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Lower intake of saturated fatty acids is associated with persistently higher arterial stiffness in patients with type 2 diabetes

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ABSTRACT

Aims/Introduction: There are few studies to investigate the relationship between macronutrients and longitudinal changes in arterial stiffness in patients with type 2 diabetes mellitus. This exploratory study sought to determine whether macronutrients were correlated with increased arterial stiffness independently of conventional atherosclerotic risk factors.

Materials and Methods: The study participants comprised 733 type 2 diabetes outpatients who had no apparent history of cardiovascular diseases. The dietary schedule was assessed with a validated, brief, self-administered diet history questionnaire. At baseline and at years 2 and 5, brachial-ankle pulse wave velocity was measured. A multivariable linear mixed-effects model was used to determine the predictive values of macronutrients and atherosclerotic risk factors for longitudinal changes in brachial-ankle pulse wave velocity.

Results: There was a significant increase in brachial-ankle pulse wave velocity values over the 5-year follow-up period. In a multivariable linear mixed-effects model that adjusted for age and sex, lower saturated fatty acid intake was significantly correlated with persistently higher brachial-ankle pulse wave velocity, independently of other atherosclerotic risk factors. Lower intake of dairy products in particular showed this correlation.

Conclusions: Our data showed that lower saturated fatty acids intake was correlated with persistently higher brachial-ankle pulse wave velocity in type 2 diabetes patients. Among food sources of saturated fatty acids, lower dairy products specifically were correlated with elevated brachial-ankle pulse wave velocity. This might be because the consumption of dairy products in Japan is much lower than in Western countries.

INTRODUCTION

Type 2 diabetes mellitus patients are at higher risk of cardiovascular disease (CVD)[1]. While lifestyle modification is a fundamental aspect of diabetes care, a recent clinical trial found that CVD in obese patients with type 2 diabetes was not decreased by lifestyle interventions focused either on calorie restriction, such as fat-restricted diets, or on increased physical activity[2]. With respect to this, greater attention should be paid to the quantity and/or quality of diets rather than to approaches based on calorie restriction.

Nutrition therapy is the most challenging part of lifestyle management for patients with type 2 diabetes. The American Diabetes Association's current clinical practice guideline dealing with nutrition therapy recommends a balanced variety of foods with appropriate portion sizes to achieve metabolic goals and delay or prevent diabetic complications, such as CVD[3]. Regarding the general population in particular, the guideline recommends limiting the intake of saturated fatty acids (SFAs) and cholesterol, and consuming higher amounts of unsaturated fatty

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acids, such as polyunsaturated fatty acids (PUFAs) and/or monounsaturated fatty acids (MUFAs), to delay or prevent CVD. The Japan Atherosclerosis Society Guidelines make similar recommendations[4]. In the general population, a previous meta-analysis showed that a reduction of SFA intake was associated with a 17% reduction in the risk of CVD, and replacing SFAs with PUFAs, but not MUFAs, was correlated with a 27% risk reduction[5]. In that study, the degree of CVD risk reduction was associated with the degree of reduced SFA intake, and the degree of increased PUFA and MUFA intake. In contrast, another meta-analysis showed that a higher intake of SFAs was not associated with coronary heart disease[6]. In addition, several cohort studies, but not all, showed an inverse relationship between the intake of SFAs and the risk of CVD[7–9]. Thus, the association between the types and amounts of dietary fat consumed and the risk of CVD is a matter of debate in the general population. In contrast, patients with type 2 diabetes have altered carbohydrate and lipid metabolism, and an abnormal prothrombotic profile. Thus, recommendations should be largely based on findings from individuals with this condition. In this regard, a very recent study showed that lower total mortality and CVD-related mortality in patients with type 2 diabetes was associated with higher PUFA intake, but was not correlated with carbohydrate or SFA intake[10]. However, the association between macronutrients, including specific dietary fats and their food sources, and cardiovascular health remains largely unclarified in patients with type 2 diabetes.

Type 2 diabetes patients have increased arterial stiffness[11]. The brachial-ankle pulse wave velocity (baPWV) is a non-invasive, convenient technique to assess arterial stiffness, and it serves as a surrogate marker for CVD in patients with type 2 diabetes[12,13]. Recent cross-sectional studies showed that increased arterial stiffness was related to conventional risk factors in patients with type 2 diabetes[11,14,15]. Conversely, a cross-sectional study showed that a diet rich in carbohydrates and MUFAs was correlated with reduced arterial stiffness in patients with type 2 diabetes[16]. However, little is known about the association between other macronutrients, including specific dietary fats, and longitudinal changes in arterial stiffness in this population.

As it is highly beneficial to identify modifiable risk factors for atherosclerosis, we carried out an exploratory study to assess the association between dietary macronutrients and longitudinal changes in arterial stiffness in type 2 diabetes patients who were free of apparent CVD. Our goal was to gain a better understanding of the optimal types and proportions of dietary nutrients for maintaining cardiovascular health.

METHODS

Study participants

The participants were enrolled from the outpatient clinic of three medical institutions, as previously described[17–19]. The study design, and inclusion and exclusion criteria were published previously[17–20]. The inclusion criteria were: (i) diagnosis of type 2 diabetes; (ii) aged ≥25 and < 70 years; and (iii) provision of written informed consent for study participation. The exclusion criteria were: (i) type 1 or secondary diabetes; (ii) presence of severe infectious disease or severe trauma before or after surgery; (iii) history of myocardial infarction, angina pectoris, cerebral stroke or cerebral infarction; (iv) chronic renal failure requiring hemodialysis; (v) liver cirrhosis; (vi) moderate or severe heart failure (New York Heart Association stage III or higher); and (8) active malignancy and so on. Among 736 outpatients enrolled between June 2013 and January 2014, two patients withdrew their consent.

The protocol of this study was approved by the ethics committee of Juntendo University Hospital. It conformed to the provision of the Declaration of Helsinki. Written informed consent was obtained from all participates. The study was registered on the University Hospital Medical Information Network Clinical Trials Registry (UMIN000010932).

Questionnaire survey

Each patient's dietary schedule during the month preceding the initiation of the study was assessed with the validated brief-type self-administered diet history questionnaire (BDHQ). Daily caloric intake was estimated using an ad hoc computer algorithm for the 56 foods and beverages[21]. The BDHQ has good validity[22] and test–retest reliability[23].

Physical activity level was assessed with the International Physical Activity Questionnaire[24].

Data collection

Blood and urine samples were collected from participants once per year. Glycated hemoglobin (HbA1c), lipid levels, and renal and liver function tests were measured with standard techniques.

Measurement of baPWV

At baseline and at 2 and 5 years, baPWV was measured with use of an automatic waveform analyzer (BP-203RPE form; Colin Medical Technology, Komaki, Japan), as described previously[17]. Briefly, measurement was carried out in the supine position after 5-min bed rest. Cuffs for occlusion and monitoring were placed snugly around both arms and both ankles. The pressure waveforms were then recorded simultaneously from the brachial arteries by the oscillometric method. All scans were carried out by well-trained observer in each institution. A previous study confirmed the high reproducibility of baPWV measurements[25]. Participants with an ankle-brachial index ≤0.90 were considered to have peripheral artery disease, and the baPWV data of these individuals were excluded from this study.

Statistical analysis

Results are expressed as the mean ± standard deviation for continuous variables, and as the number (proportion) for categorical variables. Longitudinal baPWV was analyzed using a

linear mixed-effects model that included time, patient characteristics, dietary schedule and possible atherosclerotic risk factors at baseline as fixed effects, and patient as a random effect to account for the inherent correlation of repeated measures on the same individual over time. We added the interaction term between time and each covariate in the mixed-effects model. The correlation between SFAs and possible food sources of SFAs was evaluated using Spearman's correlation coefficients. Statistical tests were two-sided, with a 5% significance level. All analyses were carried out using SAS software version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Patients characteristics

The data of 734 patients at baseline were available. A total of 99 patients were lost to follow up, as previously described[20]. One patient did not complete the BDHQ. Accordingly, the baseline characteristics of the remaining 733 type 2 diabetes patients are shown in Table 1. The mean total energy intake was 1,719 kcal/day, and the mean percentages of total energy intake from carbohydrates, proteins, fats, SFAs, MUFAs and PUFAs were 53%, 15%, 23%,7%, 9% and 6%, respectively.

Modest, but significant, increases were seen in HbA1c levels over a period of 5 years of follow up. Also, modest but significant changes occurred in body mass index (BMI), systolic and diastolic blood pressure (BP), high-density lipoprotein cholesterol and triglycerides. Also, baPWV significantly increased. All of the above data were previously described [20].

Table 1 | Patient demographic and background characteristics at baseline

	Baseline
Age (years)	57.8 ± 8.6
Male (%)	463 (63.1)
Body mass index (kg/m^2)	24.6 ± 4.0
Systolic blood pressure (mmHg)	127 ± 14
Diastolic blood pressure (mmHg)	77 ± 10
HbA1c (%)	7.0 ± 1.0
HbA1c (mmol/mol)	52.6 ± 10.9
Total cholesterol (mg/dL)	185 ± 28
HDL cholesterol (mg/dL)	59 ± 14
Triglyceride (mg/dL)	125 ± 91
Uric acid (mg/dL)	5.5 ± 1.2
Urinary albumin excretion (mg/g creatinine)	69 ± 233
Insulin therapy (*n*/%)	80 (11)
Hypotensive drugs (*n*/%)	348 (47.7)
Lipid-lowering drugs (*n*/%)	444 (60.9)
Antiplatelet agents (*n*/%)	24 (3.3)
Physical activity (METs·h/week)	43.7 ± 73.9
Current smoker (yes)	177 (24.1)
Alcohol consumption (g/day)	12.4 ± 21.6
Total caloric intake (kcal/day)	1,719 ± 585
Carbohydrate intake (g)	226 ± 76
Carbohydrate intake (% energy)	53 ± 9
Protein intake (g)	66.6 ± 29.3
Protein intake (% energy)	15 ± 4
Fat intake (g)	48.7 ± 20.4
Fat intake (% energy)	25 ± 6
SFA intake (g)	12.8 ± 6.1
SFA intake (% energy)	7 ± 2
MUFA intake (g)	17.2 ± 8.1
MUFA intake (% energy)	9 ± 2
PUFA intake (g)	12.4 ± 5.4
PUFA intake (% energy)	6 ± 2
baPWV (cm/s)	1545 ± 280

Total n = 733. Data are the mean ± standard deviation or the number of patients. *P*-values are derived using a mixed-effects model with repeated measures. % energy, the percentage of estimated daily total energy intake; baPWV, brachial-ankle pulse wave velocity; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; MUFA, monounsaturated fatty acid; PUFAs, polyunsaturated fatty acid; SFA, saturated fatty acid.

Relationships between longitudinal baPWV and saturated fatty acid

We used a linear mixed-effects model to examine the relationship between longitudinal baPWV, which was adjusted for age and sex, and each dietary nutrient. There was no significant interaction between time and each nutrient for longitudinal baPWV throughout the study period (Table 2 and data not shown). However, this analysis showed that a lower percentage of total calories from SFAs was significantly correlated with persistent higher baPWV (Table 2). Other nutrients were not significantly correlated with persistent higher baPWV (data not shown).

Next, we investigated whether dietary nutrients in type 2 diabetes patients were correlated with persistent increased arterial stiffness independently of conventional atherosclerotic risk factors. In a multivariable linear mixed-effects model that included both dietary nutrients and conventional atherosclerotic risk factors, a lower percentage of total calories from SFAs was still an independent predictive factor for persistently higher baPWV, in addition to older age, longer estimated duration of type 2 diabetes, lower BMI, higher systolic BP, lower high-density lipoprotein level, lower urinary albumin excretion and use of antiplatelet agents (Table 3).

We divided participants into three groups based on tertiles of the percentage of total calories from SFAs to further investigate their relationships. When replacing continuous variables with categorical variables, participants who consumed ≥7.4% of total calories from SFAs had persistent lower baPWV than those who consumed <5.8% of total calories from SFAs and those who consumed ≥5.8% and <7.4% of total calories from SFAs in the multivariable linear mixed-effects model (Table S1). These data might suggest linear relationships between saturated fatty acids intake and changes in baPWV.

Relationships between longitudinal baPWV and dairy products

Possible food sources of SFAs include dairy products, meats, processed meats, eggs, sweets, butter and nuts. However, as in

Table 2 | Relationships between longitudinal brachial-ankle pulse wave velocity adjusted for age and sex, and saturated fatty acid (%) using a linear mixed-effects model

Regression coefficient			
Effect	Level	Estimate (Standard error)	*P* value
Intercept		778.4 (74.2)	<0.001
Time	1 year	20.3 (5.8)	0.0005
SFA intake (% energy)	1 unit	−1,614.1 (520.8)	0.002
Time × SFA intake		40.6 (85.3)	0.63
Age	1 year	14.8 (1.1)	<0.001
Sex	Male vs female	24.3 (18.9)	0.20

The longitudinal brachial-ankle pulse wave velocity was analyzed with a linear mixed-effects model including time, saturated fatty acid (SFA), their interaction, and age and sex at baseline as fixed effects, and patient as a random effect. % energy, the percentage of estimated daily total energy intake.

Table 3 | Predictors of longitudinal brachial-ankle pulse wave velocity during 5-year follow up

	Comparison	Regression coefficient		*P*-value
Intercept		227.7	145.3	0.12
Time	1 year	20.0.0	5.8	0.0006
SFA intake (% energy)	1 unit	−1163.1	497.5	0.02
Time × SFA intake (% energy)		49.0	85.3	0.57
Age	1 year	12.5	1.1	<.0001
Sex	Male vs female	−|4.9	21.7	0.82
Physical activity	1 METs·h/week	−0.1	0.1	0.42
Current smoker	Former smoker vs Current smoker	−6.7	23.7	0.78
	Never-smoker vs Current smoker	−11.9	23.1	0.61
Estimated duration of diabetes	1 year	3.0	1.3	0.02
Body mass index	1 kg/m^2	−12.5	2.5	<.0001
Systolic BP	1 mmHg	5.7	0.6	<.0001
HbA1c	1 mmol/mol	1.9	0.9	0.03
Total cholesterol	1 mg/dL	0.5	0.4	0.12
HDL cholesterol	1 mg/dL	−1.4	0.7	0.05
Triglyceride: log-transformed value	1 mg/dL	0.2	0.1	0.12
Insulin therapy	Yes vs no	12.3	29.2	0.68
Antihypertension drugs	Yes vs no	−3.9	17.8	0.83
Antihyperlipidemia drugs	Yes vs no	−22.9	17.5	0.19
Antiplatelet drugs	Yes vs no	108.1	47.4	0.02
Diabetic retinopathy	Yes vs no	16.6	18.4	0.37
Diabetic neuropathy	Yes vs no	−23.0	19.5	0.24
Urinary albumin excretion	mg/g creatinine	−34.9	18.1	0.05
Uric acid	1 mg/dL	22.3	7.7	0.004

Longitudinal brachial-ankle pulse wave velocity was analyzed with a linear mixed-effects model using time and lifestyle habits, and possible atherosclerotic risk factors at baseline as fixed effects, and patient as a random effect. % energy, the percentage of estimated daily total energy intake; BP, blood pressure; HDL, high-density lipoprotein; SFA, saturated fatty acid.

a general Japanese population[22], the study patients consumed almost no butter or nuts (Table 4). We evaluated the correlations between the baseline intakes of SFAs and their possible food sources, and found correlations between SFAs and each of the aforementioned food sources, excluding butter and nuts (Table 4). Next, we investigated whether different food sources of SFAs were correlated with persistent increased arterial stiffness independent of conventional atherosclerotic risk factors. Lower intake of dairy products was an independent predictive factor for persistently higher baPWV, along with older age, longer estimated duration of type 2 diabetes, higher HbA1c level, lower BMI, higher systolic BP, higher uric acid level, lower urinary albumin excretion and use of antiplatelet agents (Table 5).

Table 4 | Correlation between saturated fatty acid and possible food sources of saturated fatty acids at baseline

	g/day (mean ± SD)	Correlation coefficient (95% confidence interval)	*P*-value
Dairy products	118 ± 98	0.59 (0.54–0.63)	<0.001
Meats	52.2 ± 39.9	0.54 (0.49–0.59)	<0.001
Processed meats	8.4 ± 8.8	0.47 (0.41–0.52)	<0.001
Eggs	30.0 ± 24.4	0.41 (0.35–0.47)	<0.001
Sweets	37.1 ± 35.8	0.47 (0.42–0.53)	<0.001
Butter	0 ± 0	–	–
Nuts	0 ± 0	–	–

Total (n = 733). By Spearman's rank correlation analysis. CI, confidence interval.

DISCUSSION

This might be the first prospective longitudinal study to investigate the intake of SFAs or their possible food sources in relation to arterial stiffness in type 2 diabetes patients. We showed that lower intake of SFAs, particularly in the form of dairy products, correlated with persistent higher baPWV in type 2 diabetes patients, in this exploratory study.

Higher intake of SFAs is considered to undermine cardiovascular health, because these compounds negatively affect cholesterol metabolism[26]. Impaired health of the vascular wall is an important contributor to CVD. Indeed, published guidelines recommend limiting the intake of SFAs to delay or prevent CVD[4].

In contrast, Japanese type 2 diabetes patients appear to consume far lower amounts of SFAs than American patients[10]. The National Health and Nutrition Examination Survey in 2017 reported that Japanese people aged ≥20 years consumed approximately 17.6 g of SFAs per day[27]. The consumption of SFAs in the present study was slightly lower, at 12.8 g per day, but was very similar to that observed in patients with type 2 diabetes in other studies. The Fukuoka Diabetes Registry used the BDHQ questionnaire to determine that patients with type 2 diabetes consumed approximately 12.3 g of SFAs per day[28]. In addition, the Japan Diabetes Complications Study reported that SFA intake was likely to be approximately 8 g per day according to the Food Frequency Questionnaire[29]. Thus, the amount of daily SFA intake in Japanese patients with type 2 diabetes is likely to be lower than that in the general population. The exact reason for this difference is currently unclear. However, one

Table 5 | Predictors of longitudinal brachial-ankle pulse wave velocity during 5-year follow up

	Comparison	Regression coefficient		*P*-value
Intercept		179.1	141.1	0.204
Time	1 year	21.2	2.48	<0.0001
Dairy products intake	g	−0.28	0.10	0.006
Time × dairy product intake		0.02	0.07	0.30
Age	1 year	13.0	1.13	<0.0001
Sex	Male vs female	5.1	22.0	0.83
Physical activity	1 METs·h/week	−0.07	0.12	0.57
Current smoker	Former smoker vs current smoker	−5.75	23.7	0.81
	Never-smoker vs current smoker	−8.60	23.1	0.71
Estimated duration of diabetes	1 year	3.11	1.28	0.016
Body mass index	1 kg/m^2	−13.1	2.51	<0.0001
Systolic BP	1 mmHg	5.70	0.63	<0.0001
HbA1c	1 mmol/mol	1.84	0.86	0.03
Total cholesterol	1 mg/dL	0.46	0.35	0.19
HDL cholesterol	1 mg/dL	−1.19	0.73	0.10
Triglyceride	1 mg/dL	0.21	0.12	0.07
Insulin therapy	Yes vs no	9.77	29.2	0.74
Antihypertension drugs	Yes vs no	−2.55	17.7	0.88
Antihyperlipidemia drugs	Yes vs no	−24.8	17.5	0.16
Antiplatelet drugs	Yes vs no	112.7	47.2	0.02
Diabetic retinopathy	Yes vs no	14.8	18.4	0.42
Diabetic neuropathy	Yes vs no	−24.25	19.5	0.21
Urinary albumin excretion	mg/g creatinine	−36.2	18.1	0.045
Uric acid	1 mg/dL	22.3	7.7	0.004
Total caloric intake	1 kcal	−0.01	0.02	0.55

Longitudinal brachial-ankle pulse wave velocity was analyzed with a linear mixed-effects model using time and dairy product intake at baseline as fixed effects, and patient as a random effect. BP, blood pressure; HDL, high-density lipoprotein.

possibility is that patients with type 2 diabetes pay more attention to their SFA intake as a result of their healthcare providers' advice. Also, the diet histories of overweight individuals might underreport SFA intake[30], as patients with type 2 diabetes have been shown to have a higher BMI than the general population in Japan.

Intriguingly, a cohort study carried out in Japan showed that SFA intake was inversely correlated with the incidence of lacunar infarction and deep intraparenchymal hemorrhage in a Japanese general population[31]. In that study, participants had a relatively low SFA intake averaging 16.3 g per day. The authors found that SFA intake of approximately 20 g per day was the threshold for the inverse association between SFA intake and stroke. Consistent with this finding, the SFA intake in the present study participants was 12.8 g per day, and we showed that a lower percentage of calories from SFAs was associated with a persistently higher baPWV. In addition, we found the linear relationships between saturated fatty acids intake and changes in baPWV (Table S1). This result might be due largely to relatively low SFA intake averaging 17.0 g per day, even in highest tertile group.

It is possible that the association between lower SFA intake and persistently higher baPWV partly depends on the food sources of SFAs. Interestingly, of the several food sources we examined, only dairy products were associated with persistently higher baPWV independently of other possible risk factors for atherosclerosis. The consumption of dairy products has been considered to be detrimental to cardiovascular health, because their SFA content might increase low-density lipoprotein cholesterol levels[32]. However, one of two recent studies showed an inverse relationship between dairy product intake and arterial stiffness in the general population[33,34]. Furthermore, recent studies, but not all, showed that dairy product intake was inversely associated with the risk of CVD and mortality in the general population[35–37]. In contrast, there are limited data on whether type 2 diabetes patients who are susceptible to CVD[1] are more likely to develop atherosclerosis if they consume fewer dairy products, which is the case in the general population. In this regard, this is the first longitudinal study to show that lower intake of dairy products was correlated with persistent higher baPWV in type 2 diabetes patients. This association seemed to be affected by the basal intake of dairy products. Indeed, compared with no intake of dairy products, consumption of more than two servings per day was associated with a lower risk of mortality and CVD in low- and middle-income countries where dairy product consumption is low[36]. As dairy product consumption in Japan is much lower than that in Western countries[38,39], increasing the amount of SFA intake from dairy products might not be detrimental in terms of preventing the progression of atherosclerosis in Japan.

Although it remains largely unknown how lower intake of dairy products induces arterial stiffness, we propose the following possibilities. First, bioactive peptides, such as casein-derived casokinins and whey-derived lactokinins, are capable of inhibiting the action of angiotensin-converting enzyme[40], therefore reducing BP and increasing endothelium-dependent vasorelaxation. In addition, recent studies reported that intake of dairy products had a beneficial effect on BP[41,42]. This effect might explain why a higher intake of dairy products has a beneficial effect on arterial stiffness. In fact, lower intake of dairy products was modestly, but significantly, correlated with higher systolic BP in the present study ($r = -0.10$, $P = 0.006$). Second, dairy products are rich in magnesium, potassium and calcium. These minerals might have an impact on BP and arterial stiffness through their effects on vasodilator production[43]. Ultimately, the combined effects of a variety of biologically active components are likely to underlie the mechanism by which lower intake of dairy products induces arterial stiffness, as dairy products are recognized as providing a broad spectrum of essential nutrients for human health[43].

There were certain limitations of the present study. First, the observational cohort study design made it impossible to evaluate whether dietary habits had a causal relationship with arterial stiffness. Second, we evaluated dietary intake by self-reported questionnaires, although this method has been successfully used in many studies. The results might have been influenced by social desirability and recall bias. Although weighed food records are more accurate for assessing an individual's diet, they are not practical in studies with large sample sizes because of the need for extensive training of the participants. We evaluated just 56 food and beverage items, which might have led to an underestimation of energy intake. Thus, we used energy-adjusted nutrition intake to deal with this potential confounder[44]. In addition, we did not investigate whether specific dairy products, such as milk, cheese or yogurt, were associated with the progression of arterial stiffness, although we did find that that lower intake of dairy products overall was associated with persistently higher baPWV. Third, we carried out analysis using dietary intake data collected only at baseline. In the future study, the changes in dietary intake when investigating the relationship between macronutrients and atherosclerosis should be considered. At least, there were no major changes in intake of each micronutrient at 2 years from baseline (Table S2). Fourth, although we adjusted for several atherosclerotic risk factors including BP, residual confounding factors, such as changes in BP and HbA1c over time, could not be ruled out. Finally, our findings could be applied to Japanese patients with type 2 diabetes, as there are regional and race differences in dietary consumption patterns and macronutrient intakes.

In conclusion, the present data showed that lower intake of SFAs, and particularly reduced consumption of dairy products, was correlated with persistent higher baPWV in Japanese type 2 diabetes patients. However, consuming very high amounts of SFAs should be avoided, as SFA intake was shown to be positively correlated with the onset of myocardial infarction[31]. The present data suggest that too great a restriction on the intake of SFAs might have a negative effect on CVD in Japanese type 2 diabetes patients. In addition, the present

results show that different food sources of SFAs might have varying effects on cardiovascular health.

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DISCLOSURE

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1 | Predictors of longitudinal brachial-ankle pulse wave velocity during 5-year follow up.

Table S2 | Macronutrients intake of each group at baseline and 2-year follow up.