

n-3 Polyunsaturated fatty acids and *trans* fatty acids in patients with the metabolic syndrome: a case–control study in Korea

Eunjeong Lee¹, Sangyeoup Lee² and Yongsoon Park^{1*}¹Department of Food and Nutrition, Hanyang University, Seoul, Korea²Center for Obesity Nutrition and Metabolism, Family Medicine Division, Pusan National University Hospital and Medical Research Institute, Pusan National University, Pusan, Korea

(Received 9 July 2007 – Revised 19 November 2007 – Accepted 13 December 2007 – First published online 28 February 2008)

n-3 and *Trans* fatty acids are considered to be the important modifiable factors of the metabolic syndrome. The purpose of this study was to test the hypothesis that lower *Omega*-3 fatty acids and/or higher *trans* fatty acids of erythrocytes (RBC) are associated with the risk of the metabolic syndrome. Forty-four patients with the metabolic syndrome, defined by three or more risk factors of the modified Adult Treatment Panel III criteria, and eighty-eight age- and sex-matched controls with less than three risk factors were recruited for the study. The mean age was 54.5 (SEM 0.8) years and 45 % of subjects were female. *Trans* fatty acids of RBC were higher in patients than controls (0.82 (SEM 0.04) v. 0.73 (SEM 0.03) %; *P*=0.043), while their *Omega*-3 indexes, the sum of EPA and DHA in RBC, did not significantly differ (11.78 (SEM 0.04) v. 12.39 (SEM 0.02) %). Multivariable-adjusted regression analysis showed positive association between *trans* fatty acid and risk of the metabolic syndrome (OR 7.13; 95 % CI 1.53, 33.27; *P*=0.013). Fasting serum insulin (7.9 (SEM 0.7) v. 4.9 (SEM 0.3) μ U/ml; *P*<0.001) and high sensitivity C-reactive protein (18 (SEM 3) v. 11 (SEM 17) mg/l; *P*=0.042) were also higher in patients than controls. There were significant positive relationships between *trans* fatty acids and waist circumference, and between *trans* fatty acids and BMI. The results suggested that RBC *trans* fatty acids might be a predictor of increased risk for the metabolic syndrome, but *n*-3 fatty acids were not in this population.

Metabolic syndrome: *Omega*-3 index: *Trans* fatty acid

The metabolic syndrome classically refers to a multi-component disorder that is characterized by abdominal obesity, hypertension, dyslipidaemia and impaired glucose tolerance⁽¹⁾. It is associated with a high risk of subsequent development of type 2 diabetes mellitus and CVD⁽²⁾. The prevalence of the metabolic syndrome defined by the Adult Treatment Panel III criteria was 23.7 % in the Third National Examination Survey in the United States, but its prevalence was found to differ among ethnic groups⁽³⁾. In Korea, the prevalence of the metabolic syndrome was 29.0 % in men and 16.8 % in women aged 30–80 years when using Asian–Pacific waist criteria⁽⁴⁾.

Serum fatty acid composition has been shown to predict the risk of diabetes⁽⁵⁾ and CVD⁽⁶⁾ and is related to components of the metabolic syndrome⁽⁷⁾. *n*-3 PUFA such as EPA (20 : 5*n*-3) and DHA (22 : 6*n*-3) have beneficial effects on improving lipid profiles^(8,9), reducing blood pressure⁽¹⁰⁾, improving insulin resistance^(8,9) and reducing markers of systemic inflammation⁽¹¹⁾. On the other hand, intake of *trans* fatty acids was inversely related with HDL-cholesterol^(12,13) and positively related to LDL-cholesterol⁽¹²⁾. *Trans* fatty acids also increased lipoprotein(a)⁽¹⁴⁾, TAG⁽¹⁵⁾ and insulin resistance⁽¹⁶⁾ and were associated with systemic inflammation and endothelial dysfunction^(17,18). Thus, *n*-3 and *trans* fatty acid tissue levels

may be a modifiable factor for the metabolic syndrome. The estimated dietary intake of fish is high in Korea⁽¹⁹⁾, so Korea is a particularly appropriate population to investigate the role of *n*-3 PUFA on the metabolic syndrome.

The purpose of the present study was to compare fatty acid composition of erythrocytes (RBC), plasma lipid profiles, high sensitivity C-reactive protein (hs-CRP), fasting glucose and insulin levels between Koreans with and without the metabolic syndrome. The *Omega*-3 index, a new blood test to measure EPA and DHA in RBC, as a good reflection of systemic *n*-3 PUFA status⁽²⁰⁾ was also compared.

Subjects and methods

Subjects

Subjects were recruited from patients visiting for regular health examinations at Pusan National University Hospital between August 2006 and January 2007. Cases consisted of patients diagnosed with the metabolic syndrome, defined by modified Adult Treatment Panel III criteria⁽¹⁾: presence of three or more of the following components: (1) a waist circumference \geq 90 cm in men and \geq 80 cm in women;

Abbreviations: ALT, alanine aminotransferase; HOMA-IR, homeostasis model assessment insulin resistance; hs-CRP, high sensitivity C-reactive protein; RBC, erythrocyte.

* **Corresponding author:** Professor Yongsoon Park, fax +82 2 2292 1226, email yongsoon@hanyang.ac.kr

(2) HDL-cholesterol levels < 400 mg/l in men and < 500 mg/l in women; (3) TAG level \geq 1500 mg/l; (4) systolic blood pressure \geq 130 mmHg or diastolic blood pressure \geq 85 mmHg or taking an anti-hypertensive medication; (5) fasting glucose levels \geq 1100 mg/l or taking an anti-diabetic medication. We selected age- and sex-matched controls with less than three risk factors of the modified Adult Treatment Panel III criteria. The current study was approved by the Institutional Review Board of Pusan National University Hospital and informed, written consent was obtained from all subjects before participating.

Procedures

Medical history and lists of medications such as oral hypoglycaemic agents, insulin, lipid-lowering, anti-hypertensive or oestrogen agents were obtained. Weekly total fish intakes were additionally obtained from all subjects. Subjects taking a supplement containing *n*-3 fatty acids were excluded. Height and body weight was measured using a digital scale with the subjects wearing a light gown. BMI was calculated as weight (kg)/height (m²). Using a tape measure, waist circumference was measured up to 0.1 cm unit at the midpoint between the lower costal margin and the iliac crest by well-trained examiners. Total body fat (%) was determined using a bioelectric impedance analyser (Inbody 3.0; Biospace Co., Ltd., Seoul, Korea). Resting blood pressure was measured using an automatic sphygmomanometer (BP203RV-II; Nippon Colin, Japan) after > 10 min at rest in a sitting position at 08.00 hours to 10.00 hours.

Subjects refrained from smoking or ingesting caffeine for 30 min prior to having their blood samples drawn. Fasting blood samples (> 12 h) were collected from the antecubital vein to determine serum concentrations of total cholesterol, TAG, HDL-cholesterol, fasting glucose, insulin, hs-CRP, alanine aminotransferase (ALT) and alkaline phosphatase. All biochemical analyses were carried out within 2 h of blood sampling, using an autoanalyser (model 7600-110; Hitachi Corp., Tokyo, Japan) and commercially available kits. LDL-cholesterol was calculated using the Friedewald formula⁽²¹⁾. Homeostasis model assessment insulin resistance (HOMA-IR) was calculated from the fasting concentration of insulin and glucose using the following formula⁽²²⁾:

$$\text{HOMA-IR} = (\text{fasting insulin } (\mu\text{U/ml}) \times \text{fasting glucose (mg/dl)})/405.$$

RBC were used for fatty acid analysis⁽²⁰⁾. Boron trifluoride methanol-benzene (B1252; Sigma-Aldrich, MO, USA) was added to RBC and samples were methylated for 10 min at 100°C. Fatty acid methyl esters were analysed by GC (Shimadzu 2010AF; Shimadzu Scientific Instrument, Japan) with a 100 mm SP2560 capillary column (Supelco; Bellefonte, PA, USA). Standard (GLC-727; Nu-Check Prep, Elysian, MN, USA) was used for identifying fatty acids and correcting inter-assay variation. In the standard, 18:1t peak was the mixture of 18:1n-12t, C18:1n-9t and 18:1n-7t, while 18:2n-6t peak contained 18:2n-6tt. The Omega-3 index was calculated as the sum of EPA and DHA in RBC. The control sample composed of pooled RBC and CV was 6.2%.

Statistical analysis

All data were expressed as mean with their standard errors of the mean. Subjects with and without the metabolic syndrome were compared using the independent *t* test, and correlation between variables was tested by partial correlation analysis after adjusting age and sex. OR were computed for specific fatty acids of interest using multivariable logistic regression analysis after adjusting for age, sex, height, weight, blood pressure, aspartate aminotransferase, ALT, hs-CRP, glucose, insulin, TAG, total cholesterol, HDL-cholesterol, LDL-cholesterol and waist circumference. Fatty acid values were categorized into quartiles based on the control data only and then second and third quartiles were combined. Statistical analysis was performed using SPSS 12.0 (SPSS Inc., Chicago, IL, USA). A *P* value of < 0.05 was considered statistically significant.

Results

General characteristics of subjects

The characteristics of subjects are shown in Table 1. Weight, BMI and waist circumference were significantly (*P*<0.001) higher in the patients with the metabolic syndrome than those without it. Waist circumference (95.5%) was the most common determinant risk factor in cases, and there were 63.6% of cases with three risk factors and 34.1% and 2.3% of cases with four and five risk factors, respectively. On the other hand, 52.4%, 23.8%, 23.8% of controls had one, none, two risk factor(s), respectively.

Metabolic parameters and fish intake

Diastolic and systolic blood pressure, ALT, hs-CRP, fasting blood glucose, serum insulin, HOMA-IR and TAG were significantly (*P*<0.05) higher in the patients with the metabolic syndrome than those without it (Table 2). On the other hand, HDL-cholesterol was significantly (*P*<0.001) lower in the patients than in controls. There was no significant difference in the weekly fish consumption between the patients and the control subjects (2.80 servings/week v. 3.11 servings/week). However, subjects with higher fish consumption had a greater Omega-3 index (Fig. 1).

Table 1. General characteristics of subjects†
(Mean values with their standard errors)

	Cases (<i>n</i> 44)		Controls (<i>n</i> 88)		<i>P</i> value
	Mean	SEM	Mean	SEM	
Males (<i>n</i>)	24		48		
Females (<i>n</i>)	20		40		
Age (years)	55.0	1.8	54.3	0.8	0.717
Height (cm)	162.5	1.3	163.3	0.9	0.583
Weight (kg)	72.6	1.7	65.9*	1.1	0.001
BMI (kg/m ²)	27.4	0.4	24.6*	0.3	<0.001
Total body fat (%)	27.6	0.7	26.2	0.7	0.162
Waist circumference (cm)	93.7	0.9	85.3*	0.8	<0.001

Mean values were significantly different: **P*<0.001 (independent *t* test).
† For details of subjects and procedures, see Subjects and methods.

Table 2. Metabolic parameters of subjects†
(Mean values with their standard errors)

	Cases (<i>n</i> 44)		Controls (<i>n</i> 88)		<i>P</i> value
	Mean	SEM	Mean	SEM	
Systolic blood pressure (mmHg)	132	2.4	124*	1.7	0.008
Diastolic blood pressure (mmHg)	80	1.6	76*	1.1	0.042
AST (IU/l)	28	2.3	24	1.5	0.121
ALT (IU/l)	34	3.3	25*	2.3	0.023
hs-CRP (mg/l)	18	3.0	11*	1.7	0.042
Fasting blood glucose (mg/l)	102	3.9	90**	1.3	< 0.001
Fasting serum insulin (μU/ml)	7.9	0.7	4.9**	0.3	< 0.001
HOMA-IR	2.0	0.2	1.1**	0.1	< 0.001
TAG (mg/dl)	1900	138	960**	36	< 0.001
Total cholesterol (mg/l)	2040	61	1950	30	0.141
HDL-cholesterol (mg/l)	470	17	550**	13	< 0.001
LDL-cholesterol (mg/l)	1200	54	1210	29	0.342

AST, aspartate aminotransferase; ALT, alanine aminotransferase; hs-CRP, high sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance, calculated from (fasting insulin (μU/ml) × fasting glucose (mg/dl))/405.

Mean values were significantly different: **P*<0.05; ***P*<0.001 (independent *t* test).

† For details of subjects and procedures, see Subjects and methods.

Erythrocyte fatty acid composition

Fatty acid composition of RBC is presented in Table 3. *Trans* fatty acids of RBC were significantly (*P*=0.043) higher in patients than controls, while the Omega-3 index did not differ between groups. Total PUFA was significantly lower, but 14:0, 16:1*n*-7, 18:1*n*-9c, 18:2*n*-6t, 18:3*n*-3 and MUFA were significantly (*P*<0.05) higher in the patients with than those without the metabolic syndrome. However, multivariable-adjusted regression analysis showed that only total *trans* fatty acids and 18:2*n*-6t were positively (*P*<0.05) associated with risk of the metabolic syndrome after adjusting for age, sex, height, weight, blood pressure, aspartate aminotransferase, ALT, hs-CRP, glucose, insulin, TAG, total cholesterol, HDL-cholesterol, LDL-cholesterol and waist circumference (Table 4). Subjects in the highest quartile of total *trans* fatty acids and 18:2*n*-6t had seven and fourteen times higher risk of the metabolic syndrome, even after adjusting for all confounding variables. Total *trans* fatty acids (*P*=0.01), 16:1*n*-7t (*P*=0.045) and 18:2*n*-6t (*P*=0.007), 14:0 (SFA; *P*<0.001) and MUFA were positively (*P*=0.014) related with waist circumference

(Table 5). BMI was positively associated with 14:0 (*P*<0.001) and MUFA (*P*=0.031), but negatively associated with PUFA (*P*=0.023) and *n*-6 PUFA (*P*=0.006). TAG levels were positively related with 14:0 (*P*<0.001), 18:1*n*-9c (*P*<0.001), 16:1 *n*-7t (*P*=0.009) and MUFA (*P*<0.001). C-reactive protein was positively related with SFA (*P*=0.023), but negatively with PUFA (*P*=0.004) and *n*-6 PUFA (*P*=0.036). In addition, 14:0 was positively associated with glucose (*P*=0.009), insulin (*P*<0.001) and HOMA-IR (*P*<0.001).

Table 3. Fatty acid composition of erythrocytes in subjects†
(Mean values with their standard errors of the mean)

% of total fatty acids	Cases		Controls		<i>P</i> value
	Mean	SEM	Mean	SEM	
14:0	0.42	0.02	0.34**	0.11	< 0.001
16:0	21.93	0.35	21.50	0.13	0.159
16:1 <i>n</i> -7t	0.14	0.01	0.12*	0.01	0.025
16:1 <i>n</i> -7c	5.40	0.17	5.09	0.16	0.228
18:0	15.12	0.23	15.30	0.16	0.525
18:1 <i>n</i> -9t	0.19	0.01	0.20	0.01	0.624
18:1 <i>n</i> -9c	11.95	0.19	11.25*	0.10	0.001
18:2 <i>n</i> -6t	0.50	0.03	0.41*	0.02	0.038
18:2 <i>n</i> -6c	8.66	0.20	9.10	0.16	0.104
18:3 <i>n</i> -6	0.09	0.01	0.07	0.01	0.092
18:3 <i>n</i> -3	0.26	0.02	0.20*	0.01	0.008
20:4 <i>n</i> -6	11.45	0.28	11.84	0.17	0.210
20:5 <i>n</i> -3	2.54	0.16	2.78	0.16	0.178
22:5 <i>n</i> -3	2.94	0.08	3.09	0.04	0.086
22:6 <i>n</i> -3	9.25	0.27	9.61	0.14	0.183
Total SFA	37.73	0.50	37.38	0.17	0.418
Total MUFA	17.74	0.20	16.73**	0.14	< 0.001
Total PUFA	38.75	0.61	40.16*	0.33	0.029
Total <i>n</i> -3 PUFA	15.00	0.43	15.68	0.23	0.129
Total <i>n</i> -6 PUFA	23.75	0.44	24.48	0.31	0.178
Omega-3 index	11.78	0.04	12.39	0.02	0.123
Total <i>trans</i> fatty acids	0.82	0.04	0.73*	0.03	0.043

Omega-3 index, DHA + EPA.

Mean values were significantly different: **P*<0.05; ***P*<0.001 (independent *t* test).

† For details of subjects and procedures, see Subjects and methods.

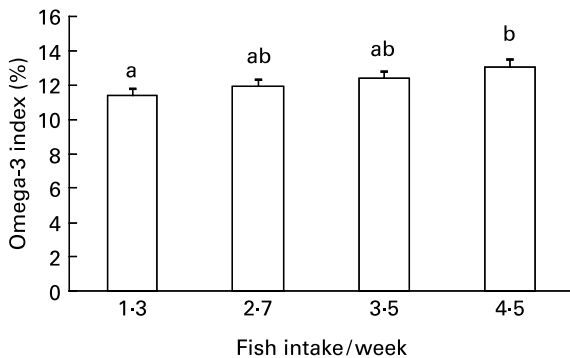


Fig. 1. Quartile of weekly fish intake and Omega-3 index (thirty-three in each). ^{a,b}Mean values with different letters were significantly different: *P*<0.05 (ANOVA with *post-hoc* by Tukey's test).

Table 4. OR and 95% CI associated with fatty acid composition and the risk of the metabolic syndrome by multivariable regression analysis*

	Quartile of RBC fatty acid concentration			P value
	1	2†	4	
14:0				
No. of cases/controls	14/22	14/44	16/22	
Blood fatty acid cut-off	≤0.28	0.28 < to ≤ 0.40	>0.40	
OR (95% CI)‡	1.00	0.40 (0.03, 4.92)	0.13 (0.01, 2.51)	0.171
16:1n-7t				
No. of cases/controls	10/22	16/44	18/22	
Blood fatty acid cut-off	≤0.09	0.09 < to ≤ 0.14	>0.14	
OR (95% CI)	1.00	2.30 (0.26, 20.70)	1.99 (0.24, 16.47)	0.585
18:1n-9c				
No. of cases/controls	4/22	20/44	20/22	
Blood fatty acid cut-off	≤10.54	10.54 < to ≤ 11.94	>11.94	
OR (95% CI)	1.00	2.55 (0.26, 24.98)	8.86 (0.60, 130.36)	0.107
18:2n-6tt				
No. of cases/controls	3/22	26/44	15/22	
Blood fatty acid cut-off	≤0.22	0.22 < to ≤ 0.58	>0.58	
OR (95% CI)	1.00	6.09 (1.08, 34.40)	14.22 (2.16, 93.51)	0.005
Total MUFA				
No. of cases/controls	4/22	17/44	23/22	
Blood fatty acid cut-off	≤15.95	15.95 < to ≤ 17.63	>17.63	
OR (95% CI)	1.00	3.78 (0.28, 50.93)	5.14 (0.36, 74.39)	0.284
Total trans fatty acids				
No. of cases/controls	4/22	25/44	15/22	
Blood fatty acid cut-off	≤0.50	0.5 < to ≤ 0.92	>0.92	
OR (95% CI)	1.00	3.58 (0.87, 14.73)	7.13 (1.53, 33.27)	0.013

RBC, erythrocytes.

* For details of subjects and procedures, see Subjects and methods.

† Second quartile + third quartile.

‡ OR was adjusted for age, sex, height, weight, blood pressure, aspartate aminotransferase, alanine aminotransferase, high sensitivity C-reactive protein, glucose, insulin, TAG, total cholesterol, HDL-cholesterol, LDL-cholesterol and waist circumference.

Discussion

In the present study, we observed that RBC *trans* fatty acids were higher in patients with than without the metabolic syndrome and associated with risk of the metabolic syndrome after adjusting for age, sex, height, weight, blood pressure, aspartate aminotransferase, ALT, hs-CRP, glucose, insulin, TAG, total cholesterol, HDL-cholesterol, LDL-cholesterol and waist circumference. However, the Omega-3 index might not be associated with the metabolic syndrome in this population. Total MUFA, PUFA, *trans* fatty acid, 14:0, 16:1n-7t, 18:1n-9c, 18:2n-6tt and 18:3n-3 differed between patients

and controls, but after adjusting for all metabolic parameters only *trans* fatty acids and 18:2n-6tt were significantly different. Correlation analysis showed that RBC fatty acids were significantly related with mostly TAG, waist circumference and BMI, which might be the major factors accounted for the OR analysis.

Trans fatty acids are positively related with lipoprotein(a)⁽¹⁴⁾, systemic inflammation, endothelial dysfunction and plasma TAG levels⁽¹⁵⁾ and strongly associated with CVD^(18,23). Thus, it is possible that *trans* fatty acids play a role in the development of the metabolic syndrome and type 2 diabetes mellitus^(17,18). In a large prospective study of

Table 5. Correlation between fatty acid composition and metabolic parameters by partial correlation analysis†

	Hs-CRP (mg/l)	Glucose (mg/l)	Insulin (μU/ml)	HOMA-IR	TAG (mg/l)	Waist circumference (cm)	BMI
Total SFA	0.199*	0.054	0.049	0.057	-0.019	-0.064	0.115
14:0	0.161	0.229*	0.316**	0.346**	0.314**	0.321**	0.342**
Total MUFA	0.073	0.089	0.061	0.074	0.341**	0.216*	0.189*
18:1n-9c	-0.019	-0.100	0.056	-0.006	0.366**	0.083	0.080
Total PUFA	-0.254*	-0.134	-0.085	-0.104	-0.089	-0.079	-0.199*
Total n-6 PUFA	-0.184*	-0.149	-0.109	-0.127	-0.004	-0.116	-0.242*
Total trans fatty acids	0.091	0.040	0.003	-0.001	0.082	0.226*	0.151
16:1n-7t	0.118	0.013	0.101	0.092	0.228*	0.176*	0.130
18:2n-6t	0.087	0.012	0.031	0.008	0.080	0.234*	0.166

hs-CRP, high sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance, calculated from (fasting insulin (μU/ml) × fasting glucose (mg/dl))/405.

All values were significantly different: *P<0.05; **P<0.001 (partial correlation coefficient adjusted by age and sex).

† For details of subjects and procedures, see Subjects and methods.

women, intake of trans fatty acids was positively associated with type 2 diabetes⁽²⁴⁾. Sun *et al.*⁽²³⁾ reported that the risk for CHD among subjects in the highest quartile of erythrocyte trans fatty acid content was three times higher than that of subjects in the lowest quartile. Troisi *et al.*⁽¹²⁾ reported that intake of trans fatty acids was positively related to LDL-cholesterol and inversely related to HDL-cholesterol. Meta-analysis of Mensink *et al.*⁽¹³⁾ showed that trans fatty acids raised the serum total cholesterol:HDL ratio. Koh-Banerjee *et al.*⁽²⁵⁾ reported a positive association between intake of trans fatty acids and abdominal adiposity in the prospective cohort. Kavanagh *et al.*⁽²⁶⁾ also showed that trans fatty acids were an independent factor for abdominal fat deposition and impaired insulin sensitivity, both of which are linked to the metabolic syndrome.

Recently, the Korean Food and Drug Administration reported that the average intake of trans fat was estimated as 0.7% total energy or 1.54 g trans fat per d, which was lower than the WHO recommendation of less than 1% total energy⁽²⁷⁾. The average trans fatty acid of the current subjects was 0.73% in RBC, which was also lower than those of the USA (2.0%) and Denmark (1.2%)^(27,28). Although RBC trans fatty acids were relatively low in all subjects, they were different between patients and controls, possibly suggesting the association between trans fatty acid and the metabolic syndrome.

Interestingly, we found higher 18:2n-6tt and lower 18:1t in RBC of subjects as compared with those of Westerners. The main contributors for trans 18:2n-6tt are vegetable oils (maize oil, soyabean oil, sesame oil), mayonnaise and canned tuna, while dairy products such as cheese, milk, ice cream, sour cream and butter contain 18:1t^(29,30). It is known that consumption of dairy products is relatively low among Koreans. Thus, this discrepancy can be explained by the dietary pattern between Koreans and Westerners.

Studies have suggested that the genetic regulatory effects of PUFA may protect against the adverse signs of the metabolic syndrome by mediating insulin and carbohydrate control of lipogenic and glycolytic genes, inhibiting fat storage and promoting fat oxidation^(31,32). Tai *et al.*⁽³³⁾ found significant gene-nutrient interactions between the PPAR- α gene-leucine to valine (PPAR α -L162V) polymorphism and PUFA intake on plasma TAG and apo C-III concentrations in a Framingham Heart Study. In addition, the fatty acid composition in patients with insulin resistance and the metabolic syndrome is typically characterized by high levels of SFA and low levels of PUFA⁽³⁴⁾. The present study did not find a difference in PUFA between patients and controls, but PUFA was negatively correlated with hs-CRP and BMI.

n-3 PUFA have beneficial effects in reducing plasma TAG⁽⁸⁾, blood pressure⁽¹²⁾ and markers of systemic inflammation such as hs-CRP⁽¹³⁾ and also in improving the lipoprotein profile by decreasing the fraction of atherogenic small dense LDL-cholesterol and improving insulin resistance^(8,9). However, studies showed that EPA and DHA were not significantly different in patients with the metabolic syndrome^(34,35). We also found no significant association between fish consumption and the metabolic syndrome, and between the Omega-3 index and the metabolic syndrome. In the present study, average fish consumption was three servings per week and was greater than that of US residents, who consumed less than one serving/week^(36,37). Although the Omega-3

index was not significantly (11.8 (SEM 2.5) % v. 12.4 (SEM 1.9) %, $P=0.123$) different between patients with and without the metabolic syndrome, it was higher than in US residents and Europeans (4%). The current subjects consumed more than the American Heart Association recommendation of fish⁽³⁸⁾ and had a higher Omega-3 index than the recommended value of 8–10% to prevent CHD⁽²⁰⁾. This may be explained by the fact that Pusan is a major port for the Korean fish market; thus, most people may have higher fish consumption than the general population. The average Omega-3 index was 4% in the USA⁽³⁹⁾ and Europe⁽⁴⁰⁾; thus, Korea is a particularly appropriate population to investigate the role of n-3 PUFA.

In conclusion, this study showed that RBC trans fatty acid content was higher in patients with the metabolic syndrome compared with controls and was associated with risk of the metabolic syndrome after adjusting for age, sex and metabolic parameters. Although causal relationships cannot be ascertained in such a case-control study, these findings have suggested that trans fatty acids might contribute to the metabolic syndrome phenotype. Even though there was no relationship with the Omega-3 index, further studies in populations with lower fish intake regarding the relationship between fish intake and the metabolic syndrome should be undertaken.

Acknowledgements

This work was supported by the Korea Science and Engineering Foundation (KOSEF) grant founded by the Korean government (MOST) (R01-2007-000-10 613-0).

References

1. National Cholesterol Education Program (2001) Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *JAMA* **295**, 2486–2497.
2. Grundy SM, Cleeman JL, Daniels SR, *et al.* (2005) Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* **112**, 2735–2752.
3. Ford ES, Giles WS & Dietz WH (2002) Prevalence of the metabolic syndromes among US adults: findings from the Third National Health and Nutrition Examination Survey. *JAMA* **287**, 356–359.
4. Oh JY, Hong YS & Sung YA (2004) Prevalence and factor analysis of metabolic syndromes in urban Korean population. *Diabetes Care* **27**, 2027–2032.
5. Wang L, Folsom AR, Zheng ZJ, Pankow JS & Eckfeldt JH (2003) Plasma fatty acid composition and incidence of diabetes in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Clin Nutr* **78**, 91–98.
6. Wang L, Folsom AR & Eckfeldt JH (2003) Plasma fatty acid composition and incidence of coronary heart disease in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. *Nutr Metab Cardiovasc Dis* **13**, 256–266.
7. Tremblay AJ, Despres JP, Piche ME, *et al.* (2004) Associations between the fatty acid content of triglyceride, visceral adipose tissue accumulation, and components of the insulin resistance syndrome. *Metabolism* **53**, 310–317.

8. Mori TA, Burke V, Puddey IB, *et al.* (2000) Purified eicosapentaenoic and docosahexaenoic acids have differential effects on serum lipids and lipoproteins, LDL particle size, glucose, and insulin in mildly hyperlipidemic men. *Am J Clin Nutr* **71**, 1085–1094.
9. Holness MJ, Greenwood G, Smith N & Sugden M (2003) Diabetogenic impact of long chain omega-3 acids on pancreatic beta-cell function and the regulation of endogenous glucose production. *Endocrinology* **144**, 3958–3968.
10. Prisco D, Paniccio R, Bandinelli B, *et al.* (1998) Effect of medium-term supplementation with a moderate dose of *n*-3 polyunsaturated fatty acids on blood pressure in mild hypertensive patients. *Thromb Res* **91**, 103–112.
11. Harris WS, Park YS & Isley WL (2003) Cardiovascular disease and long-chain omega-3 fatty acids. *Curr Opin Lipidol* **14**, 9–14.
12. Troisi R, Willett WC & Weiss ST (1992) Trans-fatty acid intake in relation to serum lipid concentrations in adult men. *Am J Clin Nutr* **56**, 1019–1024.
13. Mensink RP, Zock PL, Kester AD & Katan MB (2003) Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr* **77**, 1146–1155.
14. Nestel P, Noakes M, Belling B, *et al.* (1992) Plasma lipoprotein lipid and Lp[a] changes with substitution of elaidic acid for oleic acid in the diet. *J Lipid Res* **33**, 1029–1036.
15. Katan MB, Zock PL & Mensink RP (1995) Trans fatty acids and their effects on lipoproteins in humans. *Annu Rev Nutr* **15**, 473–493.
16. Hu FB, Manson JE, Stampfer MJ, *et al.* (2001) Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* **345**, 790–797.
17. Lopez-Garcia E, Schulze MB, Meigs JB, *et al.* (2005) Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. *J Nutr* **135**, 562–566.
18. Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ & Willett WC (2006) Trans fatty acids and cardiovascular disease. *N Engl J Med* **354**, 1601–1613.
19. Nogi A, Yang J, Li L, Yamasaki M, Watanabe M, Hashimoto M & Shiwaku K (2007) Plasma *n*-3 polyunsaturated fatty acid and cardiovascular disease risk factors in Japanese, Korean and Mongolian workers. *J Occup Health* **49**, 205–216.
20. Harris WS & Von Schacky C (2004) The omega-3 index: a new risk factor for death from coronary heart disease? *Prev Med* **39**, 212–220.
21. Friedwald WT, Levy RI & Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* **18**, 499–502.
22. Matthews DR, Hosker JP, Rudenski AS, *et al.* (2003) Impact of glucose intolerance and insulin resistance on cardiac structure and function: sex-related differences in the Framingham Heart Study. *Circulation* **107**, 448–454.
23. Sun Q, Ma J, Campos H, Hankinson SE, *et al.* (2007) A prospective study of trans fatty acids in erythrocytes and risk of coronary heart disease. *Circulation* **115**, 1858–1865.
24. Salmeron J, Hu FB, Manson JE, *et al.* (2001) Dietary fat intake and risk of type 2 diabetes in women. *Am J Clin Nutr* **73**, 1019–1022.
25. Koh-Banerjee P, Chu N, Spiegelman D, Rosner B, Colditz G, Willett W & Rim E (2003) Prospective study of the association of changes in dietary intake, physical activity, alcohol consumption, and smoking with 9-y gain in waist circumference among 16587 US men. *Am J Clin Nutr* **78**, 719–727.
26. Kavanagh K, Jones KL, Sawyer J, Kelley K, Carr JJ, Wagner JD & Rudel LL (2007) Trans fat diet induces abdominal obesity and changes in insulin sensitivity in monkeys. *Obesity* **15**, 1675–1684.
27. Hunter JE (2006) Dietary trans fatty acids: review of recent human studies and food industry response. *Lipids* **41**, 967–992.
28. Dyerberg J, Eskesen DC, Andersen PW, *et al.* (2004) Effects of trans- and *n*-3 unsaturated fatty acids on cardiovascular risk markers in healthy males. An 8 weeks dietary intervention study. *Eur J Clin Nutr* **58**, 1062–1070.
29. Karabulut I (2007) Fatty acid composition of frequently consumed foods in Turkey with special emphasis on trans fatty acids. *Int J Food Sci Nutr* **1**, 1–10.
30. Baylin A, Siles X, Donovan-Palmer A, Fernandez X & Campos H (2007) Fatty acid composition of Costa Rican foods including trans fatty acid content. *J Food Comp Analysis* **20**, 182–192.
31. Clarke SD (2000) Polyunsaturated fatty acid regulation of gene transcription: a mechanism to improve energy balance and insulin resistance. *Br J Nutr* **8**, S59–S66.
32. Clarke SD (2001) Polyunsaturated fatty acid regulation of gene transcription a molecular mechanism to improve the metabolic syndrome. *J Nutr* **131**, 1129–1132.
33. Tai ES, Corella D, Demissie S, *et al.* (2005) Polyunsaturated fatty acids interact with the PPARA-L162V polymorphism to affect plasma triglyceride and apolipoprotein C-III concentrations in the Framingham Heart Study. *J Nutr* **135**, 397–403.
34. Warensjö E, Sundström J, Lind L & Vessby B (2006) Factor analysis of fatty acids in serum lipids as a measure of dietary fat quality in relation to the metabolic syndrome in men. *Am J Clin Nutr* **84**, 442–448.
35. Klein-Platat C, Draï J, Oujaa M, Schlienger JL & Simon C (2005) Plasma fatty acid composition is associated with the metabolic syndrome and low-grade inflammation in overweight adolescents. *Am J Clin Nutr* **82**, 1178–1184.
36. Sands SA, Reid KJ, Windsor SL & Harris WS (2005) The impact of age, body mass index, and fish intake on the EPA and DHA content of human erythrocytes. *Lipids* **40**, 343–347.
37. Mozaffarian D, Bryson CL, Lemaitre RN, *et al.* (2005) Fish intake and risk of incident heart failure. *J Am Coll Cardiol* **45**, 2015–2021.
38. Kris-Etherton PM, Harris WS, Appel LJ & American Heart Association Nutrition Committee (2002) Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* **106**, 2747–2757.
39. Albert CM, Campos H, Stampfer MJ, *et al.* (2002) Blood levels of long-chain *n*-3 fatty acids and the risk of sudden death. *N Engl J Med* **346**, 1113–1118.
40. GISSI-Prevenzione Investigators (1999) Dietary supplementation with *n*-3 polyunsaturated fatty acids and vitamin E in 11,324 patients with myocardial infarction: results of the GISSI-Prevenzione trial. *Lancet* **354**, 447–455.