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Lifetime cigarette smoking is associated with abdominal obesity in a community-based sample of Japanese men: The Shiga Epidemiological Study of Subclinical Atherosclerosis (SESSA)

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ABSTRACT

Studies from Western countries suggest that smokers tend to display greater abdominal obesity than non-smokers, despite showing lower weight. Whether this holds true in a leaner population requires clarification. Using indices of abdominal obesity including visceral adipose tissue, we examined whether lifetime cigarette smoking is associated with unfavorable fat distribution among Japanese men.

From 2006 to 2008, we conducted a cross-sectional investigation of a community-based sample of Japanese men at 40–64 years old, free of cardiovascular diseases and cancer. Areas of abdominal visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) were calculated using computed tomography. We divided participants into four groups: never-smokers; and tertiles of pack-years of smoking among ever-smokers. Using multivariable linear regression, we calculated adjusted means of obesity indices (VAT, SAT, VAT-SAT ratio [VSR], and waist-hip ratio [WHR]) for each group, and mean differences between consecutive groups.

We analyzed 513 men (median age, 58.2 years; current smokers, 40.1%). Two-thirds showed body mass index (BMI) < 25 kg/m^2 (median, 23.5 kg/m^2). Overall, greater lifetime smoking group was associated with greater WHR and VSR. On average, one higher smoking group was associated with 0.005 higher WHR (95% CI, 0.001–0.008; $P = 0.005$) and 0.041 greater VSR (95% CI, 0.009–0.073; $P = 0.012$) after adjustment for potential confounders, including BMI. In this sample of relatively lean Japanese men, greater lifetime smoking was associated with a metabolically more adverse fat distribution. Although smoking is commonly associated with lower BMI, minimizing the amount of lifetime smoking should be advocated.

1. Introduction

Smokers tend to be leaner than non-smokers, although the long-term effects of smoking on weight remain unclear and can be variable (Audrain-McGovern and Benowitz, 2011; Chiolero et al., 2008). The idea that cigarette smoking is helpful in controlling body weight has remained popular (Audrain-McGovern and Benowitz, 2011), and the fear of gaining weight discourages smokers from quitting (Chiolero et al., 2008). Importantly, many population-based studies have suggested that cigarette smoking is associated with a greater degree of abdominal obesity (Bamia et al., 2004; Barrett-Connor and Khaw, 1989; Kim et al., 2012; Shimokata et al., 1989b), despite the lower weight/body mass index (BMI) observed in smokers (Canoy et al., 2005; Jee et al., 2002). In most of those studies, however, abdominal obesity was assessed using anthropometric measures such as waist

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circumference (WC) or waist-to-hip ratio (WHR). Whether smoking is associated with either visceral adipose tissue (VAT) or subcutaneous adipose tissue (SAT), or both thus remains unclear. This question is important, as VAT has been suggested to play a more important role than SAT in the pathogenesis of cardiometabolic derangements such as diabetes mellitus (DM) and atherosclerosis (Farb and Gokce, 2015; Perrini et al., 2008). In addition, most relevant studies have been conducted in the United States or Europe, where BMI is generally higher than in other regions, including Japan. We therefore aimed to examine cross-sectional associations between lifetime cigarette smoking and measures of abdominal obesity, including computed tomography (CT)-based assessments of VAT and SAT, in a population-based sample of Japanese men.

2. Methods

2.1. Subjects

This is a cross-sectional investigation of an observational population-based study. The subjects were male participants in a population-based cohort study conducted in Japan, the Shiga Epidemiological Study of Subclinical Atherosclerosis (SESSA). SESSA is a study of subclinical atherosclerosis and its determinants on a sample of Japanese residents, and details of the methods of enrollment have been reported previously (Kadota et al., 2013). In brief, from 2006 to 2008, we randomly selected and invited 2381 Japanese men aged 40 to 79 years who were residents of Kusatsu City, Shiga, based on the Basic Residents' Register of the city. The Register contains information on name, sex, birth date, and address of residents (Sekikawa et al., 2007). A total of 1094 men agreed to participate (The participation rate was 46%) (Kadota et al., 2013). The city, located in central Japan, has an industrial structure similar to the average of Japan: approximately two thirds and one-third are tertiary (i.e. service industries) and secondary (mining, manufacturing, construction industries) sectors, respectively, and the remaining few percent is primary sector (agriculture, forestry and fishery industry) according to the Ministry of Health, Labour and Welfare. For the present study, we limited our analyses *a priori* to those 40–64 years old who were free of cardiovascular disease and cancer at baseline (519 men). We chose the age cut-off of 64 years as an exclusion criterion to minimize the potential for older age to confound the association between smoking and obesity. Japanese men tend to start losing weight, as reflected by a decline in BMI, at around 60–69 years old (Yatsuya et al., 2011). According to the National Health and Nutrition Surveys in Japan, the proportion of current male smokers starts to decrease around the same age range (60–69 years), and continues to drop progressively with age (JAPAN HEALTH PROMOTION & FITNESS FOUNDATION, 2008). This simultaneous decline in body weight and smoking rates, likely rooted in both biological and socio-behavioral bases, may introduce further complexities and confounding to the relationship between exposure and outcome (Hu, 2008), which we therefore intended to avoid in our analyses.

The present study was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and approved by the institutional review board of Shiga University of Medical Science (Nos. 17–19, 17–83).

2.2. Measurements

Data on medical history, use of medications, smoking, alcohol intake, and other lifestyle factors were collected from each participant using a self-administered questionnaire. Trained technicians confirmed the completed questionnaire with participants.

We assessed the amount of lifetime cigarette smoking in staged questions. First, participants were asked "Have you smoked in the past 30 days? (Yes/No)". Those answering "Yes" were categorized as current smokers, and queried the average number of cigarettes he smokes each day, and further asked the following question: "At what age did you start smoking cigarettes regularly? (Age)". For those who answered "No", the second question was "Have you smoked in the past?" If the answer was "No", we categorized the individual as a never-smoker, and if the answer was "Yes", we categorized him as a former smoker and asked for further information on the ages at which he started and ceased regular smoking, and the average number of cigarettes smoked each day during those periods. Based on the resulting information, we calculated the lifetime amount of cigarette smoking in pack-years, defined as the number of cigarettes smoked each day divided by 20, then multiplied by the number of years of smoking. Among the former smokers we categorized, three individuals reported same age for both initiation and cessation of smoking. We treated those individuals as former smokers with estimated pack-years of smoking of zero. The frequency of physical activity in leisure time was asked and categorized as "often", "occasional", or "rare to never."

Body weight and height were measured while the participant was wearing light clothing without shoes. Circumferences of the waist and hip were measured twice at the levels of the umbilicus and maximal protrusion of the hip, respectively, in the end-exhalation phase while the participant was standing upright. The mean of the two measurements was used for analysis. Blood pressure was measured twice consecutively in the right arm of the seated participant after sitting quietly for 5 min, using an automated sphygmomanometer (BP-8800; Colin Medical Technology, Komaki, Japan). The mean of these two measurements was used for analyses. Blood specimens were obtained early in the clinic visit after a 12-hour fast, and used for laboratory testing including lipids and glucose concentrations, and other detailed were reported previously. Serum lipid concentrations were determined at a single laboratory (Shiga Laboratory; MEDIC, Shiga, Japan) that had been certified for standardized lipid measurements according to the protocols of the US Centers for Disease Control and Prevention/Cholesterol Reference Method Laboratory Network. Concentrations of glycated hemoglobin (HbA1c) were measured using a latex agglutination inhibition assay according to the standardized method of the Japan Diabetes Society. DM was defined from a fasting serum glucose ≥126 mg/dL (≥6.99 mmol/L), HbA1c ≥6.1% (as per the Japan Diabetes Society protocol during the examination period; equivalent to ≥6.5% in the National Glycohemoglobin Standardization Program (Kashiwagi et al., 2012)), or current treatment for DM.

2.3. Abdominal adipose tissue areas

Areas of VAT and SAT were assessed using CT. Abdominal VAT was defined as the fat enclosed by the inner aspect of the abdominal wall. Abdominal SAT was defined as the fat outside the outer aspects of the abdominal wall, but not including that fat located within the muscular fascia. While participants were supine, serial CT images were obtained using a protocol similar to one described previously (Kadowaki et al., 2006). A single CT image of the L4–L5 vertebral space was selected to estimate areas of VAT and SAT. Adipose tissue was identified as showing attenuation between −190 and −30 Hounsfield units combined with anatomical interpretation by a reader. Studies of human cadavers have shown that the area measured by CT offers an accurate estimate of abdominal VAT,(Rossner et al., 1990) and the same or similar ranges of attenuation have been adopted to estimate VAT/SAT in population studies (DeNino et al., 2001; Ding et al., 2008; Fox et al., 2007; Wheeler et al., 2005). The inner and outer aspects of the abdominal walls were manually tracked, and respective areas were calculated using image analysis software (SliceOmatic; Tomovision, Montreal, Canada). Two types of CT scanner were used during the examination period: a GE-Imatron C150 Electron Beam Tomography system (EBCT; GE Medical Systems, South San Francisco, CA; slice thickness, 6 mm) for participants examined from May 2006 through to August 2007 and a 16-row multidetector row CT system (MDCT, Aquilion-16™; Toshiba Medical Systems, Tochigi, Japan; slice thickness, 7 mm) for participants examined thereafter. All CT images were analyzed at Shiga University of Medical Science by a trained

physician-researcher who was blinded to participant characteristics. Overall findings were similar between the CT types, so combined results are presented with adjustment for CT type in statistical models.

2.4. Statistical analysis

Among the 519 eligible men, we limited our analyses to those with no missing CT-based abdominal obesity indices (VAT, SAT) and pertinent variables including pack-years of smoking, resulting in the inclusion of 513 men for analysis. We divided these participants into four groups based on reported smoking habits and pack-years of smoking: never-smokers and tertiles of pack-years among current and former smokers combined. To assess linear trends in the demographics of participants according to estimated lifetime smoking, we treated the smoking group variable as ordinal (0 = never, 1 = first tertile, 2 = second tertile, and 3 = third tertile), then calculated *P*-values using linear regressions for continuous variables and the Mantel-Haenszel chi-square test for categorical variables. We sought age-adjusted Pearson's correlation coefficients among BMI and abdominal obesity indices (WC, WHR, VAT, SAT, and VAT-SAT ratio [VSR]). For main analyses, we first obtained adjusted means of abdominal obesity indices for each smoking group under no linear assumption between lifetime smoking and the indices. We then tested linear trends and obtained estimates of average difference (and 95% confidence intervals (95% CIs)) between consecutive smoking groups using linear regression. Adjusting covariates were as follows: Model 1, age (years) and CT-type (EBCT versus MDCT); Model 2, education (years), treated DM (yes/no), frequency of physical activity in leisure time (often, occasional, or rare-never), and drinking habit (current, former, or never) in addition to Model 1; and Model 3, BMI in addition to Model 2. Treated DM was defined as use of any antidiabetic medications.

In subgroup analyses, we separately repeated regression analyses on current smokers alone and former smokers alone using each group-specific tertile of pack-years. In sensitivity analyses, we used DM (Yes/No) to replace treated DM in regression models of the main analyses. Because WHR was missing for 35 individuals (19 current smokers, 12 former smokers, and 4 never smokers), we conducted multiple imputations to consider this missing value with a set of 100 plausible substitutes on the assumption of "missing at random" using the Markov Chain Monte Carlo method, and presented the results of the main analyses. In sensitivity analyses, we examined whether the main results differed by the use of complete data (n = 478) or multiple imputations (n = 513). Values of $P < 0.05$ were considered significant and all analyses were two-tailed. SAS version 9.4 software (SAS Institute, Cary, NC) was used for all statistical analyses.

3. Results

For the 513 men studied, median age was 58.2 years, and 40.0%, 43.3%, and 16.7% of participants reported themselves as current, former, and never-smokers, respectively. Two-thirds of study participants (350 of the 513) showed BMI < 25 kg/m^2. Median [25th, 75th percentile] values for lifetime smoking and BMI were 24 pack-years [5, 41 pack-years], and 23.5 kg/m^2 [21.5, 25.7 kg/m^2], respectively. Demographics of the participants according to estimated lifetime smoking are shown in Table 1. Higher levels of smoking were associated with older age, lower concentration of high-density lipoprotein cholesterol, higher concentration of triglycerides, and higher systolic blood pressure, but not with higher BMI. Age-adjusted Pearson's correlation coefficients (r) among BMI and each index of abdominal obesity are shown in Table 2. BMI was most strongly correlated with WC ($r = 0.853$), followed by SAT ($r = 0.818$), VAT ($r = 0.725$) and WHR ($r = 0.574$). VSR showed a moderate positive correlation with VAT ($r = 0.439$) and a moderate negative correlation with SAT ($r = -0.310$).

3.1. Main analyses

Unadjusted and adjusted means of abdominal obesity indices are shown according to estimated lifetime smoking in Table 3. Throughout the models, with or without adjustment for BMI, greater lifetime smoking showed significant, positive associations with higher WHR and VSR. For example, adjusted means of WHR for never-, 1st, 2nd, and 3rd tertiles of smokers were 0.908, 0.915, 0.918, and 0.924, with mean differences per one group of 0.005 (95% CI: 0.001, 0.008; $P_{trend} = 0.005$) after adjusting for age, CT type, years of education, treated DM, physical activity in leisure time, drinking, and BMI (Model 3). Overall, results of WC were similar to WHR.VAT tended to be greater in groups with greater lifetime smoking, but no significant difference was found in any of the models. No clear pattern was seen between SAT and lifetime smoking.

3.2. Subgroup analyses

Tables 4 and 5 summarize the results of analyses restricted to current smokers alone (n = 205) and former smokers alone (n = 222), respectively. Among current smokers, we no longer observed significant trends in any of the obesity indices. For WHR and VSR, however, the overall positive pattern was consistent with the main results. Results were similar when indices were regressed according to the number of cigarettes smoked per day (data not shown). Among former smokers, we observed positive associations between greater lifetime smoking and not only WHR and VSR, but also VAT across the models. Sensitivity analysis replacing DM with treated DM (in Models 2 and 3) resulted in a slight attenuation of the magnitude of relationships, as evidenced by the average difference per one higher category, but overall patterns remained similar to the main results (Appendix B. Table A.1). Sensitivity analyses comparing estimates of WHR from unimputed (complete data, N = 478) and from 100-times imputed data (N = 513) showed similar results (Appendix B. Tables A.2). Results were similar across the strata by education level (highest education attained <16 years, vs ≥16 years, data not shown), and we did not stratify by other socio-economic status due to lack of other appropriate variables for stratification.

4. Discussion

In this population-based, cross-sectional study of Japanese men, higher amount of lifetime smoking was associated with greater indices of abdominal obesity, namely WHR and VSR. The relationship between smoking and obesity is complex and not yet completely understood. On the one hand, numerous cross-sectional studies have indicated that body weight and/or BMI are lower in smokers than in non-smokers (Chiolero et al., 2008). On the other hand, however, many population-based studies, conducted mostly in the United States (Barrett-Connor and Khaw, 1989; Shimokata et al., 1989b) or Europe (Akbartabartoori et al., 2005; Bamia et al., 2004; Canoy et al., 2005; Rosmond and Bjorntorp, 1999; Seidell et al., 1991), have associated cigarette smoking with a greater degree of abdominal obesity (assessed using either WHR or WC)(Bamia et al., 2004; Barrett-Connor and Khaw, 1989; Kim et al., 2012; Shimokata et al., 1989b) despite the lower BMI observed in smokers (Canoy et al., 2005; Jee et al., 2002). The positive association between pack-years of smoking and abdominal obesity identified in our study is in line with these previous studies. Furthermore, our study is one of only a few studies (Kim et al., 2012) to show differential associations of smoking with two types of abdominal adipose tissue assessed on CT: VAT and SAT. We observed a positive association of lifetime smoking with an increased ratio of VAT to SAT. This finding is intriguing because VAT and SAT correlated not only with each other (r = 0.66) but also with BMI (r = 0.73, 0.82, respectively). Since VAT, as compared to SAT, may be more strongly associated with adverse cardiometabolic profiles such as inflammation, insulin resistance (Shah et al., 2014), DM (Farb and Gokce, 2015; Perrini et al., 2008), and

Table 1
Demographics of men according to estimated pack-years of smoking (40–64 years, examined in 2006–2008, Shiga, Japan).

	Never smoker		Current and former smoker						P
				T1		T2		T3	
n	86			143		144		140	
Pack-years (range)	(0)		(0−20)		(21–39)		(39–152)		
Age, years	58.3	[48.1–62.3]	56.9	[46.5–61.4]	56.5	[49.3–61.4]	60.2	[56.3–62.5]	<0.001
Education, years	14	[12–16]	12	[12–16]	12	[12–16]	12	[12–16]	0.025
Height, cm	168	[165–172]	170	[166–174]	169	[165–173]	168	[165–172]	0.462
Weight, kg	66.9	[61.5–72.9]	67.5	[61.8–72.9]	67.8	[59.9–74.9]	66.3	[60.0–74.4]	0.845
BMI, kg/m^2	23.6	[21.7–25.4]	23.3	[21.5–25.4]	23.5	[21.2–26.1]	23.6	[21.6–25.7]	0.885
Total-c, mg/dL	206	[182–233]	212	[192–237]	208	[190–232]	208	[188–231]	0.786
HDL-c, mg/dL	61	[48–72]	59	[51–70]	58	[47–68]	50	[44–63]	<0.001
TG, mg/dL	98	[67–145]	101	[72–150]	118	[76–178]	126	[84–189]	<0.001
Glucose, mg/dL	95	[90–103]	97	[90–105]	96	[91–107]	99	[91–110]	0.100
HbA1c (NGSP*), %	5.7	[5.4–6.0]	5.7	[5.5–6.0]	5.7	[5.5–6.0]	5.8	[5.6–6.4]	0.001
Systolic BP, mmHg	129	[117–138]	128	[118–141]	130	[121–145]	133	[121–147]	0.019
DM, %	11.6		8.4		16.7		24.3		0.001
Treated DM, %	9.3		2.8		4.2		10.7		0.285
Hypertension, %	34.9		35.0		44.4		47.9		0.014
Smoking, %									<0.001
Current	0.0		24.5		55.6		64.3		
Former	0.0		75.5		44.4		35.7		
Never	100.0		0.0		0.0		0.0		
Drinking, %									0.838**
Current	74.4		84.6		84.7		77.9		
Former	1.2		2.1		2.8		5.0		
Never	24.4		13.3		12.5		17.1		
Frequency of PA in leisure time, %									0.764
Often	18.6		18.9		23.6		17.1		
Occasional	46.5		39.9		36.1		49.3		
Rare to never	34.9		41.3		40.3		33.6		
CT-type, EBCT, %	64.0		62.2		66.7		86.4		<0.001

1) Values for continuous variables are given as median [inter-quartile range]. 2) T1, T2, T3 denote first, second and third tertiles of pack-years of cigarette smoking among current and former smokers combined. 3) *HbA1c was measured in accordance with the protocol of the Japan Diabetes Society (JDS), then converted to the equivalent value for the National Glycohemoglobin Standardization Program (NGSP) using the following formula: 1.02 × HbA1c (JDS) (%) + 0.25. 4) Treating the smoking category variable (never, T1–T3 for smokers) as ordinal, *P*-values were sought using linear regressions for continuous variables, and the Mantel-Haenszel chi-square test for categorical variables. ** *P*-value was obtained after collapsing the drinking category to "current" vs "non-current" because former drinkers were too few to allow testing the Mantel-Haenszel chi-square test.
Abbreviations: BMI, body mass index; VAT, abdominal visceral adipose tissue; SAT, abdominal subcutaneous adipose tissue; VSR, VAT-SAT ratio; Total-c, total-cholesterol, HDL-c, high density lipoprotein cholesterol; TG, triglycerides; BP, blood pressure; DM, diabetes mellitus; PA, physical activity; EBCT, electron-beam computed tomography.

atherosclerosis (Farb and Gokce, 2015), this finding offers further support for the idea that a greater amount of lifetime smoking is linked to a metabolically more adverse fat distribution (Canoy et al., 2005). The well-documented association between smoking and DM (Pan et al., 2015; Willi et al., 2007) could be explained in part by visceral fat accumulation (Chiolero et al., 2008), and our finding is consistent with this hypothesis. Our study adds an important piece to the body of scientific evidence against a popular belief that smoking is an efficient way to control body weight (Potter et al., 2004) as we showed that smoking was associated with (relative) increase in abdominal obesity at a given body mass (Morris et al., 2015).

Importantly, our study sample seems to show one of the lowest levels of BMI among the relevant studies. For example, Kim et al. reported that greater WC and greater CT-measured abdominal VAT were associated with higher life-time smoking in their hospital-based cross-sectional study in Korea (Kim et al., 2012). BMI for their sample (mean, 26.4 kg/m^2; standard deviation, 4.8 kg/m^2) was similar or closer to those studies from the United States and Europe (Akbartabartoori et al., 2005; Bamia et al., 2004; Canoy et al., 2005; Shimokata et al., 1989a), and much higher than BMI for our study sample (mean, 23.7 kg/m^2; standard deviation, 3.0 kg/m^2). Our findings thus add to the literature confirming the association between smoking and abdominal obesity even in leaner populations.

In subgroup analyses of current or former smokers alone, the positive association between lifetime smoking and abdominal obesity was significant only in former smokers, not in current smokers. In current smokers, however, most of our models showed a graded increase in point estimates of WHR and VSR across tertiles. Smoking has probable acute anorexic effects and metabolic properties that favor weight control (Chiolero et al., 2008), but also has other properties that may predispose to abdominal obesity, such as insulin resistance related to the release of catecholamines (Benowitz, 2003) and cortisol (Chiolero et al., 2008). In fact, other population-based studies have reported a positive association between amount of smoking and abdominal obesity within current smokers (Canoy et al., 2005; Clair et al., 2011; Kim et al., 2012). The

Table 2
Age-adjusted Pearson's correlation coefficients among obesity indices ($n = 478$).

	BMI (kg/m^2)	WC (cm)	WHR	VAT (cm^2)	SAT (cm^2)
WC	0.853	–	–	–	–
WHR	0.574	0.797	–	–	–
VAT	0.725	0.794	0.641	–	–
SAT	0.818	0.846	0.624	0.658	–
VSR	−0.066***	0.005**	0.095*	0.439	−0.310

Unless otherwise specified, all *P*s < 0.0001.
Because 35 of the 513 participants had missing WHR, all coefficients were obtained from the remaining 478 participants.
Abbreviations. BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; VAT, area of abdominal visceral adipose tissue; SAT, area of abdominal subcutaneous tissue.
* $P = 0.039$.
** $P = 0.911$.
*** $P = 0.149$.

Table 3
Unadjusted and adjusted means of abdominal obesity indices according to estimated lifetime smoking among all participants (513 men, aged 40–64 years, examined in 2006–2008, Shiga, Japan).

			Current and former smokers					
		Never smokers	T1	T2	T3			
N		86	143	144	140	Estimated mean difference per 1 higher category (95% CI)		Trend *P*
Pack-years (range)		(0)	(0–20)	(21–39)	(39–152)			
WC, cm	Mean (unadjusted)	84.5	85.0	85.6	86.1	0.540	(−0.10, 1.18)	0.100
	Model 1	84.6	85.0	85.6	86.6	0.687	(0.03, 1.34)	0.040
	Model 2	85.9	86.3	87.1	87.6	0.590	(−0.06, 1.24)	0.076
	Model 3	84.3	85.1	85.0	85.9	0.462	(0.11, 0.82)	0.010
WHRa	Mean (unadjusted)	0.906	0.910	0.916	0.925	0.006	(0.002, 0.010)	0.002
	Model 1	0.907	0.911	0.918	0.925	0.006	(0.002, 0.010)	0.004
	Model 2	0.915	0.920	0.927	0.931	0.005	(0.001, 0.010)	0.010
	Model 3	0.908	0.915	0.918	0.924	0.005	(0.001, 0.008)	0.005
VAT, cm^2	Mean (unadjusted)	114	114	119	121	2.8	(−1.5, 7.2)	0.202
	Model 1	114	114	119	124	3.8	(−0.7, 8.2)	0.094
	Model 2	119	118	124	127	3.1	(−1.3, 7.6)	0.165
	Model 3	109	111	112	117	2.5	(−0.6, 5.5)	0.118
SAT, cm^2	Mean (unadjusted)	122	124	126	117	−1.7	(−6.1, 2.7)	0.449
	Model 1	123	124	128	126	1.0	(−3.4, 5.4)	0.652
	Model 2	136	137	141	136	0.2	(−4.2, 4.6)	0.925
	Model 3	125	129	127	125	−0.6	(−3.1, 2.0)	0.669
VSR	Mean (unadjusted)	0.960	0.961	1.013	1.112	0.055	(0.023, 0.086)	0.001
	Model 1	0.945	0.951	0.996	1.060	0.041	(0.009, 0.073)	0.012
	Model 2	0.879	0.875	0.923	0.990	0.041	(0.009, 0.073)	0.013
	Model 3	0.885	0.879	0.930	0.996	0.041	(0.009, 0.073)	0.012

Adjusting covariates: Model 1: age (years), CT type; Model 2: education (years), treated DM (yes/no), frequency of physical activity in leisure time (often, occasional, rare-to-never), and drinking habit (current, former, never) in addition to Model 1; Model 3: body mass index (kg/m^2) in addition to Model 2. Abbreviations: T1, T2, and T3 denote first, second, and third tertiles of pack-years of smoking among current and former smokers combined. WC, waist circumference; WHR, waist-to-hip ratio; VAT, area of abdominal visceral adipose tissue (cm^2); SAT, area of abdominal subcutaneous adipose tissue (cm^2); VSR, VAT-SAT ratio.
Trend Ps were calculated using an ordinal variable for the 4 groups (never, tertiles of smokers) in the linear regression models.
[a] Estimates for WHR were obtained using 100-times imputed plausible WHR values for the 35 participants with missing data for WHR.

reasons for the inconsistency between our study and such previous studies remain unclear. One speculative explanation is that the relationship in current smokers may be less strong as compared to that in former smokers, given the acute anorexic effect of smoking (Jessen et al., 2005; Perkins et al., 1991). A greater sample size and/or wider range of BMIs may thus be required to demonstrate the relationship among current

Table 4
Unadjusted and adjusted means of each index of abdominal obesity according to estimated lifetime smoking among current smokers (205 men, aged 40–64 years, examined in 2006–2008, Shiga, Japan).

		T1	T2	T3			
n		68	69	68	Estimated mean difference per 1 group higher category (95% CI)		Trend *P*
Pack-years (range)	(1–29)	(30–44)	(44–113)				
WC, cm	Mean (unadjusted)	85.4	86.5	85.9	0.27	(−1.09, 1.63)	0.698
	Model 1	84.7	86.7	86.4	0.81	(−0.68, 2.30)	0.285
	Model 2	86.5	88.5	87.9	0.66	(−0.84, 2.16)	0.386
	Model 3	85.5	85.9	86.5	0.47	(−0.33, 1.28)	0.248
WHRa	Mean (unadjusted)	0.912	0.922	0.924	0.006	(−0.002, 0.014)	0.161
	Model 1	0.913	0.923	0.925	0.006	(−0.003, 0.015)	0.196
	Model 2	0.931	0.941	0.941	0.005	(−0.005, 0.014)	0.330
	Model 3	0.927	0.931	0.935	0.004	(−0.004, 0.012)	0.337
VAT, cm^2	Mean (unadjusted)	118	121	113	−2.3	(−11.3, 6.7)	0.611
	Model 1	115	125	119	1.8	(−8.0, 11.6)	0.717
	Model 2	121	131	125	1.7	(−8.3, 11.6)	0.744
	Model 3	115	115	116	0.6	(−6.1, 7.3)	0.869
SAT, cm^2	Mean (unadjusted)	130	130	112	−9.2	(−19.0, 0.6)	0.066
	Model 1	120	132	118	−1.5	(−12.0, 9.0)	0.776
	Model 2	135	147	132	−1.9	(−12.5, 8.6)	0.718
	Model 3	128	129	122	−3.2	(−9.0, 2.5)	0.271
VSR	Mean (unadjusted)	0.939	1.041	1.081	0.071	(0.008, 0.134)	0.028
	Model 1	0.991	1.038	1.058	0.033	(−0.035, 0.101)	0.341
	Model 2	0.904	0.953	0.976	0.036	(−0.033, 0.105)	0.309
	Model 3	0.912	0.974	0.988	0.037	(−0.031, 0.106)	0.285

Adjusting covariates: Model 1: age (years), CT type; Model 2: education (years), treated DM (yes/no), frequency of physical activity in leisure time (often, occasional, rare-to-never), and drinking habit (current, former, never) in addition to Model 1; Model 3: body mass index (kg/m^2) in addition to Model 2. Abbreviations: T1, T2, and T3 denote first, second, and third tertiles of pack-years of smoking among current smokers. WC, waist circumference; WHR, waist-to-hip ratio; VAT, area of abdominal visceral adipose tissue (cm^2); SAT, area of abdominal subcutaneous adipose tissue (cm^2); VSR, VAT-SAT ratio.
Trend Ps were calculated using an ordinal variable for the 4 groups (never, tertiles of smokers) in the linear regression models.
[a] Estimates for WHR were obtained using 100-times imputed plausible WHR values for the 19 current smokers with missing data for WHR.

Table 5
Unadjusted and adjusted means of each index of abdominal obesity according to estimated lifetime smoking among former smokers (222 men, aged 40–64 years, examined in 2006–2008, Shiga, Japan).

		T1	T2	T3			
n		74	75	73	Estimated mean difference per 1 group higher category (95% CI)		Trend *P*
Pack-years (range)		(0−13)	(14–32)	(33–152)			
WC, cm	Mean (unadjusted)	84.8	84.0	86.9	1.06	(−0.21, 2.33)	0.102
	Model 1	85.1	84.6	88.0	1.44	(0.16, 2.72)	0.028
	Model 2	85.3	85.1	87.9	1.29	(−0.01, 2.59)	0.052
	Model 3	84.2	83.9	84.9	0.29	(−0.38, 0.96)	0.399
WHR[a]	Mean (unadjusted)	0.906	0.908	0.930	0.012	(0.004, 0.020)	0.004
	Model 1	0.908	0.910	0.932	0.012	(0.004, 0.020)	0.003
	Model 2	0.907	0.911	0.931	0.012	(0.004, 0.020)	0.005
	Model 3	0.902	0.906	0.917	0.007	(0.001, 0.014)	0.029
VAT, cm^2	Mean (unadjusted)	109	113	134	12.3	(3.5, 21.0)	0.006
	Model 1	107	113	137	14.6	(5.7, 23.6)	0.002
	Model 2	99	108	128	14.2	(5.3, 23.1)	0.002
	Model 3	94	102	111	8.6	(2.2, 15.0)	0.009
SAT, cm^2	Mean (unadjusted)	123	111	128	2.5	(−6.0, 11.1)	0.558
	Model 1	128	119	143	7.4	(−0.8, 15.6)	0.078
	Model 2	136	128	148	5.8	(−2.6, 14.2)	0.177
	Model 3	130	121	130	0.0	(−5.4, 5.4)	0.991
VSR	Mean (unadjusted)	0.922	1.059	1.124	0.101	(0.033, 0.169)	0.004
	Model 1	0.867	0.996	1.040	0.087	(0.019, 0.155)	0.013
	Model 2	0.712	0.871	0.908	0.100	(0.031, 0.168)	0.005
	Model 3	0.711	0.871	0.907	0.100	(0.030, 0.169)	0.005

Adjusting covariates: Model 1: age (years), CT type; Model 2: education (years), treated DM (yes/no), frequency of physical activity in leisure time (often, occasional, rare-to-never), and drinking habit (current, former, never) in addition to Model 1; Model 3: body mass index (kg/m^2) in addition to Model 2. Abbreviations: T1, T2, and T3 denote first, second, and third tertiles of pack-years of smoking among former smokers. WC, waist circumference; WHR, waist-to-hip ratio; VAT, area of abdominal visceral adipose tissue (cm^2); SAT, area of abdominal subcutaneous adipose tissue (cm^2); VSR, VAT-SAT ratio.
Trend Ps were calculated using an ordinal variable for the 4 groups (never, tertiles of smokers) in the linear regression models.
[a] Estimates for WHR were obtained using 100-times imputed plausible WHR values for the 12 former smokers with missing data for WHR.

smokers. The reason we observed a strong association in former smokers may be related to post-cessation weight gains. An important finding of our study was that, among former smokers, VAT was significantly greater in those with higher lifetime smoking even after adjusting for BMI. Former smokers with a greater amount of lifetime smoking, and thus likely being more nicotine-dependent, are well documented to be at risk of gaining more weight after tobacco cessation (Audrain-McGovern and Benowitz, 2011; Chiolero et al., 2008), making them prone to abdominal obesity (Xu et al., 2007).

4.1. Limitations and strengths

Because of the observational and cross-sectional nature of this study, we were unable to prove the direction of causality of the observed association between smoking and abdominal obesity. Likewise, we were unable to refute the possibility of residual confounding, such as the one by socio-economic status, despite our attempts to minimize such influences, or the possibility that smoking merely offers a marker of a clustering of unhealthy lifestyle factors that favor abdominal obesity, such as lower levels of physical activity and poor dietary habits.(Chiolero et al., 2006) We conducted our study only on a relatively small sample size (especially for non-smokers) of men aged 40–64 years from one city, which may limit the applicability of our results to only men with similar age and demographics to our sample. Furthermore, the possibility of selection bias needs to be considered when generalizing our findings as the participation rate of the study was 46%. Another limitation relates to the fact that our method of assessing smoking status and pack-years relies primarily on self-report, thus, leading to potential misclassification. Although we attempted to minimize it by verifying the participant's response by trained technicians with the participant, additional use of biochemical verification and/or information from participant's proxy could yield more accurate classification. Strengths of our study include the population-based enrollment, use of a standardized protocol in assessing outcomes, such as CT-based VAT and SAT, and other adjusting covariates.

5. Conclusions

We found that greater lifetime smoking was cross-sectionally associated with a greater degree of abdominal obesity in a relatively lean population-based sample of Japanese men. Our findings, consistent with previous studies, suggest that those with a greater amount of lifetime smoking tend to show metabolically more adverse fat distributions linked to cardiometabolic diseases. Although smoking is commonly associated with lower BMI, our findings and the other well-known health hazards of smoking suggest that emphasis should be placed on avoiding the initiation of smoking or, failing that, minimizing the amount of lifetime smoking.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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Appendix B. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.pmedr.2016.06.013.

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