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Serum adiponectin and TNFα concentrations are closely associated with epicardial adipose tissue fatty acid profiles in patients undergoing cardiovascular surgery

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ABSTRACT

Background: Epicardial adipose tissue (EAT) releases both adiponectin and TNFα, and these two adipokines play important roles in heart diseases such as coronary arterial disease. The aim of the present study was to clarify whether fatty acid (FA) profiles in EAT are linked to the serum concentration of these adipokines. The relationships between serum adipokine levels and FA profiles in patients undergoing cardiovascular surgery were analyzed.

Methods: Patients ($n = 21$) undergoing cardiovascular surgery (11 males, 70.4 ± 9.0 years, BMI 26.0 ± 5.1 kg/m^2) were included. EAT samples were taken. We measured clinical biochemical data and FA profiles in venous blood and EAT samples using gas chromatography. Serum adiponectin and TNFα concentrations were also measured.

Results: The adiponectin and TNFα levels were not correlated with any fatty acid concentration in serum lipids. In contrast, there was a positive correlation between the serum adiponectin level and epicardial level of nervonic acid (C24:1ω9, $r = 0.525$, $P = 0.025$). In multiple regression analysis, adiponectin showed a positive association with the epicardial C24:1ω9 concentration after controlling for age and BMI, or TG, non-HDL-C, and BNP. The serum TNFα concentration was negatively correlated with the epicardial C18:3ω3, C12:0 and C18:0 content. In multiple regression analysis, the serum TNFα concentration showed a positive association with the epicardial C18:3ω3 level ($\beta = -0.575$, $P = 0.015$).

Conclusions: These results suggest that there is a close relationship between epicardial FA profiles and serum levels of adiponectin and TNFα. Dietary therapy to target FA profiles may be helpful to modulate inflammation.

1. Introduction

Fatty acids (FAs) are monovalent carboxylic acids that contain long chain hydrocarbon. They are components of lipids and important sources of fuel, and play a number of key roles in metabolism as essential components of all membranes. The FA composition of cell membranes affects cellular function including intracellular signaling [1]. Also, essential polyunsaturated FAs (PUFAs) consist of both ω6 and ω3 FAs and exert a broad range of beneficial effects on the cardiovascular system including modulation of the inflammatory response [2]. Consumption of a large amount of fish or marine mammals rich in ω3 FAs contributes to a low incidence of cardiovascular disease (CVD) among the Greenland Eskimos [3]. In addition, evidence from both epidemiologic studies and clinical trials demonstrates substantial cardioprotective effects of α-linolenic acid [4,5]. In contrast, several studies showed that an increase in circulatory linoleic acid is associated with reduced inflammation and cardiovascular risk, as well as improved outcomes [6,7]. Thus, dietary therapy that targets FA profiles may be helpful to modulate inflammation that could prevent CVD.

The relationship between the amount of PUFAs in the diet and the corresponding proportions of the same FAs in plasma lipids is strong. This is usually true for essential FAs, such as linoleic (18:2ω6) and α-linolenic acid (18:3ω3). However, most other types of FAs reflect endogenous FA metabolites and are synthesized from precursors,

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particularly saturated fatty acids (SFAs). SFAs can be synthesized de novo in the human body from acetyl coenzyme A and can be elongated or desaturated. Thus, FA profiles in serum and tissues can serve as a biomarker of the type of dietary fat intake as well as an indicator of the risk of diseases such as metabolic syndrome and CVD [8,9].

Adipose tissue is not only a lipid storage unit, but it also serves as an endocrine and paracrine organ, playing a key role in the homeostasis of body energy and the metabolism of lipids and carbohydrates [10,11]. In particular, epicardial adipose tissue (EAT), which interacts locally with the myocardium and coronary arteries, is a metabolically active organ that has a high rate of secretion of inflammatory adipokines such as TNFα [12,13]. EAT is also an important source of adiponectin, an anti-inflammatory and anti-atherosclerotic adipokine, and secretion of adiponectin from EAT can alter adiponectin levels in the systemic circulation [14,15]. Thus, adipokines released from EAT play an important role in diseases such as obesity, metabolic syndrome, and CVD including coronary arterial disease (CAD) [16]. Until now, several studies have reported the relationships between serum TNFα/adiponectin concentrations and FA profiles in serum [17,18]. Thus, it is likely that the FA composition of adipose tissue affects adipose function such as adipokine secretion, which plays an essential role in heart diseases. However, there are few reports on the relationships between serum TNFα/adiponectin concentrations and FA profiles in EAT and their underlying mechanisms.

2. Objectives

We investigated the relationships between serum adipokine levels/laboratory markers and FA profiles of EAT in patients undergoing cardiovascular surgery.

3. Materials

3.1. Participants

From October 2015 to December 2016, we evaluated 21 patients who underwent cardiovascular surgery at Dokkyo Medical Hospital. The proposal was approved by the Regional Ethics Committee of Dokkyo Medical University Hospital. The baseline characteristics of the patients are summarized in Table 1. The mean age was 70.4 ± 9.0 years, and the body mass index (BMI) was 26.0 ± 5.1 kg/m^2.

Fasting venous blood samples were obtained in tubes with and without EDTA sodium (1 mg/ml) and in polystyrene tubes without an anticoagulant. Serum and plasma were immediately separated by centrifugation at 3000 rpm at 4 °C for 10 min. Fasting blood sugar (FBS), total cholesterol (TC), hemoglobin A1c (HbA1c), brain natriuretic peptide (BNP), low-density lipoprotein (LDL)-cholesterol (LDL-C), high density lipoprotein (HDL)-cholesterol (HDL-C), non-HDL-C, triglycerides (TG), and estimated glomerular filtration rate (eGFR) were measured before the operation. The eGFR was calculated as follows.

eGFR (ml/min/1.73 m^2) = 194 × creatinine-1.094 × age − 0.287 (in men)

eGFR (ml/min/1.73 m^2) = 194 × creatinine-1.094 × age − 0.287 × 0.739 (in women)

All patients had medical treatment including statins (52.4%), β-blocking agents (42.9%), angiotensin receptor blockers (ARB)/angiotensin converting enzyme inhibitors (ACEI) (71.4%), diuretics (28.6%), and antidiabetic drugs (24%). Fasting blood glucose (FBS) and biochemical data were analyzed by routine chemical methods in the clinical laboratory of Dokkyo Medical University Hospital. Levels of the inflammatory marker, high-sensitivity C-reactive protein (hs-CRP), were measured by a latex-enhanced nephelometric immunoassay (N Latex CRP II and N Latex SAA, Dade Behring Ltd., Tokyo, Japan).

Table 1
Patient characteristics.

Number	21	Coronary artery disease, %	%
Male:Female	11:10	0-vessel disease	47.6
Age, y	70.4 ± 9.0	1-vessel disease	0
BMI, kg/m^2	26.0 ± 5.1	2-vessel disease	9.5
Risk factors, %	%	3-vessel disease	42.9
Hypertension	81.0	Cardiovascular surgery, %	%
Diabetes	33.3	CABG	52.4
Dyslipidemia	52.4	Valve replacement/repair	47.6
Smoking	4.7	Others	28.6
Hemodialysis	14.3	Drugs, %	%
NYHA class	2.3 ± 1.1	β-blockers	42.9
Laboratory blood data		Ca-blockers	47.6
HbA1c, %	6.0 ± 0.7	α-blockers	9.5
Fasting blood glucose, mg/dl	112 ± 31	ACE-I/ARB	71.4
eGFR	56 ± 27	Diuretics	28.6
Total cholesterol, mg/dl	173 ± 42	Statin	52.4
Triglycerides, mg/dl	125 ± 73	Sulfonylurea	14.3
HDL cholesterol, mg/dl	51 ± 15	α-GI	14.3
LDL cholesterol, mg/dl	98 ± 32	Biguanide	4.8
non-HDL cholesterol, mg/dl	117 ± 48	DPP4 inhibitor	9.5
hsCRP, mg/dl	0.28 ± 0.40	Insulin	4.8
BNP, pg/ml	466 ± 882		
Adiponectin, μg/ml	7.3 ± 7.3		
TNFα, pg/ml	3.2 ± 2.8		

The mean ± SD values are shown. NYHA, New York Heart Association; FBS, fasting blood sugar; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hsCRP, high-sensitivity C-reactive protein; BNP, brain natriuretic peptide; TNFα, tumor necrosis factor α; CABG, coronary artery bypass grafting; ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; α-GI, α-glucosidase inhibitor.

3.2. Blood collection for measurement of adiponectin and TNFα

To measure fasting serum adiponectin and TNFα levels, peripheral venous blood was drawn into pyrogen-free tubes without EDTA in 18 of 21 patients on the morning of the cardiovascular surgery. The serum was stored in aliquots at −80 °C for ELISA and Luminex assays.

3.3. Enzyme-linked immunosorbent assay (ELISA) and Luminex

Serum adiponectin level was measured by the Human Total Adiponectin/Acrp30 Quantikine ELISA Kit (R&D Systems, USA). The detection threshold was 0.24 ng/ml. Samples, reagents, and buffers were prepared according to the manufacturer's instructions. A Luminex assay was applied to determine serum levels of TNFα. The serum concentrations of TNFα were calculated by comparing the assay readings on a Luminex200™ system (Luminex Co., Austin TX, USA). The detection threshold was 1.2 pg/ml.

3.4. Adipose tissue sampling

Adipose tissue samples were obtained before the initiation of cardiovascular surgery as previously described [19]. Epicardial adipose tissue (EAT) samples (average 0.5 to 1.0 g) were taken near the proximal right coronary artery. The specimens were stored at −80 °C for later analysis.

3.5. Determination of FA composition

3.5.1. Serum FAs

Approximately 0.2 ml of serum sample and 2 ml of chloroform-methanol (2:1) solution (1 ml water, 666 μl methanol, and 333 μl chloroform) were placed in Pyrex centrifuge tubes, homogenized with a Polytron (PCU2-110, KINEMATICA GmbH, Switzerland), and then centrifuged at 3000 rpm for 10 min. An aliquot of the chloroform-methanol extract was transferred to another Pyrex tube and dried under a stream of nitrogen gas. The dried specimens were dissolved in 100 μl 0.4 M

potassium methoxide-methanol/14% boron trifluoride-methanol solution, and the FAs concentrations in the solution were measured with a gas chromatograph (Shimazu GC 17A, Kyoto, Japan) at SRL, Inc. The contents of FAs were expressed for each fatty acid as a percentage of the total fat extracted. These were then converted to masses by multiplying the lipid percentage by the mass of lipid per gram of tissue (μg/g).

3.5.2. FA composition of adipose tissue

Lipids were extracted from approximately 200–250 mg adipose tissue. The adipose tissue and 100 μl water and 1 ml of chloroform-methanol (2:1) solution (666 μl methanol and 333 μl chloroform) were placed in polypropylene centrifuge tubes, homogenized with a disperser (T10 basic ULTRA-TURRAX®, IKA®, Wilmington, DE, USA), and then centrifuged at 2000 rpm for 5 min. All of the supernatant of the chloroform-methanol extract in upper layer was transferred to another polypropylene tube. In addition, the remaining material and 1.52 ml of chloroform-methanol solution (800 μl methanol, 400 μl chloroform, and 320 μl water) were again placed in a polypropylene centrifuge tube, homogenized with the disperser, and then centrifuged at 2000 rpm for 5 min. All of the supernatant of the chloroform-methanol extract was added to the polypropylene tube containing the first extract, and mixed with 1.4 ml of chloroform solution (0.7 ml water and 0.7 ml chloroform), then centrifuged at 2000 rpm for 5 min. The lower part that contained lipids was transferred to a glass container, and kept at 37 °C overnight to evaporate the chloroform. The lipid was applied to a gas-liquid chromatograph (SRL, Inc.) as described above.

3.6. Statistical analysis

Data were analyzed using SPSS software. Baseline data are expressed as means ± standard deviation or percentages (categorical data). The comparison of mean variables between groups was carried out using independent sample *t*-test. Correlations were analyzed by Spearman's rank correlation method. Univariate and multivariate linear regression analyses were performed. Multivariate linear regression analyses with serum adiponectin levels as the dependent variable was performed to identify independently associated factors in the study subjects. From the results of the univariate analyses, TG, non-HDL, and BNP were analyzed as covariates in addition to age and BMI. A P value <0.05 was considered statistically significant.

4. Results

4.1. Characteristics of study patients

We assessed the presence of conventional risk factors such as diabetes (DM), hypertension (HT), hyperlipidemia (HL), and current smoking as shown in Table 1. Perioperative functional status was assessed with the New York Heart Association (NYHA) class. Six patients were class I, 6 were class 2, 5 were class 3, and 4 were class 4. Six patients underwent coronary artery bypass grafting (CABG), and 4 patients had valve replacement/repair (mitral valve replacement (MVR), tricuspid valve annuloplasty (TAP), and aortic valve replacement (AVR)). Five patients had CABG and valve replacement (AVR, TAP) combined. The subjects with acute coronary syndrome were excluded. The remaining 6 patients had aortic vascular surgery. As shown in Table 1, the fasting blood glucose was 112 ± 31 mg/dl, and HbA1c was 6.0 ± 0.7%. Seven patients had DM, and they were treated with sulfonylureas, α-glucosidase inhibitors (GI), biguanide, dipeptidyl peptidase IV (DPP4) inhibitors, or insulin. The blood total cholesterol level was 173 ± 42 mg/dl, and the HDL-C concentration was 51 ± 15 mg/dl. The LDL-C level was 117 ± 48 mg/dl, and the non-HDL-C level was 117 ± 48 mg/dl. Eleven of 21 patients were treated with a statin to lower their cholesterol. The fasting serum adiponectin concentration was 7.3 ± 7.3 μg/ml, and the serum TNFα level was 3.2 ± 2.8 pg/ml.

Table 2
Sex differences of fatty acid compositions of serum and epicardial fat.

	Serum μg/ml (%)		Epicardial fat μg/g (%)	
Fatty acids	Male	Female	Male	Female
C12:0	0.9 (0.043)	1.6 (0.065)	199.9 (0.22)	274.5 (0.31**)
C14:0	11.8 (0.56)	17.4 (0.73)	1714.9 (1.9)	2041.9 (2.2)
C14:1ω5	0.8 (0.034)	1.3 (0.053*)	229.2 (0.24)	288.8 (0.33)
C16:0	441.9 (21.9)	525.4 (21.8)	21,207.1 (23.4)	20,219.5 (22.2)
C16:1ω7	42.7 (2.0)	58.1 (2.4)	3920.4 (4.4)	5517.1 (6.2)
C18:0	131.6 (6.7)	159.1 (6.6)	2972 (3.4)	2884.5 (3.1)
C18:1ω9	422.0 (20.8)	490.3 (20.3)	41,341.3 (45.9)	42,130.3 (45.2)
C18:2ω6	516.2 (25.8)	630.1 (26.2)	12,990.2 (14.5)	13,602.8 (14.5)
C18:3ω6	5.3 (0.27)	8.4 (0.35)	93.4 (0.10)	100.9 (0.11)
C18:3ω3	16.3 (0.80)	20.1 (0.84)	937.5 (1.0)	1070.4 (1.1)
C20:0	5.1 (0.26)	6.1 (0.26)	90.7 (0.11)	91.8 (0.098)
C20:1ω9	4.0 (0.21)	5.0 (0.21)	1002.1 (1.1)	839.5 (0.90*)
C20:2ω6	4.8 (0.25)	5.9* (0.25)	385.3 (0.43)	317.5 (0.35*)
C20:3ω9	1.4 (0.061)	2.2 (0.090)	30.7 (0.032)	25.7 (0.029)
C20:3ω6	22.6 (1.1)	34.7* (1.4*)	255.7 (0.29)	288.4 (0.32)
C20:4ω6	136.9 (7.1)	175.7* (7.3)	513.0 (0.56)	458.6 (0.51)
C20:5ω3	65.5 (3.3)	56.3 (2.4)	165.5 (0.18)	184.5 (0.19)
C22:0	10.4 (0.53)	12.8 (0.54)	13.6 (0.016)	12.8 (0.012)
C22:1ω9	1.3 (0.033)	1.3 (0.038)	49.5 (0.055)	39.7 (0.042)
C22:4ω6	3.2 (0.17)	3.7 (0.16)	365.6 (0.40)	293.1 (0.33)
C22:5ω3	15.2 (0.75)	15.6 (0.65)	582.5 (0.63)	622.4 (0.67)
C24:0	10.4 (0.52)	12.8 (0.54)	11.7 (0.015)	9.0 (0.0090)
C22:6ω3	104.1 (5.3)	125.2 (5.2)	939.8 (1.1)	1191.6 (1.2)
C24:1ω9	29.3 (1.5)	33.5 (1.4)	17.7 (0.021)	16.1 (0.015)

The data are shown as mean value. Calculated with unpaired *t*-test.
* $P < 0.05$.
** $P < 0.01$ vs. male.

4.2. FA concentration/composition in serum lipids and EAT

Sex differences in the concentration (μg/g) and composition (mol%) of FAs in serum lipids and EAT are shown in Table 2. In serum lipids, the concentration (μg/g) of eicosadienoic acid (C20:2ω6), dihomo-γ-linolenic acid (C20:3ω6) and arachidonic acid (C20:4ω6) in females was significantly higher than that in males. The composition (mol %) of myristoleic acid (C14:1ω5) and dihomo-γ-linolenic acid (C20:3ω6) was also higher in females. In EAT lipids, no significant differences in the concentrations of FAs (μg/g) were observed between men and women. In EAT, a significant sex difference was observed in the composition (mol%) of lauric acid (C12:0), eicosenoic acid (C20:1ω9), and eicosadienoic acid (C20:2ω6) (all $P < 0.05$).

4.3. Correlation between serum adiponectin/TNFα concentrations and clinical data

The correlations between serum adiponectin/TNFα concentrations and the clinical data are shown in Table 3. No correlations were found

Table 3
Correlation matrix between serum TNFα/adiponectin concentration and clinical data.

	Adiponectin	TNFα
Clinical data	*r* value (*P*)	*r* value (*P*)
Age	0.275 (0.269)	−0.135 (0.592)
Sex	0.750 (0.768)	0.367 (0.134)
BMI	−0.360 (0.142)	−0.362 (0.140)
eGFR	−0.158 (0.531)	−0.604 (0.008**)
BNP	0.725 (0.001**)	0.474 (0.047*)
HDL-C	0.104 (0.680)	−0.584 (0.011*)
LDL-C	−0.327 (0.185)	−0.048 (0.851)
Non-HDL-C	−0.670 (0.002**)	−0.036 (0.886)
TG	−0.699 (0.001**)	−0.079 (0.755)
FBS	0.058 (0.820)	−0.067 (0.791)
HbA1C	0.044 (0.865)	0.144 (0.580)
hsCRP	0.160 (0.540)	0.218 (0.400)

* $P < 0.05$.
** $P < 0.01$.

between these adipokines and age, sex, or body mass index (BMI). However, the serum adiponectin concentration was negatively correlated with blood TG ($r = -0.699$, $P = 0.001$) and non-HDL-C ($r = -0.670$, $P = 0.002$), and positively correlated with BNP levels ($r = 0.725$, $P = 0.001$) (Table 3). The concentration of serum TNFα was negatively correlated with eGFR ($r = -0.604$, $P = 0.008$), and HDL-C concentration ($r = -0.584$, $P = 0.011$), and positively correlated with BNP levels ($r = 0.474$, $P = 0.047$).

4.4. Correlation between FA profiles in serum and EAT and serum adiponectin/TNFα concentrations

The correlations between serum adiponectin/TNFα concentrations and the concentrations of FAs in serum lipids and EAT are shown in Table 4. The serum adiponectin and TNFα level were not correlated with any FA component in serum. In contrast, univariate correlation analysis showed a positive correlation between the serum adiponectin level and the epicardial level of nervonic acid (C24:1ω9, $r = 0.525$, $P = 0.025$, Fig. 1Aa), but not linolenic acid (C18:3ω3, Fig. 1Ab). The serum adiponectin concentration tended to correlate with the concentration of erucic acid (C22:1ω9, $r = 0.414$, $P = 0.088$, Fig. 1Ac). In multiple regression analysis, the serum adiponectin level showed a positive association with epicardial nervonic acid concentration (C24:1ω9, β = 0.575, $P = 0.019$) after adjusting for age and BMI (Table 6A(1)).

The serum TNFα level was negatively correlated with linolenic acid (C18:3ω3, $r = -0.655$, $P = 0.003$, Fig. 1Ba), stearic acid (C18:0, $r = -0.629$, $P = 0.005$), lauric acid (C12:0, $r = -0.528$, $P = 0.024$, Fig. 1Bc), linoleic acid (C18:2ω6, $r = -0.497$, $P = 0.036$) and behenic (C22:0, $r = -0.48$, $P = 0.044$), total ω6 content ($r = -0.483$, $P = 0.042$), and PUFAs ($r = -0.505$, $P = 0.032$), but not with nervonic acid (C24:1ω9, Fig. 1Bb) in EAT (Table 2). In univariate regression analysis (Table 6B(1)), the serum TNFα concentration showed a negative association with epicardial linolenic acid (C18:3ω3, β = −0.561, $P = 0.015$), lauric acid (C12:0, β = −0.504, $P = 0.033$) and stearic acid (C18:0, β = −0.492, $P = 0.038$). Furthermore, multiple regression analysis (Table 6B(2)) showed that the serum TNFα concentration was positively associated with the epicardial linolenic acid (C18:3ω3) level (β = −0.575, $P = 0.015$), although there was no correlation with C18:3ω3, C12:0, and C18:0 levels.

4.5. Correlation between the FA profiles in EAT and the clinical data

The correlations between FA profiles in EAT and the clinical data are shown in Table 5. As shown in Table 5, the blood TG level was negatively correlated with the concentrations of monounsaturated FAs (MUFAs), erucic acid (C22:1ω9, $r = -0.455$, $P = 0.038$) and nervonic acid (C24:1ω9, $r = -0.585$, $P = 0.005$) in EAT. The non-HDL-C concentration was also correlated with nervonic acid (C24:1ω9, $r = -0.465$, $P = 0.034$) in EAT, and tended to correlate with erucic acid (C22:1ω9, $r = -0.391$, $P = 0.080$). The eGFR was only weakly correlated with eicosadienoic acid (C22:1ω9 C20:2ω6, $r = -0.443$, $P = 0.044$) in EAT, but not linolenic acid (C18:3ω3). The plasma BNP level was negatively correlated with the erucic acid (C22:1ω9, $r = -0.490$, $P = 0.024$) concentration in EAT (Table 5).

Since our results showed that blood TG and non-HDL levels were negatively correlated with the serum adiponectin concentration and the EAT concentration of nervonic acid (C24:1ω9), multiple regression

Table 4
Correlation matrix between the epicardial fatty acid density (μg/g) and the serum adiponectin/TNFα concentration.

	Epicardial fat		Serum	
	Adiponectin	TNFα	Adiponectin	TNFα
	r value (*P*)	*r* value (*P*)	*r* value (*P*)	*r* value (*P*)
C12:0	−0.005 (0.984)	−0.528 (0.024*)	−0.224 (0.372)	−0.024 (0.924)
C14:0	0.199 (0.428)	−0.249 (0.318)	−0.287 (0.248)	0.034 (0.892)
C14:1ω5	0.358 (0.145)	0.108 (0.669)	−0.104 (0.682)	0.125 (0.620)
C16:0	0.112 (0.657)	−0.323 (0.191)	−0.02 (0.938)	0.077 (0.762)
C16:1ω7	0.236 (0.345)	−0.137 (0.587)	0.115 (0.651)	0.216 (0.389)
C18:0	−0.115 (0.651)	−0.629 (0.005**)	−0.137 (0.587)	−0.091 (0.718)
C18:1ω9	0.036 (0.887)	−0.400 (0.100)	−0.162 (0.521)	0.222 (0.375)
C18:2ω6	−0.11 (0.663)	−0.497 (0.036*)	−0.046 (0.855)	0.147 (0.562)
C18:3ω6	−0.061 (0.81)	−0.426 (0.078)	−0.325 (0.188)	−0.39 (0.110)
C18:3ω3	−0.196 (0.435)	−0.655 (0.003**)	−0.455 (0.058)	0.048 (0.851)
C20:0	0.185 (0.463)	−0.366 (0.136)	−0.179 (0.478)	−0.348 (0.157)
C20:1ω9	−0.051 (0.842)	−0.222 (0.375)	0.21 (0.404)	0.152 (0.547)
C20:2ω6	−0.189 (0.453)	−0.024 (0.925)	−0.165 (0.512)	−0.048 (0.849)
C20:3ω9	0.115 (0.65)	0.033 (0.896)	−0.195 (0.512)	−0.183 (0.468)
C20:3ω6	−0.245 (0.328)	−0.157 (0.534)	−0.296 (0.233)	−0.117 (0.643)
C20:4ω6	0.042 (0.868)	−0.165 (0.521)	0.067 (0.791)	−0.319 (0.197)
C20:5ω3	0.104 (0.681)	−0.305 (0.219)	0.226 (0.367)	−0.266 (0.286)
C22:0	0.087 (0.732)	−0.48 (0.044*)	−0.238 (0.341)	−0.309 (0.213)
C22:1ω9	0.414 (0.088)	0.092 (0.718)	0.259 (0.299)	−0.174 (0.490)
C22:4ω6	−0.135 (0.593)	−0.061 (0.810)	−0.061 (0.810)	0.056 (0.826)
C22:5ω3	0.005 (0.984)	0.042 (0.868)	−0.104 (0.681)	0.011 (0.964)
C24:0	0.051 (0.841)	0.056 (0.826)	−0.129 (0.610)	−0.128 (0.611)
C22:6ω3	0.228 (0.363)	0.135 (0.593)	−0.034 (0.893)	−0.201 (0.425)
C24:1ω9	0.525 (0.025*)	−0.048 (0.849)	0.289 (0.245)	−0.149 (0.556)
Total ω3	0.005 (0.984)	−0.319 (0.197)	0.140 (0.578)	−0.158 (0.531)
Total ω6	−0.096 (0.705)	−0.483 (0.042*)	−0.073 (0.773)	0.015 (0.954)
SFA	0.123 (0.627)	−0.331 (0.180)	−0.001 (0.997)	−0.068 (0.790)
PUFA	−0.094 (0.711)	−0.505 (0.032*)	−0.030 (0.906)	0.280 (0.261)
MUFA	0.077 (0.760)	−0.392 (0.1080)	−0.133 (0.598)	0.238 (0.341)
C20:1ω9/C18:1ω9	0.125 (0.622)	0.465 (0.052)	0.375 (0.126)	−0.222 (0.375)
C22:1ω9/C20:1ω9	0.589 (0.010*)	0.222 (0.375)	0.080 (0.753)	0.181 (0.473)
C24:1ω9/C22:1ω9	0.286 (0.250)	−0.257 (0.304)	0.164 (0.651)	−0.317 (0.372)

SFAs, saturated fatty acids; PUFAs, polyunsaturated fatty acids; MUFA, monounsaturated fatty acids.
* $P < 0.05$.
** $P < 0.01$.

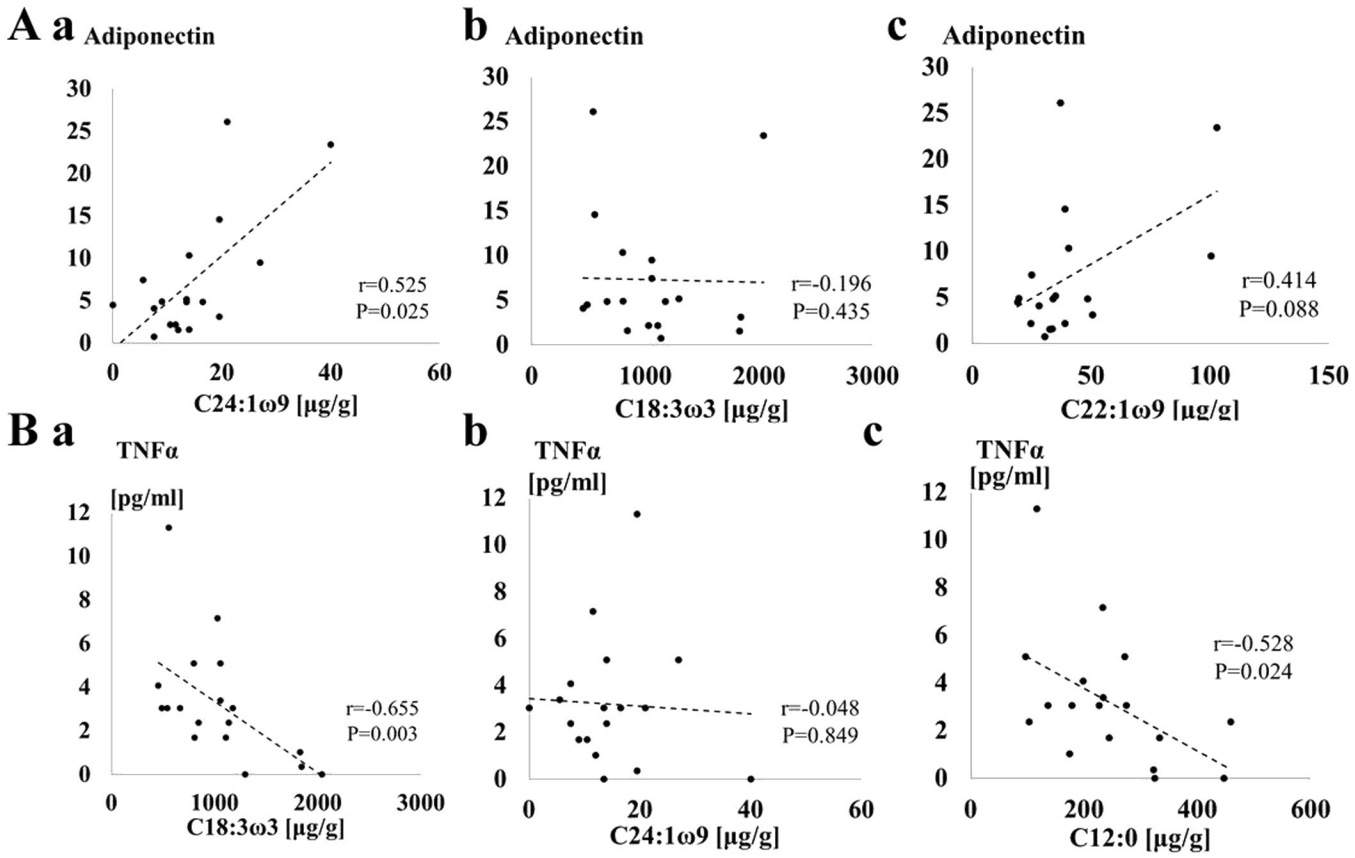

Fig. 1. Correlations between serum adiponectin/TNFα concentrations and the epicardial fatty acid concentrations. A: Relationships between the serum adiponectin concentration and epicardial nervonic acid (C24:1ω9, Aa), linolenic acid (C18:3ω3, Ab), and erucic acid (C22:1ω9, Ac). B: Relationships between the serum TNFα concentration and epicardial linolenic acid (C18:3ω3, Ba), nervonic acid (C24:1ω9, Bb), and lauric acid (C12:0, Bc).

analysis was performed to determine the relationship between the serum adiponectin concentration and the epicardial nervonic acid (C24:1ω9) concentration in EAT. As shown in Table 6A(2), the serum adiponectin level showed a positive association with the epicardial nervonic acid content (C24:1ω9, β = 0.446, $P = 0.024$) after controlling for blood TG, non-HDL, and BNP levels.

Table 5
Correlation matrix between the serum biochemical data and the epicardial fatty acid density(μg/g).

	TG	non-HDL-C	eGFR	BNP
	r value (*P*)	r value (*P*)	r value (*P*)	r value (*P*)
C12:0	0.244 (0.286)	−0.006 (0.978)	0.308 (0.175)	−0.242 (0.291)
C14:0	0.025 (0.915)	−0.225 (0.328)	−0.036 (0.876)	0.239 (0.297)
C14:1ω5	−0.005 (0.984)	−0.151 (0.515)	−0.243 (0.289)	0.273 (0.232)
C16:0	0.119 (0.608)	−0.287 (0.207)	−0.134 (0.563)	0.139 (0.548)
C16:1ω7	−0.086 (0.710)	−0.208 (0.366)	−0.016 (0.947)	0.318 (0.160)
C18:0	0.134 (0.561)	−0.266 (0.243)	−0.016 (0.947)	−0.052 (0.823)
C18:1ω9	0.025 (0.915)	−0.418 (0.059)	−0.136 (0.556)	0.073 (0.754)
C18:2ω6	0.061 (0.793)	−0.251 (0.273)	0.025 (0.915)	−0.019 (0.933)
C18:3ω6	0.147 (0.525)	−0.206 (0.369)	−0.077 (0.741)	−0.091 (0.695)
C18:3ω3	0.210 (0.362)	−0.184 (0.425)	0.157 (0.498)	−0.175 (0.449)
C20:0	−0.269 (0.238)	−0.187 (0.418)	0.085 (0.714)	0.074 (0.750)
C20:1ω9	0.057 (0.806)	−0.245 (0.284)	−0.403 (0.070)	0.069 (0.767)
C20:2ω6	0.108 (0.642)	−0.113 (0.626)	−0.443 (0.044*)	0.029 (0.902)
C20:3ω9	0.218 (0.343)	−0.214 (0.352)	−0.400 (0.073)	0.073 (0.754)
C20:3ω6	0.227 (0.322)	−0.045 (0.845)	−0.135 (0.559)	−0.065 (0.780)
C20:4ω6	0.099 (0.670)	−0.248 (0.278)	−0.296 (0.192)	0.061 (0.793)
C20:5ω3	−0.022 (0.924)	−0.277 (0.225)	−0.008 (0.973)	−0.019 (0.933)
C22:0	−0.137 (0.555)	−0.047 (0.838)	0.110 (0.636)	−0.060 (0.795)
C22:1ω9	−0.455 (0.038*)	−0.391 (0.080)	−0.196 (0.394)	0.490 (0.024*)
C22:4ω6	0.175 (0.447)	−0.069 (0.767)	−0.429 (0.053)	−0.001 (0.996)
C22:5ω3	−0.111 (0.632)	−0.305 (0.179)	−0.117 (0.614)	0.077 (0.741)
C24:0	−0.185 (0.421)	−0.080 (0.732)	−0.039 (0.866)	0.042 (0.855)
C22:6ω3	−0.285 (0.211)	−0.414 (0.062)	0.113 (0.626)	0.113 (0.626)
C24:1ω9	−0.585 (0.005**)	−0.465 (0.034*)	−0.112 (0.627)	−0.112 (0.627)

* $P < 0.05$.
** $P < 0.01$.

4.6. Correlation matrix between each epicardial FA concentration

The correlations between each FA concentration in EAT are shown in Table 7 and Fig. 2. The FAs that were positively correlated with the nervonic acid (C24:1ω9 concentration in EAT included two MUFAs, erucic acid (22:1ω9, $r = 0.906$, $P = 0.001$, Fig. 2Aa), and eicosenoic acid (C20:1ω9, $r = 0.486$, $P = 0.025$, Fig. 2Ab); and three long-chain saturated FAs (LCSFAs), eicosenoic acid (C20:0, $r = 0.745$, $P = 0.001$, Fig. 2Ac), behenic acid (C22:0, $r = 0.761$, $P = 0.001$, Fig. 2Ad), and lignoceric acid (C24:0, $r = 0.777$, $P = 0.001$, Fig. 2Ae). The nervonic acid concentration was weakly correlated with three ω3 FAs, eicosapentaenoic acid (C20:5ω3, $r = 0.458$, $P = 0.037$), docosapentaenoic acid (C22:5ω3, $r = 0.465$, $P = 0.034$), and docosahexaenoic acid (C22:6ω3, $r = 0.533$, $P = 0.013$, Fig. 2Af).

The FAs that were positively correlated with the linolenic acid (C18:3ω3) concentration in EAT included five ω6 FAs, linoleic acid (18:2ω6, $r = 0.926$, $P = 0.001$, Fig. 2Ba), dihomo-γ-linolenic acid (18:3ω6, $r = 0.698$, $P = 0.001$), eicosadienoic acid (C20:2ω6, $r = 0.549$, $P = 0.010$), eicosatrienoic acid (C20:3ω6, $r = 0.609$, $P = 0.003$), arachidonic acid (C20:4ω6, $r = 0.590$, $P = 0.005$); four SFAs, myristic acid (C14:0, $r = 0.598$, $P = 0.004$), palmitic acid (C16:0, $r = 0.774$, $P = 0.001$, Fig. 2Bb), stearic acid (C18:0, $r = 0.820$, $P = 0.001$), behenic acid (C20:0, $r = 0.435$, $P = 0.049$); and two MUFAs, oleic acid (C18:1ω9, $r = 0.832$, $P = 0.001$, Fig. 2Bc) and eicosenoic acid (C20:1ω9, $r = 0.611$, $P = 0.003$). The linoleic acid concentration was also positively correlated with three ω3 FAs, eicosapentaenoic acid (C20:5ω3, $r = 0.582$, $P = 0.006$), docosapentaenoic acid (C22:5ω3,

Table 6
A: Multiple linear regression analysis of adiponectin.
B: Univariate and multiple linear regression analysis of the serum TNFα concentration.

A.
1) Serum adiponectin concentration and C24:1ω9 content in pericardial fat

Dependent variable: serum adiponectin concentration

	Model 1*	Model 2*	Model 3*
Independent variable.	β-value (*P*)	β-value (*P*)	β-value (*P*)
C24:1ω9	**0.677 (0.002**)**	**0.592 (0.011*)**	**0.575 (0.019*)**

Model 1, unadjusted; Model 2, adjusted by Age; Model 3, adjusted by Age and BMI.

2) Serum adiponectin concentration and C24:1ω9 content in pericardial fat

Dependent variable: serum adiponectin concentration

	Model 1*	Model 2*	Model 3*	Model 4*
Independent variable	β-value (*P*)	β-value (*P*)	β-value (*P*)	β-value (*P*)
C24:1ω9	**0.677 (0.002**)**	**0.531 (0.009*)**	**0.434 (0.022*)**	**0.446 (0.024*)**

Model 1, unadjusted; Model 2, adjusted by TG; Model 3, adjusted by TG and non-HDL; Model 4, adjusted by TG, non-HDL, and BNP.

B.
1) Univariate linear regression analysis of TNFα and fatty acids

Dependent variable: serum TNFα concentration

Independent variable.	β-value (*P*)
C18:3ω3	**−0.561 (0.015*)**
C12:0	**−0.504 (0.033*)**
C18:0	**−0.492 (0.038*)**
C18:2ω6	−0.426 (0.078)
C22:0	−0.263 (0.291)

2) Multiple linear regression analysis of TNFα and fatty acids

Dependent variable: serum TNFα concentration

Independent variable (C18:3ω3, C12:0, C18:0)	β-value (*P*)
C18:3ω3	**−0.561 (0.015*)**
C12:0	N.D (0.162)
C18:0	N.D. (0.879)

N.D., not determined
* $P < 0.05$.

Table 7
Correlation matrix between C24:1ω9/C18:3ω3 content and the epicardial fatty acids density (μg/g).

	C24:1ω9	C18:3ω3
	r value (*P*)	r value (*P*)
C12:0	−0.059 (0.799)	0.516 (0.017)
C14:0	0.403 (0.070)	0.598 (0.004**)
C14:1ω5	0.308 (0.174)	0.183 (0.428)
C16:0	0.321 (0.156)	0.774 (0.001**)
C16:1ω7	0.146 (0.527)	0.189 (0.412)
C18:0	0.299 (0.188)	0.820 (0.001**)
C18:1ω9	0.343 (0.631)	0.832 (0.001**)
C18:2ω6	0.328 (0.147)	0.926 (0.001**)
C18:3ω6	0.263 (0.250)	0.698 (0.001**)
C18:3ω3	0.111 (0.631)	1
C20:0	0.745 (0.001**)	0.435 (0.049*)
C20:1ω9	0.486 (0.025*)	0.611 (0.003**)
C20:2ω6	0.293 (0.198)	0.549 (0.010*)
C20:3ω9	0.067 (0.771)	0.412 (0.064)
C20:3ω6	0.027 (0.909)	0.609 (0.003**)
C20:4ω6	0.178 (0.440)	0.590 (0.005**)
C20:5ω3	0.458 (0.037*)	0.582 (0.006**)
C22:0	0.761 (0.001**)	0.328 (0.146)
C22:1ω9	0.906 (0.001**)	0.248 (0.278)
C22:4ω6	−0.018 (0.940)	0.394 (0.077)
C22:5ω3	0.465 (0.034*)	0.505 (0.020*)
C24:0	0.777 (0.001**)	0.136 (0.556)
C22:6ω3	0.533 (0.013*)	0.508 (0.019*)
C24:1ω9	1	0.111 (0.631)

* $P < 0.05$.
** $P < 0.01$.

$r = 0.505$, $P = 0.020$), and docosahexaenoic acid (C22:6ω3, $r = 0.508$, $P = 0.019$).

5. Discussion

The major findings of the present study are as follows. (1) Serum concentration of TNFα was correlated with blood BNP, HDL-C and eGFR, whereas adiponectin was correlated with blood TG, non-HDL-C, and BNP. (2) The serum adiponectin and TNFα levels were not correlated with sex, or any FA concentration in serum lipids. (3) In multiple regression analysis, the serum adiponectin level showed a positive association with epicardial C24:1ω9 content after controlling for age and BMI ($\beta = 0.575$, $P = 0.019$), or TG, non-HDL-C, and BNP ($\beta = 0.446$, $P = 0.024$). (4) The serum TNFα level was negatively correlated with linolenic acid (C18:3ω3), stearic acid (C18:0), lauric acid (C12:0), linoleic acid (C18:2ω6) and behenic acid (C22:0). In multiple regression analysis, the serum TNFα concentration showed a positive association with the epicardial C18:3ω3 level ($\beta = -0.575$, $P = 0.015$). These results suggest that there are close relationships between epicardial FA profiles and serum levels of adiponectin and TNFα. Dietary therapy that targets FA profiles may be helpful to modulate inflammation.

Plasma concentrations of adiponectin are known to be lower in obesity, hypertension, hyperlipidemia, DM, and coronary atherosclerosis [20–22]. It has also been reported that the adiponectin mRNA expression in adipose tissue is decreased in obese ob/ob mice and obese humans [20], and is lower in patients with CAD [23–25]. In addition, studies have shown that plasma adiponectin levels are inversely correlated with TG and positively correlated with HDL-C, which suggest that

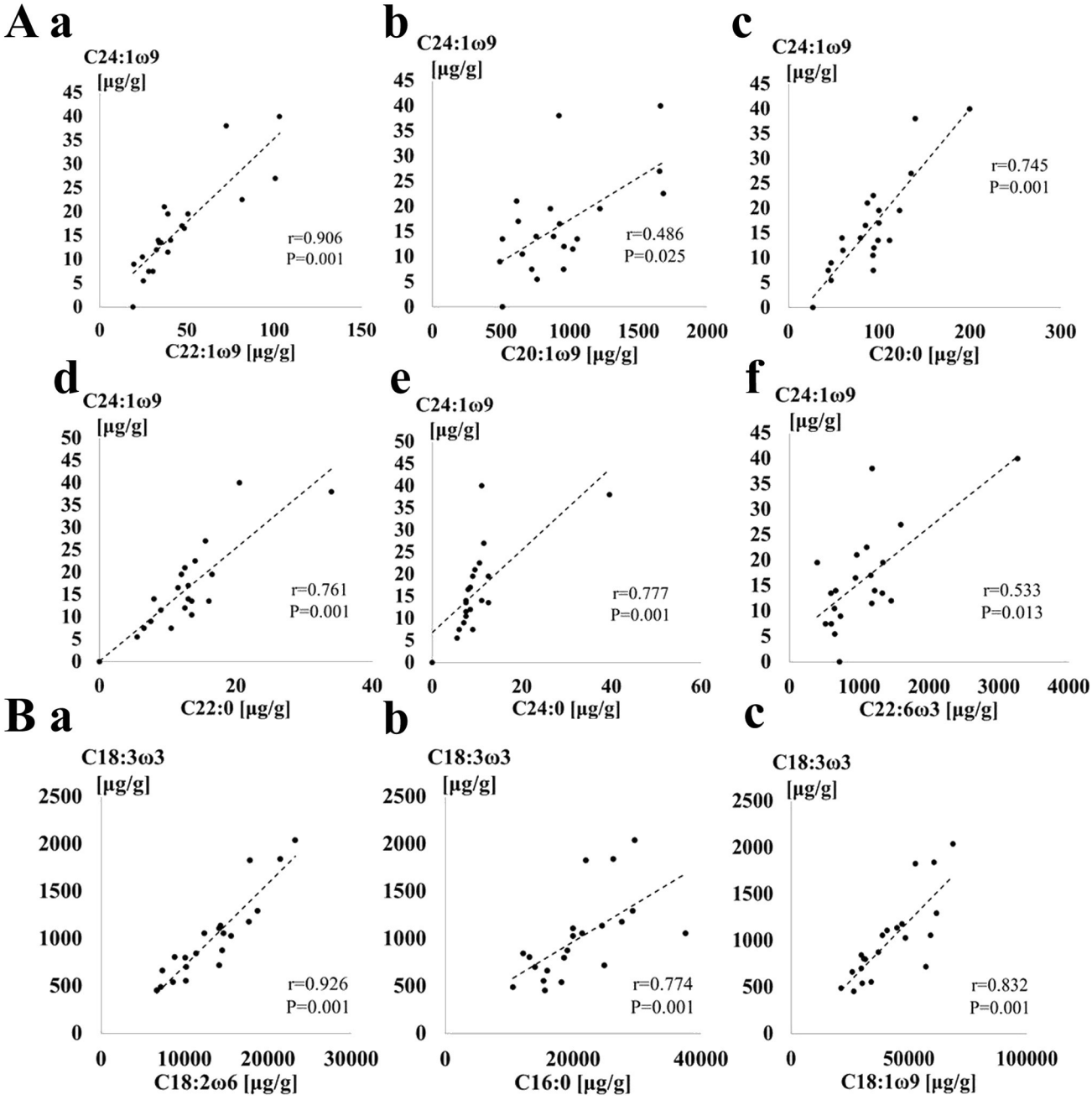

Fig. 2. Correlation matrix between each epicardial fatty acid concentration A: Relationships between the C24:1ω9 content and the content of the other fatty acids in EAT B: Relationships between the C18:3ω3 content and the content of other fatty acids in EAT.

adiponectin influences lipid metabolism [26,27]. In our study in patients undergoing cardiovascular surgery, the serum adiponectin concentration was negatively correlated with blood TG and non-HDL-C levels, though we could not exclude the influence of statin use, where 52% of patients were on statin therapy. In addition, adiponectin was negatively correlated with the serum BNP level. The relation might be limited to a small number of patients. However, the association of serum adiponectin level with the NYHA class and BNP levels has been reported in chronic heart failure (CHF) [28,29]. In contrast, TNFα, a cytokine produced mainly by macrophages, but also by adipocytes, causes inflammation under pathophysiological conditions such as chronic kidney disease (CKD) and heart failure. Several papers reported that the serum TNFα level is associated with lower eGFR, which is an independent risk factor for CKD [30], and an excellent predictor of mortality and morbidity in CHF [31]. Gormez et al. [32] also reported that TNFα gene expression in EAT increases prominently in CAD patients with metabolic syndrome, whereas adiponectin gene expression decreases significantly. In our study, the serum TNFα concentration was correlated with eGFR and the BNP concentration. It was also negatively correlated with the HDL-C concentration, which might be due to malnutrition that has been reported by Oe et al. in elderly patients with CKD [30].

A review of studies in humans showed that a fish-based diet and a ω3 FA-rich diet increase circulating adiponectin levels [33]. Also, rats fed with a soy protein diet showed higher plasma adiponectin concentrations than rats fed with a casein diet [34]. Furthermore, Itoh et al. [35] reported that treatment with eicosapentaenoic acid (C20:5ω3, EPA) increases adiponectin secretion in a rodent model of obesity and human obese patients. Yamamoto et al. [36] also showed that EPA treatment significantly increased plasma adiponectin level with an increase of serum EPA concentration in cardiac surgery patients with

hyperlipidemia. Thus, it is likely that a dietary pattern with a greater intake of ω3 PUFAs shows a clearer association with adiponectin concentration. The molecular mechanism by which ω3 PUFAs regulate adiponectin expression is still incompletely understood. A direct action of ω3 PUFAs on adipocytes has been proposed, where nuclear peroxisome proliferator-activated receptor γ (PPARγ) has been recognized as a critical regulator of adiponectin gene expression [37,38]. However, we found no relationship between the serum adiponectin concentration and the serum levels of ω3 PUFAs, suggesting that the direct effects of ω3 PUFAs did not largely contribute to serum adiponectin levels in our patients. However, our patients with CVD had a low serum level of EPA and DHA as reflected by the low EPA/AA (0.42 ± 0.23) and DHA/AA ratios (0.77 ± 0.21), and this is similar to what was previously described in patients with CAD [39]. Therefore, further studies using treatment with ω3 PUFAs are required to clarify the direct effects of ω3 PUFAs on adiponectin secretion.

Other FAs such as MUFAs may also affect the serum adiponectin level. In a study of morbidity obese patients, tissue MUFAs and SFAs were associated with an increase and decrease in adiponectin mRNA expression in EAT, respectively [40]. A cross-sectional study in healthy adults also showed a significant positive association between serum adiponectin and eicosenoic acid (C20:1ω9) in serum lipids [41]. In the present study, the serum adiponectin level was not correlated with any FA composition in serum lipids. However, we provided the first evidence of a positive correlation between the serum adiponectin level and nervonic acid content (C24:1ω9) in EAT. Therefore, it is likely that FAs measured in cells are a better reflection of the long-term dietary intake of FAs, because the turnover of FAs may be slower in cell membranes than in blood. Furthermore, changes in cellular FAs may also indicate alterations in FA metabolites and synthesis pathways in diseases such as metabolic syndrome and CVD [8,9]. In the present study, the blood TG level was negatively correlated with the concentration of MUFAs, erucic acid (C22:1ω9) and nervonic acid (C24:1ω9) in EAT, probably as a marker of disease risk in patients that required cardiovascular surgery. In multiple regression analysis, the adiponectin level showed a positive association with epicardial C24:1ω9 content after controlling for age and BMI, or TG, non-HDL-C, and BNP. The serum adiponectin concentration tended to correlate with the concentration of erucic acid (C22:1ω9) in EAT and was correlated with the C22:1ω9/C20:1ω9 ratio in EAT. These findings suggest that an increase of C20:1ω9 elongation to C22:1ω9 and the resultant increase of C24:1ω9 content may be linked to an increase of adiponectin secretion from EAT, but further studies are needed to clarify the underlying mechanisms.

It is well known that high fat feeding leads to decreased adiponectin secretion in rodents [42], and caloric restriction leads to higher circulating concentrations of adiponectin in mice and humans [43]. Interestingly, increased products of delta-9 desaturation and subsequent significant increases in C20 elongation products have been reported in rats with reduced food intake [44]. Therefore, it is speculated that reduced food intake leads to significant increases in C20 elongation products with a concomitant increase in adiponectin concentration. Nervonic acid was found to be negatively correlated with HOMA-IR, and it has been postulated to prevent obesity-related changes in metabolic parameters [45]. Roux-en-Y gastric bypass (RYGB) surgery is associated with weight loss, and improves insulin sensitivity and glucose homeostasis. RYGB also increases serum adiponectin and nervonic acid concentrations, and there is a reduction in co-morbidities such as DM and CAD, with a negative correlation between nervonic acid and HOMA-IR [46]. Furthermore, long-chain PUFAs may act as ligands for transcription factors like nuclear factor kappa B, and peroxisome-proliferator-activated receptors, which are involved in lipogenesis and FA oxidation [47]. The FA elongase, ELOVL3, is involved in the synthesis of C20-C24 saturated and monounsaturated very long-chain FAs (VLCFAs) in various tissues including adipose tissue. The ablation of ELOVL3 has been reported to reduce serum adiponectin levels with a decrease of saturated and monounsaturated C20 and C22 FAs [48]. In X-linked adrenoleukodystrophy (X-ALD), the most common progressive neurodegenerative disorder characterized by the accumulation of saturated and mono-unsaturated very long-chain fatty acids (VLCFA) and reduced peroxisomal VLCFA beta-oxidation activity. An increase in both saturated (C24:0, C26:0) and monounsaturated (C26:1ω9) FAs in plasma and adipose tissue is typically observed; the elevation of these VLCFAs in X-ALD is thought to result from increased elongation of the FA chain length. Treatment of X-ALD patients with erucic acid (C22:1ω9) results in normalization of C26:0 levels, as well as an increase of adiponectin secretion along with a significant increase in C24:1ω9, probably due to competition for the microsomal elongation system [48]. From these previous studies, adiponectin secretion by adipocytes appears to be linked to ELOVL3 expression. In the present study, nervonic acid (C24:1ω9) concentration in EAT was strongly correlated with the very long-chain MUFA, erucic acid (22:1ω9), and the LCSFAs, eicosenoic acid (C20:0), behenic acid (C22:0), and lignoceric acid (C24:0). Thus, it is likely that the FA elongase pathways involved in the synthesis of C20-C24 saturated and monounsaturated VLCFAs is linked to the nervonic acid pathway, and this linkage influences adiponectin secretion from EAT. However, further studies are needed to clarify the underlying mechanisms.

The present study showed no correlations between serum TNFα concentrations and age, sex, or BMI. In a previous paper [49], it was documented that in obese patients a high plasma levels of TNFα emerged, thus indicating a relationships between this cytokine and BMI. This discrepancy might be related to few patients analyzed in the present paper, and all characterized by similar BMI. Essential PUFAs, consisting of both ω6 and ω3 FAs, exert a broad range of effects on the cardiovascular system including modulation of the inflammatory response [3,50]. Evidence from both epidemiologic studies and clinical trials demonstrate substantial cardioprotective effects of α-linolenic acid [4,5]. In contrast, several studies showed that an increase in circulatory linoleic acid is associated with reduced inflammation and, cardiovascular risk, as well as improved outcomes [7]. Cho & Park [18] showed that serum TNFα level has a positive correlation with serum palmitic acid level and a negative correlation with serum docosahexaenoic acid (DHA) level. Ristic-Medic et al. [17] also reported that in patients on hemodialysis, the serum levels of TNFα negatively correlate with linoleic acid, DHA, and dihomo-γ-linolenic acid (DGLA). In the present study, the serum TNFα level was not significantly correlated with the FA composition in serum. However, the serum TNFα level was negatively correlated with PUFAs, linolenic acid (C18:3ω3), linoleic acid (C18:2ω6), stearic acid (C18:0), lauric acid (C12:0), and behenic acid (C22:0) levels in EAT. Furthermore, in multiple regression analysis, the serum TNFα concentration showed a negative correlation with the epicardial C18:3ω3 level. Thus, it is likely that linoleinic acid (C18:3ω3) decreases CVD risk by reducing inflammation. However, the linolenic acid (C18:3ω3) concentration in EAT was not correlated with eGFR and BNP, although the serum TNFα concentration was correlated with eGFR and BNP. Thus, it remains unclear whether FA profiles in EAT affect the pathophysiological conditions in patients with CKD and CHF. Furthermore, in the present study, the linolenic acid (C18:3ω3) concentration in EAT was strongly correlated with several FA components including MUFAs, SFAs, ω6 FAs, and ω3 FAs. This suggests that various FAs in EAT may interact to achieve a balance that subsequently decreases serum TNFα concentration in patients with CVD.

Some limitations of our study need consideration. The first weakness of the present study is a small number of patients in different setting of patients (i.e. CHF, CAD, and subjects undergoing valve repair/replacement) and the lacking control subjects. Therefore, additional studies in a larger number of patients are needed to clarify the relationship between epicardial FA profiles and serum adipokine in patients with CVD. Second, the local detailed analyses of adipokine mRNA and protein in EAT is required to clarify the relationship between EAT and the serum adipokine level. Finally, this study had a transversal design;

thus, the findings shown here are hypothesis generating. It will be necessary to demonstrate that epicardial FA profiles and serum adiponectin/TNFα concentrations can be modulated by ingestion of certain FAs or by changing the content of serum FAs.

6. Conclusions

The serum adiponectin and TNFα level were not correlated with the concentration of any FAs in serum lipids. However, the serum adiponectin level showed a positive correlation with epicardial C24:1ω9 content after controlling for age and BMI ($\beta = 0.575$, $P = 0.019$), or TG, non-HDL-C, and BNP ($\beta = 0.446$, $P = 0.024$). The serum TNFα level showed a positive correlation with the epicardial C18:3ω3 level ($\beta = -0.575$, $P = 0.015$). Thus, there is a close relationship between epicardial FA profiles and serum levels of adiponectin and TNFα. Dietary therapy that targets FA profiles may be helpful to modulate inflammation.

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Disclosures

The authors report no relationships that could be constructed as a conflict of interest.

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