAH patients and HCs. The resulting plot revealed a distinct shift in FFA profiles among groups (Figure 3A) and the specific FFAs contributing most to this separation are shown in Figure 3B. The STEMI group was characterised by increased propionic, hexadecanoic, and tetradecanoic acids, whereas the SAH group exhibited decreased isovaleric, 2-methylbutyric, hexanoic, and isobutyric acids. In contrast, the HCs were characterised by lower levels of isohexanoic, octadecanoic, and octanoic acids.

To explore potential clinical associations, Spearman correlation analyses were conducted between circulating FFAs and lipid biochemical parameters.

Acetic and 2-methylbutyric acids were negatively correlated with triglycerides, whereas decanoic acid

Table 1. Clinical characteristics of enrolled participants.

	HC	STEMI	SAH
Comorbidities			
Obesity	0 (0.0%)	15 (31.9%)	14 (82.4%)
Overweight	0 (0.0%)	25 (53.2%)	3 (17.6%)
Hypertension	0 (0.0%)	18 (39.1%)	17 (100.0%)
T2DM	0 (0.0%)	19 (41.3%)	0 (0.0%)
Dyslipidemia	6 (21.4%)	7 (14.9%)	12 (70.6%)
Smoking	0 (0.0%)	22 (47.8%)	4 (25.0%)
Alcoholism	0 (0.0%)	20 (43.5%)	11 (73.3%)
Lipid Biochemical Profile			
Total Cholesterol (mg/dL)	174.00 ± 27.34	166.72 ± 48.15	192.75 ± 36.63
Triglycerides (mg/dL)	76.35 (65.20–120.25)	128.50 (110.50–160.50)	183.20 (107.30–239.50)
c-HDL (mg/dL)	54.05 (45.23–60.12)	35.80 (30.60–44.50)	38.90 (30.20–44.10)
c-LDL (mg/dL)	109.98 ± 25.52	111.37 ± 40.95	121.49 ± 36.06

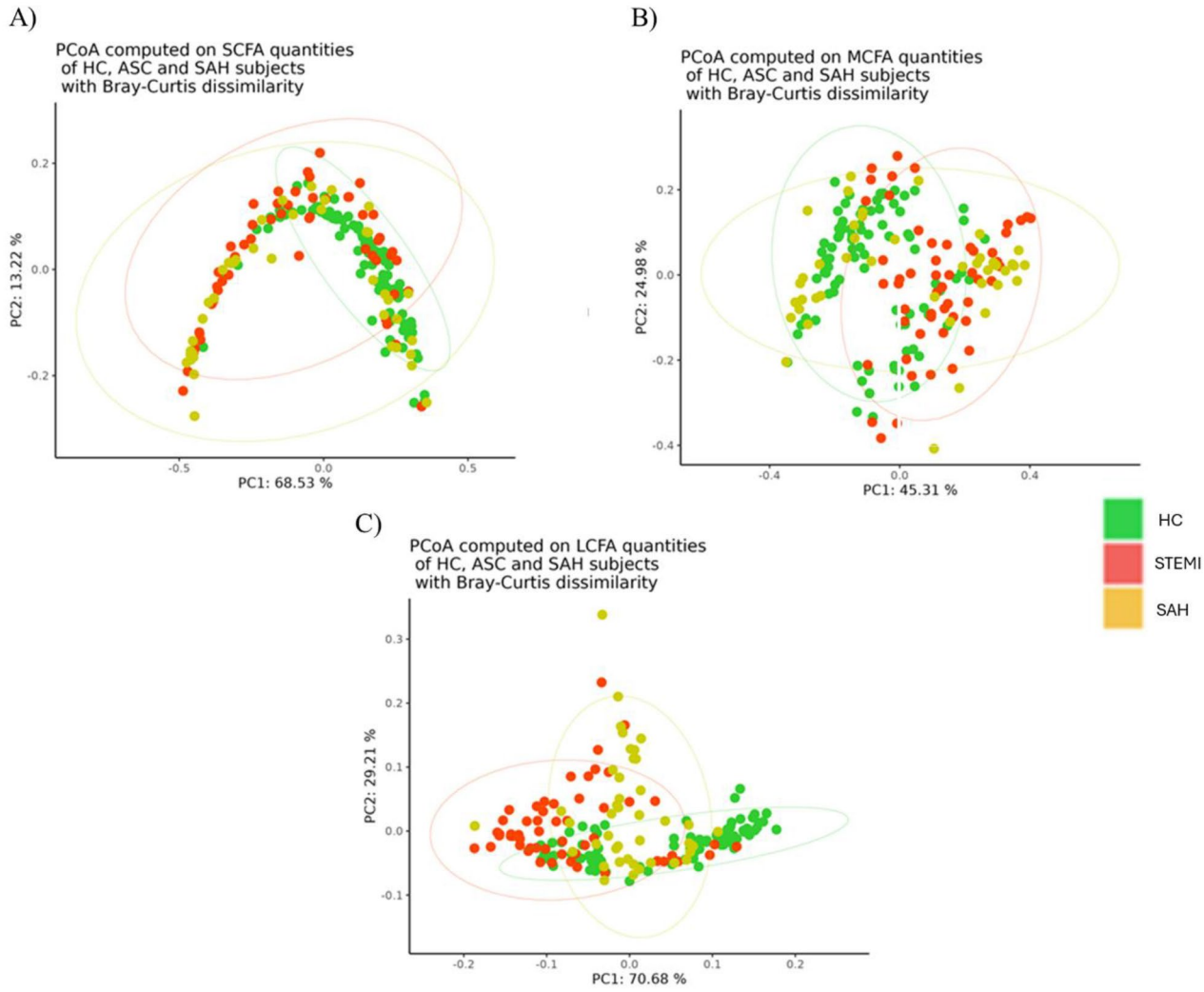

Figure 1. Principal component analysis (PCoA) conducted with the Bray–Curtis dissimilarity index revealed significant differences in the circulating SCFA (A), MCFA (B) and LCFA (C) profiles among STEMI, SAH and HC groups.

was positively correlated with total cholesterol and c-LDL. In addition, hexadecanoic acid exhibited negative correlations with triglycerides and total cholesterol (Figure 4A).

Within the STEMI group, octanoic, dodecanoic and tetradecanoic acids were positively correlated with triglycerides (Figure 4B), while no significant correlations were observed in the SAH group (Figure 4C).

4. Discussion

FFAs have recently emerged as important regulators of human health because of their role in the crosstalk between metabolic status and the immune system [17]. Notably, our previous studies documented altered FFA profiles in several immune-related diseases, including coeliac disease [18], Crohn's disease [19], pemphigus vulgaris [20], amyotrophic lateral sclerosis [21] and systemic sclerosis [22,23].

In addition to classic lipid indicators such as cholesterol and lipoproteins, changes in plasma FFA concentrations in patients with T2DM have been closely associated with the development of insulin resistance and implicated in vascular endothelial damage as well as the onset and progression of atherosclerosis [24]. Moreover, GM dysbiosis, characterised by reduced microbial diversity and overrepresentation of pro-inflammatory taxa, has been increasingly linked to CVDs, with SCFAs playing crucial roles in disease pathogenesis [25].

In this context, we recently observed altered circulating FFA profiles in patients with STEMI, including increased abundances of isobutyric and 2-methylbutyric acids relative to healthy subjects [26].

Therefore, in the present study we evaluated whether circulating FFAs provide informative metabolic signatures in patients with STEMI and SAH and in HCs. In detail, PCoA revealed clear separation of SCFA, MCFA and LCFA profiles across groups, with

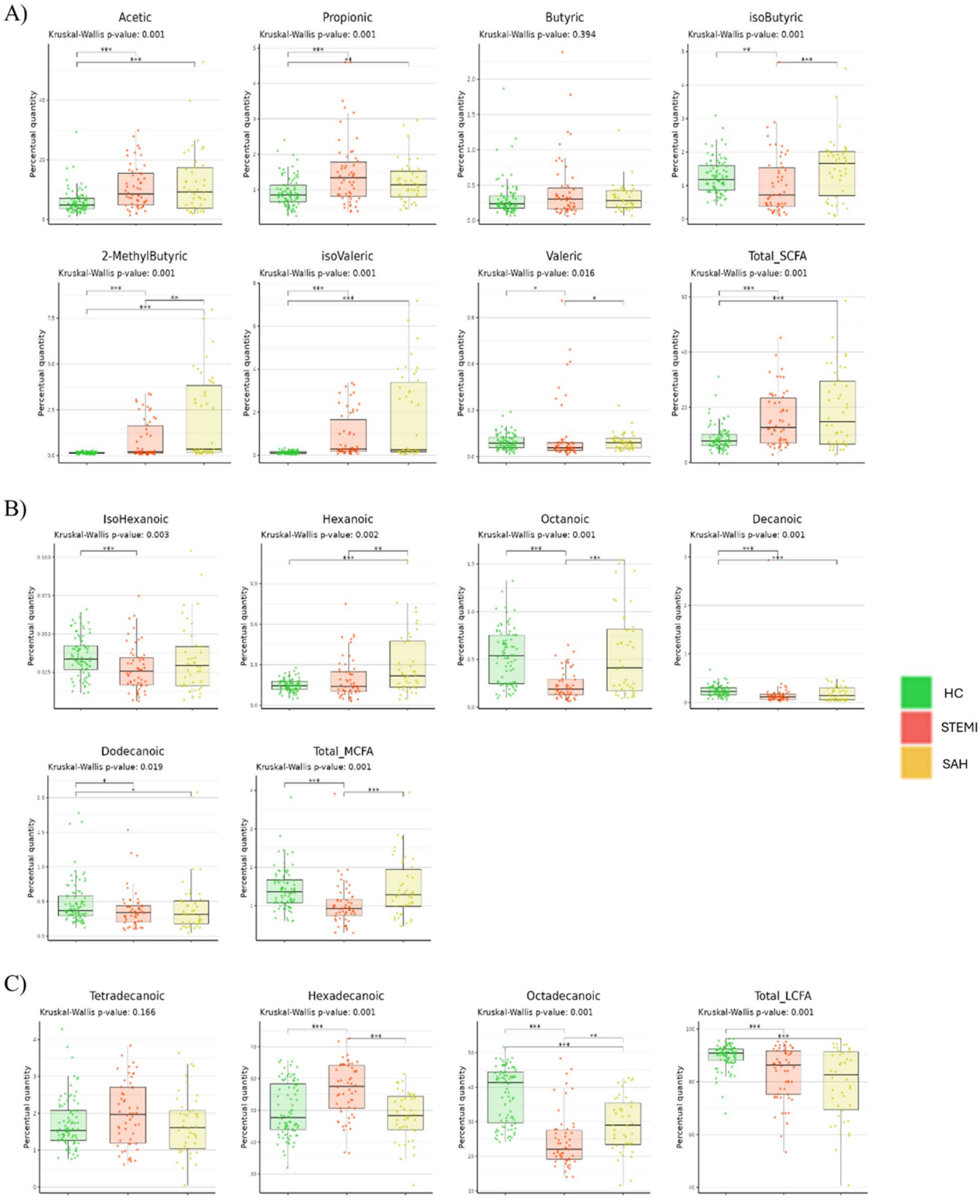

Figure 2. Box plots showing differences in the serum SCFA (A), MCFA (B) and LCFA (C) abundances among HC, STEMI and SAH groups. Statistical comparisons were performed using the Kruskal-Wallis test, followed by Dunnett's pairwise comparisons with through Benjamini-Hochberg correction. Asterisks (*) represent p adjusted values *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

distinct FFA signatures characterising STEMI and SAH patients.

Both STEMI and SAH patients exhibited increased total SCFAs and higher relative abundances of acetic, propionic, 2-methylbutyric and isovaleric acids compared with HCs. STEMI patients additionally showed reduced isobutyric and valeric acids relative to both HCs and SAH patients, and lower 2-methylbutyric acid levels than SAH patients.

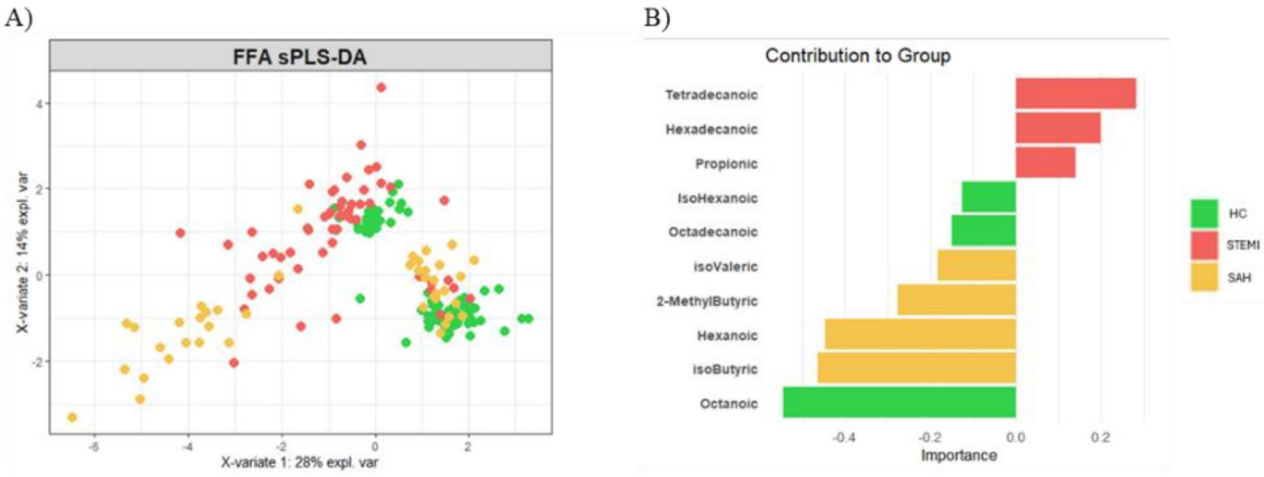

Figure 3. A) sPLS-DA analysis of circulating FFA abundances in STEMI and SAH patients and Score plot showing the separation of samples according to outcome groups. B) Contribution of specific FFA to group discrimination.

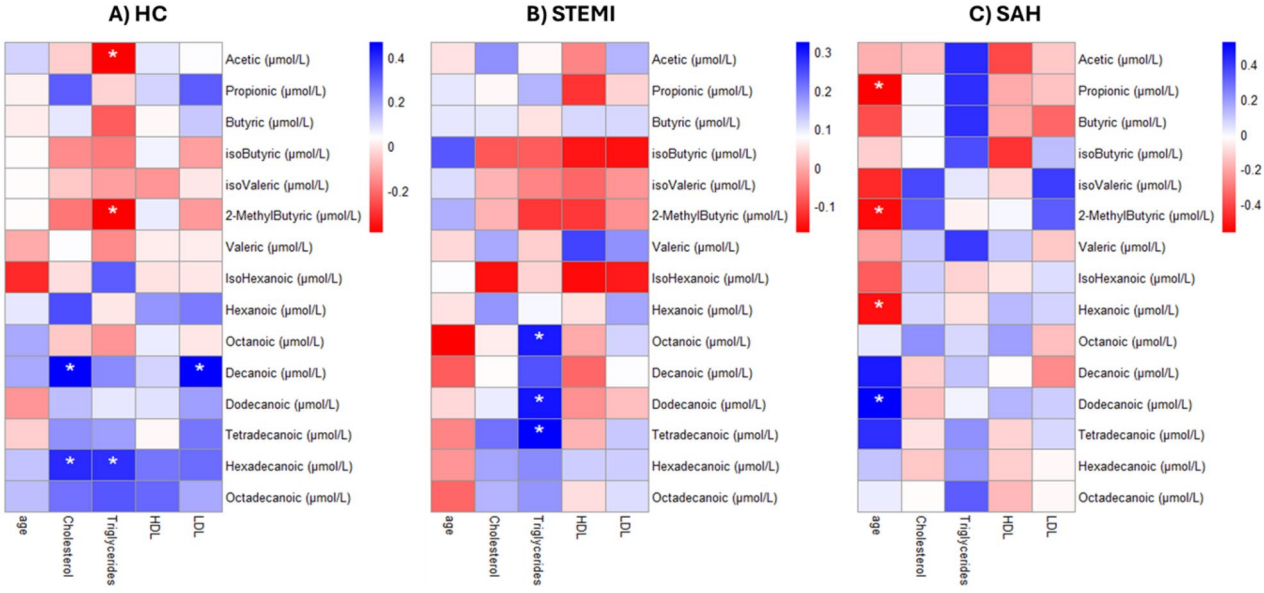

Figure 4. Correlation plot between FFAs and lipid biochemical profiles in HC (A), STEMI (B) and SAH (C) groups. Asterisks (*) represent p values $*p < 0.05$, $**p < 0.01$, $***p < 0.001$.

SCFAs are gut-derived metabolites that exert anti-inflammatory and trophic effects within the intestinal lumen; however, their biological impact depends on local versus systemic distribution. Faecal SCFA reductions are commonly associated with gut dysbiosis and decreased abundance of SCFA-producing taxa such as *Bifidobacterium* spp. and members of the Lachnospiraceae family [27]. By contrast, increases in circulating SCFAs may reflect enhanced translocation across a compromised intestinal barrier ('leaky gut'). For instance, Zhao and colleagues reported elevated circulating SCFA levels and increased ZO-1 levels in T2DM patients versus HCs, findings the authors interpreted as consistent with increased intestinal permeability in T2DM [28].

Consistent with our observations, increased serum butyric acid levels have been reported in STEMI patients [29], and accumulating evidence suggest that SCFAs influence blood pressure regulation [30]. The functional roles of SCFA-responsive G protein–coupled receptors (GPRs) can be inferred from changes in their expression across physiological conditions. Nakai and colleagues examined GPR41, GPR43, and GPR109A in immune cells from hypertensive and normotensive individuals and found that while GPR41 and GPR109A were unchanged, GPR43 was markedly reduced in hypertensive subjects and strongly negatively correlated with blood pressure [31]. These subjects also exhibited elevated plasma acetate and butyrate, suggesting that increased circulating SCFAs may not

produce blood-pressure-lowering effects when GPR43 is downregulated [32,33].

Regarding MCFAs, hexanoic acid was elevated in both STEMI and SAH patients and correlated positively with total cholesterol and triglycerides in STEMI patients, suggesting a potential pro-atherogenic or pro-inflammatory role in this clinical context. These observations align with previous studies indicating that specific MCFAs engage receptors such as GPR84, which display context-dependent actions: improving metabolic parameters in some experimental models but promoting inflammation and fibrogenesis in others [34–36]. Conversely, decanoic acid was decreased in STEMI and SAH patients versus HCs; given evidence for its antioxidant and potential cardioprotective properties, this reduction may reflect loss of a protective MCFA-mediated signal during disease [37].

For LCFAs, STEMI patients displayed increased hexadecanoic acid and decreased octadecanoic acid compared with both HC and SAH groups. Consistently, Chen and colleagues reported elevated hexadecanoic acid, a recognised risk factor for atherosclerosis, in a Chinese cohort of premature coronary artery disease patients [38]. Because some saturated LCFAs are linked to insulin resistance, inflammation, and vascular dysfunction, the LCFA pattern observed in STEMI is compatible with a shift towards a more atherogenic profile that may reflect dietary influences or disease-associated lipid remodelling [39].

Multivariate modelling (sPLS-DA) confirmed that distinct combinations of FFAs discriminate STEMI and SAH: STEMI was enriched for propionic, tetradecanoic and hexadecanoic acids, whereas SAH was characterised by lower isovaleric, isobutyric, 2-methylbutyric and hexanoic acids. These composite signatures imply that single-FFA measurements are unlikely to capture the full metabolic perturbation and that panel-based profiling may offer a more informative biomarker approach.

Notably, diet strongly influences FFA patterns: the traditional Mexican diet (centred on maize and beans) differs substantially from Western diets [40], and ongoing urbanisation towards Westernised eating habits likely shifts FFA distributions and their health effects [41].

Overall, this study is limited by a small patient cohort, lack of dietary assessment, and absence of GM characterisation in both patients and controls. Nevertheless, to our knowledge this is the first report documenting substantially altered circulating FFA profiles in STEMI and SAH patients, suggesting that microbial metabolites may contribute to cardiometabolic pathology. Longitudinal, mechanistic, and diet-integrated studies are needed to establish causality, validate FFA biomarker panels, and assess therapeutic approaches (e.g. increased dietary fibre intake, pre/probiotics, or targeted lipid interventions).

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Author contributions

SB and LACJ conducted the study, analysed the data and wrote the manuscript, SJA collected the samples, FC, IL, MM and GB performed the experiments, NAV and LMGA supervised and contributed to recruitment diagnosis and analysis of clinical parameters, AA and MMAG conceived and supervised the protocol design, review and edit the manuscript. All authors contributed to the article and approved the submitted version.

Disclosure statement

No potential competing interest was reported by the authors.

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References

[1] Yu F, Zong B, Ji L, et al. Free fatty acids and free fatty acid receptors: role in regulating arterial function. Int J Mol Sci. 2024;25(14):7853. doi: 10.3390/ijms25147853.

[2] Fusco W, Lorenzo MB, Cintoni M, et al. Short-chain fatty-acid-producing bacteria: key components of the human gut microbiota. Nutrients. 2023;15(9):2211. doi: 10.3390/nu15092211.

[3] Schönfeld P, Wojtczak L. Short- and medium-chain fatty acids in energy metabolism: the cellular perspective. J Lipid Res. 2016;57(6):943–954. doi: 10.1194/jlr.R067629.

[4] Pinkosky SL, Scott JW, Desjardins EM, et al. Long-chain fatty acyl-CoA esters regulate metabolism via allosteric

control of AMPK β1 isoforms. Nat Metab. 2020;2(9):873–881. doi: 10.1038/s42255-020-0245-2.
[5] Wojciechowicz ML, Ma'ayan A. GPR84: an immune response dial? Nat Rev Drug Discov. 2020;19(6):374–374. doi: 10.1038/d41573-020-00029-9.
[6] Zhang Y, Wu H, Jin M, et al. The gut-heart axis: unveiling the roles of gut microbiota in cardiovascular diseases. Front Cardiovasc Med. 2025;12:1572948. doi: 10.3389/fcvm.2025.1572948.
[7] Tremaroli V, Bäckhed F. Functional interactions between the gut microbiota and host metabolism. Nature. 2012;489(7415):242–249. doi: 10.1038/nature11552.
[8] Miyamoto J, Kasubuchi M, Nakajima A, et al. The role of short-chain fatty acid on blood pressure regulation. Curr Opin Nephrol Hypertens. 2016;25(5):379–383. doi: 10.1097/MNH.0000000000000246.
[9] Yang F, Chen H, Gao Y, et al. Gut microbiota-derived short-chain fatty acids and hypertension: mechanism and treatment. Biomed Pharmacother. 2020;130:110503. doi: 10.1016/j.biopha.2020.110503.
[10] Feng Y, Xu D. Short-chain fatty acids are potential goalkeepers of atherosclerosis. Front Pharmacol. 2023;14:1271001. doi: 10.3389/fphar.2023.1271001.
[11] Xia J, Wang Z, Yu P, et al. Effect of different medium-chain triglycerides on glucose metabolism in high-fat-diet induced obese rats. Foods. 2024;13(2):241. doi: 10.3390/foods13020241.
[12] Airhart S, Cade WT, Jiang H, et al. A diet rich in medium-chain fatty acids improves systolic function and alters the lipidomic profile in patients with type 2 diabetes: a pilot study. J Clin Endocrinol Metab. 2016;101(2):504–512. doi: 10.1210/jc.2015-3292.
[13] Montgomery MK, Osborne B, Brown SHJ, et al. Contrasting metabolic effects of medium- versus long-chain fatty acids in skeletal muscle. J Lipid Res. 2013;54(12):3322–3333. doi: 10.1194/jlr.M040451.
[14] Baldi S, Menicatti M, Nannini G, et al. Free fatty acids signature in human intestinal disorders: significant association between butyric acid and celiac disease. Nutrients. 2021;13(3):742. doi: 10.3390/nu13030742.
[15] Bartolucci G, Pallecchi M, Menicatti M, et al. A method for assessing plasma free fatty acids from C2 to C18 and its application for the early detection of colorectal cancer. J Pharm Biomed Anal. 2022;215:114762. doi: 10.1016/j.jpba.2022.114762.
[16] Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020;41(1):111–188. doi: 10.1093/eurheartj/ehz455.
[17] Rodríguez-Carrio J, Salazar N, Margolles A, et al. Free fatty acids profiles are related to gut microbiota signatures and short-chain fatty acids. Front Immunol. 2017;8:823. doi: 10.3389/fimmu.2017.00823.
[18] Federica R, Edda R, Daniela R, et al. Characterization of the "gut microbiota-immunity axis" and microbial lipid metabolites in atrophic and potential celiac disease. Front Microbiol. 2022;13:886008. doi: 10.3389/fmicb.2022.886008.
[19] Russo E, Cinci L, Di Gloria L, et al. Crohn's disease recurrence updates: first surgery vs. surgical relapse patients display different profiles of ileal microbiota and systemic microbial-associated inflammatory factors. Front Immunol. 2022;13:886468. doi: 10.3389/fimmu.2022.886468.
[20] Maglie R, Baldi S, Nannini G, et al. Alterations of circulating free fatty acids in patients with pemphigus vulgaris. Exp Dermatol. 2024;33(3):e15063. doi: 10.1111/exd.15063.
[21] Niccolai E, Pedone M, Martinelli I, et al. Amyotrophic lateral sclerosis stratification: unveiling patterns with virome, inflammation, and metabolism molecules. J Neurol. 2024;271(7):4310–4325. doi: 10.1007/s00415-024-12348-7.
[22] Russo E, Bellando-Randone S, Carboni D, et al. The differential crosstalk of the skin-gut microbiome axis as a new emerging actor in systemic sclerosis. Rheumatology (Oxford). 2024;63(1):226–234. doi: 10.1093/rheumatology/kead208.
[23] Bellando-Randone S, Russo E, Di Gloria L, et al. Gut microbiota in very early systemic sclerosis: the first case-control taxonomic and functional characterisation highlighting an altered butyric acid profile. RMD Open. 2024;10(4):e004647. doi: 10.1136/rmdopen-2024-004647.
[24] Liu X, Gong M, Wu N. Research progress on the relationship between free fatty acid profile and type 2 diabetes complicated by coronary heart disease. Front Endocrinol (Lausanne). 2024;15:1503704. doi: 10.3389/fendo.2024.1503704.
[25] Muttiah B, Hanafiah A. Gut microbiota and cardiovascular diseases: unraveling the role of dysbiosis and microbial metabolites. Int J Mol Sci. 2025;26(9):4264. doi: 10.3390/ijms26094264.
[26] Constantino-Jonapa LA, Aguilar-Villegas OR, Hernández-Ruiz P, et al. The link between inflammatory/SCFA profiles and oral/gut microbiome: an observational study in patients with ST-segment elevation myocardial infarction. Curr Res Microb Sci. 2025;9:100423. doi: 10.1016/j.crmicr.2025.100423.
[27] Vatanen T, Franzosa EA, Schwager R, et al. The human gut microbiome in early-onset type 1 diabetes from the TEDDY study. Nature. 2018;562(7728):589–594. doi: 10.1038/s41586-018-0620-2.
[28] Zhao L, Lou H, Peng Y, et al. Elevated levels of circulating short-chain fatty acids and bile acids in type 2 diabetes are linked to gut barrier disruption and disordered gut microbiota. Diabetes Res Clin Pract. 2020;169:108418. doi: 10.1016/j.diabres.2020.108418.
[29] Messiha D, Lange E, Tratnik A, et al. The influence of acute and chronic coronary syndrome on the gut microbiome and downstream microbiome-derived metabolites-Microbiome in acute myocardial infarction-MIAMI-Trial. Basic Res Cardiol. 2025;120(5):913–924. doi: 10.1007/s00395-025-01134-9.
[30] Xu J, Moore BN, Pluznick JL. Short-chain fatty acid receptors and blood pressure regulation: council on hypertension mid-career award for research excellence 2021. Hypertension. 2022;79(10):2127–2137. doi: 10.1161/HYPERTENSIONAHA.122.18558.
[31] Nakai M, Ribeiro RV, Stevens BR, et al. Essential hypertension is associated with changes in gut microbial metabolic pathways: a multisite analysis of ambulatory blood pressure. Hypertension. 2021;78(3):804–815. doi: 10.1161/HYPERTENSIONAHA.121.17288.

[32] Marques FZ, Nelson E, Chu P-Y, et al. High-fiber diet and acetate supplementation change the gut microbiota and prevent the development of hypertension and heart failure in hypertensive mice. Circulation. 2017;135(10):964–977. doi: 10.1161/CIRCULATIONAHA.116.024545.

[33] Kaye DM, Shihata WA, Jama HA, et al. Deficiency of prebiotic fiber and insufficient signaling through gut metabolite-sensing receptors leads to cardiovascular disease. Circulation. 2020;141(17):1393–1403. doi: 10.1161/CIRCULATIONAHA.119.043081.

[34] Puengel T, De Vos S, Hundertmark J, et al. The medium-chain fatty acid receptor GPR84 mediates myeloid cell infiltration promoting steatohepatitis and fibrosis. J Clin Med. 2020;9(4):1140. doi: 10.3390/jcm9041140.

[35] Rial SA, Ravaut G, Malaret TB, et al. Hexanoic, octanoic and decanoic acids promote basal and insulin-induced phosphorylation of the Akt-mTOR axis and a balanced lipid metabolism in the HepG2 hepatoma cell line. Molecules. 2018;23(9):2315. doi: 10.3390/molecules23092315.

[36] Nishida A, Ohue-Kitano R, Masujima Y, et al. Medium-chain fatty acid receptor GPR84 deficiency leads to metabolic homeostasis dysfunction in mice fed high-fat diet. FASEB Bioadv. 2024;6(11):526–538. doi: 10.1096/fba.2024-00075.

[37] Wu Z, Yang W, Li M, et al. Relationship between dietary decanoic acid and coronary artery disease: a population-based cross-sectional study. Nutrients. 2023;15(20):4308. doi: 10.3390/nu15204308.

[38] Chen Y, Cao Y, Li L, et al. The association between circulating palmitic acid levels and risk of premature coronary artery disease in Chinese patients: a case-control study. BMC Cardiovasc Disord. 2025;25(1):412. doi: 10.1186/s12872-025-04873-8.

[39] Annevelink CE, Sapp PA, Petersen KS, et al. Diet-derived and diet-related endogenously produced palmitic acid: effects on metabolic regulation and cardiovascular disease risk. J Clin Lipidol. 2023;17(5):577–586. doi: 10.1016/j.jacl.2023.07.005.

[40] Valerino-Perea S, Lara-Castor L, Armstrong MEG, et al. Definition of the traditional Mexican diet and its role in health: a systematic review. Nutrients. 2019;11(11):2803. doi: 10.3390/nu11112803.

[41] Jansen EC, Marcovitch H, Wolfson JA, et al. Exploring dietary patterns in a Mexican adolescent population: A mixed methods approach. Appetite. 2020;147:104542. doi: 10.1016/j.appet.2019.104542.