Coffee consumption and glucose tolerance status in middle-aged Japanese men

T. Yamaji¹ · T. Mizoue¹ · S. Tabata² · S. Ogawa² · K. Yamaguchi³ · E. Shimizu³ · M. Mineshita³ · S. Kono¹

¹ Department of Preventive Medicine, Faculty of Medical Sciences, Kyushu University, Fukuoka, Japan

² Self-Defense Forces Fukuoka Hospital, Kasuga-shi, Japan

³ Self-Defense Forces Kumamoto Hospital, Kumamoto, Japan

Abstract

Aims/hypothesis. Several studies have reported that coffee has a protective effect against the development of type 2 diabetes. However, few of these studies used the standard glucose tolerance test to diagnose type 2 diabetes. The aim of this study was to investigate the relationship between coffee and green tea consumption and glucose tolerance status as determined using a 75-g OGTT.

Methods. We performed a cross-sectional study of 3224 male officials of the self-defence forces. Glucose tolerance status was determined in accordance with the 1998 World Health Organization criteria, and average intakes of coffee and green tea over the previous year were assessed by a self-administered questionnaire. The figures obtained were adjusted for BMI, physical activity and other factors.

Results. A total of 1130 men were identified as having glucose intolerance (IFG, IGT or type 2 diabetes). Compared with those who did not consume coffee on a daily basis, fasting and 2-h post-load plasma glucose levels were 1.5% and 4.3% lower in those who drank 5 cups of coffee or more per day respectively. The adjusted odds ratios of glucose intolerance for categories of <1, 1–2, 3–4 and ≥5 cups of coffee per day were 1.0 (referent), 0.8 (95% CI 0.6–1.0), 0.7 (95% CI 0.6–0.9) and 0.7 (95% CI 0.5–0.9) respectively ($p=0.0001$ for trend). No clear association was observed between green tea drinking and glucose tolerance status.

Conclusions/interpretation. Coffee consumption may inhibit postprandial hyperglycaemia and thereby protect against the development of type 2 diabetes mellitus.

Keywords Type 2 diabetes · Coffee · Cross-sectional study · Middle-aged · Japanese · Men.

Introduction

Type 2 diabetes has become a global health burden; worldwide, the number of people with type 2 diabetes was approximately 135 million in 1995, and this fig-

ure is predicted to rise above 300 million by 2025 [1]. In Japan, it is estimated that nearly 7 million individuals suffer from type 2 diabetes, and that another 7 million have a pre-diabetic condition [2]. Of the lifestyle factors associated with the risk of type 2 diabetes, obesity and physical inactivity are the two most important factors involved in the development of the disease [3]. Additionally, it has been suggested that Japanese individuals may have a higher genetic susceptibility to type 2 diabetes [4, 5].

Recent epidemiological studies have suggested a possible protective effect of coffee against type 2 diabetes. A prospective study performed in the Netherlands reported that coffee drinking was associated with a decreased risk of type 2 diabetes [6]. This finding has since been replicated in several follow-up and cross-sectional studies [7, 8, 9, 10, 11]. However, a

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T. Yamaji (✉)

Department of Preventive Medicine,
Faculty of Medical Sciences, Kyushu University,
Higashi-ku, Fukuoka 812-8582, Japan
E-mail: taiki@kuaccm.med.kyushu-u.ac.jp
Tel.: +81-92-6426108, Fax: +81-92-6426115

Abbreviations: MET, metabolic equivalents · SDF, self-defence forces

health examination survey of the Finnish population [12] and a population-based study of Pima Indians [13] failed to observe a protective effect of coffee. Only two of these studies used the standard glucose tolerance test to diagnose type 2 diabetes [11, 13]. The aim of the present study was to investigate the relationship between daily intakes of coffee and green tea and glucose tolerance status as determined by a 75-g OGTT in middle-aged Japanese men.

Subjects and methods

Study population. Subjects were male officials in the self-defence forces (SDF) who underwent a pre-retirement health examination between January 1997 and March 2002 at the Self-Defense Forces Fukuoka Hospital and the Self-Defense Forces Kumamoto Hospital; these two hospitals cover the Kyushu district. All officials retiring from the SDF receive a pre-retirement health examination as part of a nationwide programme which offers a comprehensive medical examination. Details of the health examination have been described elsewhere [14, 15, 16, 17].

We consecutively recruited 3413 men aged 46–59 years, 3224 of whom were included in the present study. Of the remainder, five men refused to participate in the study and 184 men were excluded for the following reasons: endocrine diseases ($n=15$), chronic pancreatitis ($n=9$), chronic hepatitis or liver cirrhosis ($n=79$), use of steroids ($n=9$), past history of gastrectomy ($n=57$) and missing information as regards covariates under study ($n=20$). Some of the men met two or more of the exclusion criteria. There were 17 men whose glucose tolerance status was not determined.

The study was approved by the Ethics Committee of the Kyushu University Faculty of Medical Sciences. All study subjects gave written informed consent prior to their participation in the study.

Glucose and other measurements. Over a 5-day admission period, routine medical tests and examinations included a 75-g OGTT. After an overnight fast, venous blood was drawn for measurement of plasma glucose before and 2 h after the oral glucose load. Plasma glucose levels were determined by the glucose oxidase method using commercial reagents (Shino Test, Tokyo, Japan). Subjects were classified as having normal glucose tolerance, IFG, IGT, or type 2 diabetes in accordance with the World Health Organization (WHO) diagnostic criteria, as revised in 1998 [18]. Men with a history of dietary or drug treatment for type 2 diabetes were regarded as having known type 2 diabetes, irrespective of their glucose levels. Body weight and height were recorded, and BMI (kg/m^2) was calculated as a measure of obesity.

Assessment of coffee and green tea consumption and lifestyle characteristics. A self-administered questionnaire was used to ascertain coffee and green tea consumptions, smoking habits, alcohol use, leisure-time physical activity and other lifestyle characteristics.

Average weekly frequencies of coffee and green tea drinking over the previous year were obtained. Those drinking coffee and green tea on a daily basis reported the number of cups of each consumed per day. In a validation study based on the 28-day diet record over the past year [19], the estimated intake of each beverage showed good agreement between the two methods. The Spearman rank correlation coefficients for coffee

and green tea were 0.75 and 0.64 respectively. Caffeine ingestion was estimated using the published caffeine concentrations in coffee (0.04%) and green tea (0.02%) [20]. An average serving of one cup of coffee was estimated to be equal to 150 ml, while an average serving of one cup of green tea was estimated to be equal to 100 ml. Coffee accounted for the majority (66%) of caffeine intake. Ever-smokers were defined as individuals who had ever smoked one cigarette or more per day for at least 1 year or longer. The cumulative exposure of ever-smokers to cigarette smoking was expressed as cigarette-years, the average number of cigarettes smoked per day multiplied by years of smoking. Alcohol drinkers were defined as those who had consumed alcohol once or more per week over a period of 1 year or longer. Past-drinkers were distinguished from lifelong non-drinkers. Alcohol consumption was calculated for current drinkers based on the reported frequencies of consumption of five different alcoholic beverages (sake, shochu, beer, whisky [including brandy] and wine) and amount consumed per occasion over the previous year. Questions on leisure-time physical activity were slightly changed in April 1999. Prior to the revision, the subjects were first asked about their average frequency of regular participation in recreational exercise and sport over the previous year using a closed-ended question (none, 1–2, 3–4, 5–6 times per week or daily). If the subjects participated in recreational physical activity once per week or more frequently, they reported the type of regular exercise or sport and the time spent per occasion. Up to three types of regular exercises were recorded. In the revised questionnaire, the subjects were first asked whether they had regularly participated in recreational activity (one or more times per week) during the previous year. Those who had regularly participated reported up to three types of physical activities, together with the frequency per week and time spent per occasion on each activity. The reported type of exercise was classified as light, moderate, heavy or very heavy activity in accordance with the published energy expenditure requirements in terms of metabolic equivalents (MET) for different physical activities [21]. The time spent on recreational exercise was multiplied by the corresponding MET value (light 2, moderate 4, heavy 6 or very heavy 8) to yield a MET-hour score.

Statistical analysis. Differences in means, medians and proportions of confounding factors across the coffee and green tea consumption categories were statistically tested by one-way ANOVA, the Kruskal–Wallis test and the chi square test respectively. Analysis of covariance was used to calculate the mean concentrations of fasting and 2-h post-load plasma glucose according to the consumption of each beverage in subjects without known type 2 diabetes, with adjustment for possible confounding effects of hospital, rank in the SDF, parental history of diabetes, BMI, cigarette smoking, alcohol intake and leisure time physical activity. In addition, as coffee and green tea drinking were inversely correlated (Spearman rank correlation -0.15), we mutually adjusted for coffee and green tea consumption. Odds ratios and 95% confidence intervals of IFG, IGT, newly diagnosed type 2 diabetes and known type 2 diabetes in relation to levels of coffee and green tea consumption, were obtained from multiple logistic regression analysis while adjusting for the above-mentioned confounding variables, using normal glucose tolerance as the referent group. Trends of the association were assessed by the Wald statistic in logistic regression analysis, in which ordinal values were assigned to categories of each factor.

Categories of coffee and green tea consumption were both defined as <1, 1–2, 3–4 and ≥ 5 cups per day. BMI was divided into quartiles using the 25th, 50th and 75th percentiles in the distribution as cut-off points. Use of BMI as a continuous vari-

Table 1. Potential confounding variables according to daily coffee consumption

Variable	Coffee consumption (cups per day)								<i>p</i> value ^a
	<1		1–2		3–4		≥5		
	(n=1145)		(n=717)		(n=805)		(n=557)		
Age (years)	52.4	(0.9)	52.4	(1.0)	52.4	(0.9)	52.4	(0.9)	0.73
Examination at Fukuoka Hospital	54		62		66		73		0.001
Low ranks in the SDF	67		64		61		54		0.001
Parental history of diabetes	10		8		10		11		0.44
BMI (kg/m ²)	23.9	(2.6)	24.0	(2.7)	23.6	(2.5)	24.0	(2.7)	0.009
Ever-smoking	68		72		77		84		0.001
Cigarette-years	510	(300–640)	600	(400–720)	600	(400–750)	640	(500–900)	0.0001
Current alcohol use	86		83		82		77		0.003
Alcohol (ml/day)	48	(25–74)	46	(25–72)	45	(26–71)	44	(22–71)	0.13
MET-hours per week	16	(5–30)	16	(6–27)	14	(4–27)	13	(1–27)	0.002

Data are percentages, means (SD) or medians (interquartile ranges). ^a One-way ANOVA for mean difference, the Kruskal–Wallis test for median difference and the chi-square test for percentage difference

Table 2. Potential confounding variables according to daily green tea consumption

Variable	Green tea consumption (cups per day)								<i>p</i> value ^a
	<1		1–2		3–4		≥5		
	(n=453)		(n=622)		(n=1083)		(n=1066)		
Age (years)	52.4	(0.9)	52.4	(0.9)	52.4	(1.0)	52.4	(0.9)	0.68
Examination at Fukuoka Hospital	66		63		64		58		0.002
Low ranks in the SDF	65		60		62		63		0.45
Parental history of diabetes	10		10		10		9		0.83
BMI (kg/m ²)	24.1	(2.8)	23.8	(2.5)	23.8	(2.5)	23.9	(2.6)	0.25
Ever-smoking	74		75		75		72		0.31
Cigarette-years	600	(400–800)	600	(400–700)	600	(400–720)	600	(400–720)	0.27
Current alcohol use	85		86		84		79		0.02
Alcohol (ml/day)	45	(23–73)	47	(25–73)	45	(25–71)	45	(24–72)	0.78
MET-hours per week	12	(0–27)	15	(4–27)	16	(6–28)	16	(4–28)	0.12

Data are percentages, means (SD) or medians (interquartile ranges). ^a One-way ANOVA for mean difference, the Kruskal–Wallis test for median difference and the chi-square test for percentage difference

able did not change the results. Rank in the SDF was divided into two categories (low or high); cigarette smoking was divided into four categories (never-smokers and tertiles of cigarette-years in ever-smokers); alcohol intake was stratified into five categories (never-drinkers, past-drinkers and tertiles of alcohol consumed per day in current drinkers); and leisure time physical activity was divided into four levels (no regular exercise and tertiles of MET-hours per week in regular participants). Age was within a limited range from 46–59 years, and 98% of the subjects were aged 50–54 years. Age was thus not adjusted for in analysis. Repeated analyses controlling for age as a continuous variable produced essentially the same results as reported below. Indicator variables representing categories of the above-mentioned confounding factors were included in the models as independent variables.

Two-sided *p* values less than 0.05 were regarded as statistically significant. All analyses were performed using Statistical Analysis System (SAS), Version 6.12 (SAS Institute, Cary, N.C., USA).

Results

Among the 3224 male officials, there were 204 (6%) prevalent cases of IFG, 568 (18%) of IGT, 171 (5%) of newly diagnosed type 2 diabetes, and 187 (6%) of known type 2 diabetes.

The characteristics of the study sample varied according to the level of coffee consumption (Table 1). Men in the higher coffee consumption categories were more likely to be examinees at the Fukuoka Hospital and were more likely to have achieved a higher rank in the SDF. The frequency of ever-smokers and the cumulative amount of cigarettes smoked increased with increased coffee consumption. Furthermore, subjects with a higher intake of coffee were less likely to be current drinkers of alcohol and were less likely to participate in physical exercise during leisure time. BMI varied with coffee consumption; however, this associa-

Table 3. Plasma glucose concentrations according to daily consumption of coffee or green tea

	Daily consumption (cups per day)								<i>p</i> value for trend
	<1		1–2		3–4		≥5		
	Crude mean (SEM)								
Coffee									
Fasting (mmol/l)	5.63	(0.02)	5.52	(0.03) ^a	5.51	(0.03) ^a	5.49	(0.03) ^a	0.0003
2-h post-load (mmol/l)	6.92	(0.06)	6.74	(0.08)	6.60	(0.07) ^a	6.66	(0.09) ^a	0.001
Green tea									
Fasting (mmol/l)	5.60	(0.04)	5.57	(0.03)	5.53	(0.02)	5.55	(0.02)	0.18
2-h post-load (mmol/l)	6.76	(0.10)	6.71	(0.08)	6.68	(0.06)	6.86	(0.06)	0.23
	Adjusted mean (SEM) ^b								
Coffee									
Fasting (mmol/l)	5.60	(0.02)	5.52	(0.03) ^a	5.53	(0.03) ^a	5.52	(0.03) ^a	0.02
2-h post-load (mmol/l)	6.92	(0.06)	6.74	(0.07)	6.63	(0.07) ^a	6.63	(0.09) ^a	0.001
Green tea									
Fasting (mmol/l)	5.59	(0.04)	5.57	(0.03)	5.53	(0.02)	5.54	(0.02)	0.16
2-h post-load (mmol/l)	6.71	(0.09)	6.72	(0.08)	6.69	(0.06)	6.86	(0.06)	0.15

Men with known type 2 diabetes were excluded from the analysis. ^a $p < 0.05$ vs drinking <1 cup per day; ^b adjusted for hospital, rank, parental history of diabetes, BMI, smoking, alcohol intake, leisure time physical activity, and either green tea or coffee intake

Table 4. Odds ratio for each glucose tolerance status according to level of coffee consumption

Glucose tolerance status		Coffee consumption (cups per day)				<i>p</i> value for trend
		<1	1–2	3–4	≥5	
Normal	No.	680	475	557	382	
IFG	No.	81	42	49	32	
	Crude OR	1.0 (referent)	0.7 (0.5–1.1)	0.7 (0.5–1.1)	0.7 (0.5–1.1)	0.07
	Adjusted OR ^a	1.0 (referent)	0.8 (0.5–1.2)	0.9 (0.6–1.3)	0.9 (0.6–1.4)	0.53
IGT	No.	234	138	116	80	
	Crude OR	1.0 (referent)	0.8 (0.7–1.1)	0.6 (0.5–0.8)	0.6 (0.5–0.8)	<0.0001
	Adjusted OR ^a	1.0 (referent)	0.8 (0.6–1.1)	0.6 (0.5–0.8)	0.6 (0.4–0.8)	<0.0001
Newly diagnosed type 2 diabetes	No.	70	30	40	31	
	Crude OR	1.0 (referent)	0.6 (0.4–1.0)	0.7 (0.5–1.0)	0.8 (0.5–1.2)	0.18
	Adjusted OR ^a	1.0 (referent)	0.6 (0.4–1.0)	0.8 (0.5–1.2)	0.8 (0.5–1.3)	0.37
Known type 2 diabetes	No.	80	32	43	32	
	Crude OR	1.0 (referent)	0.6 (0.4–0.9)	0.7 (0.4–1.0)	0.7 (0.5–1.1)	0.06
	Adjusted OR ^a	1.0 (referent)	0.6 (0.4–1.0)	0.7 (0.4–1.0)	0.7 (0.4–1.1)	0.09

Data are odds ratios (95% CI). ^a Adjusted for hospital, rank, parental history of diabetes, BMI, smoking, alcohol intake, leisure time physical activity and green tea intake. OR, odds ratio

tion was not simple. Few variables were associated with green tea consumption (Table 2). Subjects with a higher intake of green tea were less likely to have undergone their health examination at the Fukuoka Hospital and were less likely to be current alcohol users.

Table 3 summarises the crude and adjusted mean concentrations of fasting and 2-h post-load plasma glucose according to coffee and green tea consumption, excluding those with known type 2 diabetes. Subjects who drank coffee on a daily basis had lower

fasting and post-load plasma glucose levels. Surprisingly, the reduction in post-load plasma glucose concentrations with increasing levels of coffee intake was more pronounced than the corresponding decrease in fasting plasma glucose concentrations. Compared with those who did not consume coffee on a daily basis, fasting and post-load glucose concentrations were 1.5% and 4.3% lower in men who drank 5 cups of coffee or more per day respectively. Green tea consumption was not inversely associated with either fasting or

Table 5. Odds ratio for each glucose tolerance status according to level of green tea consumption

Glucose tolerance status		Green tea consumption (cups per day)				<i>p</i> value for trend
		<1	1–2	3–4	≥5	
Normal	No.	277	414	735	668	
IFG	No.	35	48	64	57	
	Crude OR	1.0 (referent)	0.9 (0.6–1.5)	0.7 (0.4–1.1)	0.7 (0.4–1.1)	0.04
	Adjusted OR ^a	1.0 (referent)	0.9 (0.6–1.5)	0.7 (0.4–1.1)	0.6 (0.4–1.0)	0.02
IGT	No.	86	103	180	199	
	Crude OR	1.0 (referent)	0.8 (0.6–1.1)	0.8 (0.6–1.1)	1.0 (0.7–1.3)	0.85
	Adjusted OR ^a	1.0 (referent)	0.8 (0.6–1.2)	0.8 (0.6–1.1)	1.0 (0.7–1.3)	0.85
Newly diagnosed type 2 diabetes	No.	25	33	49	64	
	Crude OR	1.0 (referent)	0.9 (0.5–1.5)	0.7 (0.4–1.2)	1.1 (0.7–1.7)	0.69
	Adjusted OR ^a	1.0 (referent)	1.0 (0.6–1.7)	0.8 (0.5–1.3)	1.1 (0.7–1.9)	0.56
Known type 2 diabetes	No.	30	24	55	78	
	Crude OR	1.0 (referent)	0.5 (0.3–0.9)	0.7 (0.4–1.1)	1.1 (0.7–1.7)	0.15
	Adjusted OR ^a	1.0 (referent)	0.6 (0.3–1.0)	0.7 (0.4–1.2)	1.1 (0.7–1.7)	0.25

Data are odds ratios (95% CI). ^a Adjusted for hospital, rank, parental history of diabetes, BMI, smoking, alcohol intake, leisure time physical activity and coffee intake. OR, odds ratio

post-load plasma glucose concentrations. Those with the highest green tea intake had higher post-load plasma glucose concentrations; however, this trend was not statistically significant.

Tables 4 and 5 show the crude and adjusted odds ratios of IFG, IGT, newly diagnosed type 2 diabetes and known type 2 diabetes according to levels of coffee and green tea consumption, with normal glucose tolerance as the referent group. Coffee intake was not independently associated with IFG. Odds ratios of IGT, newly diagnosed type 2 diabetes and known type 2 diabetes were generally lower than unity among coffee drinkers, although not all of the decreases in odds ratios were statistically significant. The inverse association was particularly evident for IGT ($p < 0.0001$ for trend). No clear association was observed between green tea drinking and glucose tolerance status, although green tea drinkers had a reduced odds ratio for IFG.

The adjusted odds ratios of glucose intolerance (IFG, IGT and type 2 diabetes) for categories of <1, 1–2, 3–4 and ≥5 cups of coffee per day were 1.0 (referent), 0.8 (95% CI 0.6–1.0), 0.7 (95% CI 0.6–0.9) and 0.7 (95% CI 0.5–0.9) respectively ($p = 0.0001$ for trend). The corresponding values for green tea were 1.0 (referent), 0.8 (95% CI 0.6–1.1), 0.8 (95% CI 0.6–1.0) and 1.0 (95% CI 0.8–1.2) respectively ($p = 0.95$ for trend).

We also performed an analysis of caffeine intake, with adjustment for hospital, rank in the SDF, parental history of diabetes, BMI, cigarette smoking, alcohol intake and leisure time physical activity. As caffeine ingestion was strongly correlated with coffee consumption (Spearman correlation coefficient 0.89), coffee and caffeine were not simultaneously included in the analysis. The adjusted mean concentrations of

fasting and post-load plasma glucose according to quartile of daily caffeine intake were 5.63, 5.53, 5.55 and 5.50 mmol/l ($p = 0.004$ for trend) and 6.88, 6.78, 6.75 and 6.62 mmol/l ($p = 0.01$ for trend) respectively. Compared with those in the lowest quartile of daily caffeine intake, fasting and post-load plasma glucose concentrations were 2.2% and 3.8% lower in men in the highest quartile. The adjusted odds ratios of glucose intolerance according to quartile of daily caffeine consumption were 1.0 (referent), 0.8 (95% CI 0.6–1.0), 0.8 (95% CI 0.6–1.0) and 0.7 (95% CI 0.5–0.8) respectively ($p = 0.0005$ for trend).

Discussion

In the present study, we have demonstrated an inverse relationship between coffee consumption and glucose intolerance, particularly IGT, by using the standard glucose tolerance test. Our study adds to increasing evidence that coffee affords protection against the development of type 2 diabetes. The present findings are consistent with those of recent prospective studies [6, 8, 9, 10] and cross-sectional studies [7, 11], but are in disagreement with the observations reported by population-based studies in the Finnish population [12] and among Pima Indians [13]. With regard to the assessment of type 2 diabetes, the majority of studies used self-reported questionnaires and/or registers of diabetic patients receiving treatment, whereas few studies adopted the standard glucose tolerance test [11, 13].

Although coffee contains many compounds which mediate a variety of physiological functions, the main biological effects of coffee drinking have been attributed to caffeine [22]. A prospective study in the

US reported that total caffeine estimated from coffee and other sources was associated with a statistically significant lower risk of type 2 diabetes, and that this association remained significant after adjustment for coffee consumption [8]. A cross-sectional study in Japan also demonstrated that total caffeine estimated from coffee and three types of tea was associated with lower fasting glucose concentrations, and that the inverse association between caffeine from coffee alone and fasting plasma glucose was stronger than that for total caffeine [7]. In our study, total caffeine estimated from coffee and green tea was inversely related to fasting and post-load plasma glucose and to the risk of type 2 diabetes. The magnitude of the inverse relationship between caffeine and glucose intolerance was similar to that observed for coffee. We were not able to address the question of whether or not coffee is related to glucose intolerance independently of caffeine, because coffee consumption and caffeine intake were strongly correlated with each other.

Of particular interest were the findings that coffee consumption was more strongly associated with decreased concentrations of post-load plasma glucose than fasting plasma glucose, and that coffee consumption was almost unrelated to IFG. These results suggest that coffee consumption may inhibit postprandial hyperglycaemia and thereby afford protection against the development of type 2 diabetes mellitus.

The present study had several associated strengths in addition to the use of a 75-g OGTT. Almost all SDF officials in the Kyushu district participated in the health examination programme at two SDF hospitals prior to their retirement. Thus, the study population was almost unselected. In addition, the study population was relatively large. The subjects were relatively homogeneous in terms of social background as well as age range.

One of the limitations of the present study was its cross-sectional nature. An association observed in a cross-sectional study does not necessarily indicate a causal relationship. As diabetes may have affected coffee consumption levels, we treated men with a history of diabetes separately in the analysis. Another limitation was that the observed relationship between coffee drinking and glucose intolerance may be attributed in part to undetermined characteristics of coffee drinkers, although important factors associated with type 2 diabetes were statistically adjusted for. Caffeine ingestion was estimated based on only coffee and green tea consumption; thus, caffeine intake may have been misclassified to some extent. However, other caffeine-containing beverages, such as black tea and cola, are probably consumed to a far lesser extent by middle-aged men in Japan, as suggested by the survey on beverage preference [23]. Finally, the study subjects were men who served in the SDF up to retirement, and may therefore differ from the general population with respect to various lifestyle characteristics.

Consequently, our findings may not be directly applied to the general population.

In conclusion, using a 75-g OGTT to diagnose diabetes, the present study of middle-aged Japanese men provides further evidence for the protective role of coffee or caffeine in the pathogenesis of type 2 diabetes. The biological effects of caffeine and other constituents of coffee deserve further investigation.

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