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The combined relations of adiposity and smoking on mortality

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Abstract

Background—Smoking and high adiposity are strong independent health risk factors but are also interrelated. Smoking is related to a lower body mass index (BMI) but not necessarily with a smaller waist circumference. Smoking cessation is associated with increased body weight and substantial increase in waist circumference. How this affects mortality risk is unknown.

Objective—This study examined the combined relations of smoking status with BMI and waist circumference and smoking status to all-cause mortality.

Design—Data were from 149,502 men and 88,184 women, aged 51–72 participating in the NIH-AARP Diet and Health Study. All-cause mortality was assessed over 10 years of follow-up from 1996 to 2006.

Results—Current smokers with a BMI<18.5 kg/m^2 or a BMI ≥35 kg/m^2 had a 6 to 8 times higher mortality risk compared to persons within the normal BMI range who never smoked. Current smokers with a large waist circumference had about a 5 times higher mortality risk compared to never smokers with a waist circumference in the second quintile.

Conclusion—Both smoking and adiposity are independent predictors of mortality but the combination of current or recent smoking with a BMI greater or equal to 35 kg/m^2 or a large waist circumference is related to an especially high mortality risk.

INTRODUCTION

The prevalence of overweight and obesity is increasing across the age spectrum (1,2). Overweight and obesity have been associated with increased risk of diabetes, heart disease,

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AK conceptualized the idea, analyzed the data and wrote the first draft of the paper; MFL conceptualized the idea, contributed to the data analyses, interpreted the data and contributed to drafts of the article; AS initiated the NIH-AARP Diet and Health Study interpreted the statistical analyses and reviewed drafts of the paper; KFA and JThMvE interpreted the statistical analyses and reviewed drafts of the paper; ARH helped conceptualize the NIH-AARP Diet and Health Study, interpreted the statistical analyses and reviewed drafts of the paper; TBH contributed to the conceptualization of the idea, interpreted the data and contributed to drafts of the article.

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arthritis, and cancer (3–5). However, the association between body weight and mortality remains controversial. Most previous studies have found an increased risk of mortality among underweight and obese people (6–8). However, not all studies found an increased risk of mortality among overweight persons. In addition to total body fat, fat distribution may be an important determinant of morbidity and mortality. Increased abdominal fat has been associated with metabolic disease risk (9,10) independent of overall adiposity (11,12). A large waist circumference has also been related to increased mortality risk (13,14).

Cigarette smoking is a major lifestyle risk factor strongly associated with morbidity and mortality (15). Current smoking and adiposity are independent health risk factors but are also interrelated. Smoking is associated with both a lower body weight (16,17) and an increased risk of death and therefore plays an important role in the association between adiposity and mortality. There seems to be only a weak association between BMI and mortality in current smokers while the association is much stronger in non-smokers (6,7). Smoking cessation is associated with increased body weight due to increased body fat (18). While current smoking is related to a lower body mass index (BMI), it is not necessarily associated with a smaller waist circumference (16,19,20). In fact, there is some evidence to suggest that smoking is related to visceral fat accumulation (21). A recent study showed that smoking cessation is associated with a substantial increase in waist circumference (22). How this affects mortality risk and whether this is independent of total adiposity is unknown. The combined relations of BMI and smoking on mortality have not been studied extensively (23) and to our knowledge the combined effects of waist circumference and smoking have not been previously studied.

Using data from the NIH-AARP Diet and Health Study we examined the joint effects of BMI and smoking status and waist circumference and smoking status on all-cause mortality. The relations with waist circumference were examined after adjustment for BMI to determine whether the combined relations of waist circumference and smoking on mortality were independent of overall adiposity.

METHODS

Study population

The National Institutes of Health-AARP (formerly known as the American Association of Retired Persons) Diet and Health Study was initiated in 1995–1996 when an extensive baseline questionnaire was mailed to 3.5 million AARP members between 50 and 71 years old who resided in one of six US states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) or two metropolitan areas (Atlanta, GA, and Detroit, MI) (24). Out of 617,119 questionnaires returned (17.6%), 567,169 (16.2%) were satisfactorily completed. In 1996–1997, a second questionnaire was sent to participants who successfully completed the baseline questionnaire to collect additional information on diet, family history of cancer, anthropometry (including waist circumference), physical activity, and use of menopausal hormone therapy. A total of 334,908 respondents completed the second questionnaire. We excluded 83,860 persons who provided no data on waist circumference, those with a waist circumference less than 60 centimeters (n=549), those with missing data on height or weight (n=4,425), and those with a BMI less than 15 kg/m^2 or higher than 60 kg/m^2 (n=543). Persons with extreme values for waist circumference and BMI were excluded because of biological plausibility. Furthermore, 7,845 persons with missing smoking data were excluded, resulting in 237,686 participants for the present analysis. The NIH-AARP Study was approved by the Special Studies Institutional Review Board of the U.S. National Cancer Institute.

Measures

Mortality—From 1996–1997 through December 31, 2006, vital status was determined by annual linkage of the cohort to the Social Security Administration Death Master File on deaths in the United States (25) and follow-up searches of the National Death Index. We estimate that the follow-up for deaths in our cohort is more than 93% complete (26,27).

Body mass index—Current height was reported in feet and inches; and weight to the nearest pound. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m^2) and divided into 6 categories: <18.5, 18.5–<23.5, 23.5–<25, 25–<30, 30–<35, and ≥35 kg/m^2. In accordance with the paper by Adams et al we used the group with a BMI between 23.5 and 25 kg/m^2 as the reference group (6).

Waist circumference—Using a pictured instruction, participants were requested to measure their waist with a tape measure one inch above the navel while standing and to report values to the nearest quarter inch. Self-reported waist circumference has been found to be a valid assessment of measured waist (28,29). For example, a study among 123 men aged 40–75 years and 140 women aged 41–65 years reported crude Pearson correlation coefficients comparing self-reported and measured waist circumference of 0.95 for men and 0.89 for women (30). Sex-specific quintiles of waist circumference were created and the second quintile was used as the reference group (31).

Smoking—Information on cigarette smoking included the number of years and the number of cigarettes per day a person smoked. Smoking status was categorized as never smoker, former smoker who stopped smoking 10 or more years ago, former smoker who stopped smoking less than 10 years ago, and current smoker. Smoking intensity, defined as the number of cigarettes per day a person smoked, was categorized as 1–10, 11–20, 21–30, 31,40, 41–60, and 61 or more.

Covariates—Information on covariates was collected using a self-administered, mailed questionnaire. Sociodemographic variables included age and race or ethnic group (non-Hispanic white, non-Hispanic black, Hispanic, Asian, and Pacific Islander or American Indian). Categories of level of education were 11 years or less, 12 years or completed high school, post-high school or some college, college graduate, and postgraduate. Physical activity was assessed by a question in the baseline questionnaire about how often a person participated in physical activities at work or home including exercise, sports, and activities such as carrying heavy loads for at least 20 minutes that caused increases in breathing, heart rate, or working up a sweat during a typical month in the past 12 months. Categories of physical activity were never, rarely, 1–3 times per month, 1–2 times per week, 3–4 times per week, and 5 or more times per week. Alcohol consumption over the past 12 months was assessed as part of a food frequency questionnaire (24). From the total alcohol intake in grams per day, 4 categories were created: 0, 0–<5, 5–<15 and ≥15 g/day. Information on chronic diseases was collected by means of the following question: ‘Have you ever been told by a doctor that you had any of the following conditions?’ Diseases included cancer, heart disease, stroke, diabetes, emphysema, and renal failure.

Statistical Analysis

Differences in baseline characteristics between BMI, waist circumference, or smoking status groups were tested using chi-square tests for categorical and analysis of variance for continuous variables. Age-standardized mortality rates were calculated standardized to the age distribution of the cohort in men and women using 5 year age categories. Cox proportional hazard models were fitted to study the individual and joint effects of BMI and smoking and waist circumference and smoking on time to death in men and women. People were cross-classified

based on their smoking status and BMI or waist circumference group. The group never smokers with a normal BMI or waist circumference was used as the reference group. Analyses were adjusted for age, race or ethnic group, smoking intensity, education, physical activity, and alcohol consumption. For the analyses with waist circumference we additionally adjusted for height and BMI. In additional analyses, people with chronic diseases at baseline were excluded. We further excluded the first two years of follow-up to exclude persons who died during the first two years. The proportional hazards assumption was investigated by testing the constancy of the log hazard ratio over time by means of log-minus-log survival plots; according to the test, the proportional hazard assumption was not violated. Analyses were performed using SPSS, version 15.0 (SPSS Inc., Chicago, IL).

RESULTS

During 10 years of follow-up, 19,699 men and 7,371 women died. The baseline characteristics of the study population according to BMI, waist circumference and smoking status are shown in Table 1. Men and women with the highest BMI or the largest waist circumference had a lower education, were less likely to currently smoke, were less physically active, and had a lower alcohol intake compared to those with a normal BMI (18.5–<25 kg/m^2) or a smaller waist circumference (all $p<0.01$). Current smokers had a lower education, lower physical activity levels, and a higher alcohol intake compared to never smokers (all $p<0.01$).

After adjustment for BMI, waist circumference, and all covariates, former and current smoking were associated with significantly higher mortality risks in both men and women (not tabulated). Compared to never smokers, former smokers who stopped smoking more than 10 years ago had a more than 80% higher mortality risk (men: HR:1.96, 95%CI:1.79, 2.14; women: HR:1.83, 95%CI:1.37, 2.43), former smokers who stopped smoking less than 10 years ago had a more than 3 times higher risk (men: HR:3.42, 95%CI:3.11, 3.75; women: HR:3.13, 95%CI:3.43, 6.12), and the highest mortality risks were found among current smokers (men: HR:4.85, 95%CI:4.41, 5.34; women: HR:4.58, 95%CI:3.43, 6.12). The individual relations of BMI and waist circumference on mortality have been shown previously, using the same data (6,32). Adams et al showed that being underweight (BMI<18.5 kg/m^2), overweight, or obesity were associated with increased risk of death (6) and we showed that a large waist circumference was associated with about a 25% higher mortality risk after adjustment for BMI (32). For the present study, two-way interactions between BMI and smoking and waist circumference and smoking were formally tested and were all statistically significant ($p<0.01$). Interactions between the combination of BMI and smoking and sex were also statistically significant ($p<0.01$) and between the combination of waist circumference and smoking and sex was borderline significant ($p=0.06$).

Age standardized mortality rates and adjusted hazard ratios of mortality for the combined relations of smoking and BMI are shown in Table 2. Overall mortality rates were higher in the very low and high BMI groups. In each BMI group, mortality rates were highest in former smokers who stopped smoking less than 10 years ago and current smokers. Compared to never smoking men with a BMI of 23.5 to less than 25 kg/m^2, never smokers with a BMI between 25 and 30 kg/m^2 had an increased mortality risk (HR:1.11, 95%CI:1.01, 1.22) as well as men with a BMI between 30 and 35 kg/m^2 (HR:1.41, 95%CI:1.26, 1.59) or a BMI greater than or equal to 35 kg/m^2 (HR:2.44, 95%CI:2.10, 2.82). A significantly higher mortality risk was also found in men in the normal BMI range (23.5–<25 kg/m^2) who were former smokers who stopped smoking 10 years or more ago (HR:2.15, 95%CI:1.89, 2.45), former smokers who quit smoking less than 10 years ago (HR:4.09, 95%CI:3.53, 4.74) and current smokers (HR:6.15, 95%CI:5.34, 7.08). The highest mortality risks were found in current smokers and particularly in current smokers who were underweight (<18.5 kg/m^2) (HR:8.36, 95%CI:6.27, 11.15) and those with morbid obesity (≥35 kg/m^2) (HR:8.13, 95%CI:6.61, 10.01). A similar pattern was

found in women. In additional analyses we excluded people with chronic diseases at baseline. In this healthy group, results were similar and people with a BMI less than 18.5 kg/m^2 still had a significantly higher mortality risk across all smoking groups (data not shown). In additional analyses we further excluded the first two years of follow-up to exclude persons who died during the first two years; very similar results were found (data not shown).

The analyses on the combined effects of waist circumference and smoking on mortality were additionally adjusted for BMI. In each waist circumference group, mortality rates were highest in current smokers in both men and women (Table 3). In never smokers and former smokers who stopped smoking 10 or more years ago, mortality rates were highest in people with a large waist circumference. In former smokers who stopped smoking less than 10 years ago and current smokers, higher mortality rates were also found in those with the smallest waist circumferences. Compared to never smoking men with a waist circumference in the second quintile, never smokers with the largest waist circumference had a significantly higher mortality risk (men: HR:1.35, 95%CI:1.22, 1.49; women: HR:1.47, 95%CI:1.28, 1.69). Risks increased in former smokers with a large waist circumference and the highest mortality risks were found among current smokers with a large waist circumference (men: HR:5.58, 95%CI: 4.87, 6.39; women: HR:5.27, 95%CI:3.82, 7.27). High mortality risks were also found in current smokers with the smallest waist circumference (men: HR:6.13, 95%CI:5.39, 6.96; women: HR:5.73, 95%CI:4.19, 7.84). A similar pattern was found in people without chronic conditions (data not shown). Similar results were found when the first two years of follow-up were excluded (data not shown).

DISCUSSION

In this large 10-year prospective cohort study, the joint relations of adiposity and smoking were examined. Compared to people within the normal BMI range who never smoked, mortality rates increased with increments of BMI and increased from never to former to current smoking. A similar pattern was found for waist circumference. Current smokers with a BMI less than 18.5 kg/m^2 or a BMI greater or equal to 35 kg/m^2 had a 6 to 8 times higher mortality risk compared to persons within the normal BMI range who never smoked. Current smokers with a large waist circumference had a more than 5 times higher mortality risk compared to never smokers with a waist circumference in the second quintile, independent of BMI.

Several previous studies have shown the BMI-mortality association stratified by smoking status (6,7). However, only a few studies specifically presented the joint effects of BMI and smoking on mortality (23); the joint effects of waist circumference and smoking on mortality risk have not been shown previously. A study among Japanese-American men reported that compared to never smokers with a BMI between 21.2 and 26.3 kg/m^2, mortality risk was significantly higher in men who smoked regardless of BMI levels (33). Another recent study showed the highest mortality risk among obese people who smoked; risks were especially high for circulatory disease mortality in people aged less than 65 years (23). That study did not show the results for the group with a BMI less than 18.5 kg/m^2.

Previous studies that examined the BMI-mortality association showed significantly higher mortality rates among underweight persons (8,28). One of the explanations for the higher mortality risk among underweight people is residual confounding by smoking. People who smoke have a higher mortality risk and are more often underweight. In the present study, we observed a higher mortality risk in low BMI groups across all smoking groups compared to never smokers within the normal BMI range. That smoking distorts the relation between BMI and mortality is seen among former smokers who stopped smoking less than 10 years ago and current smokers where mortality rates were not markedly different between normal weight, overweight and obese (BMI 30–<35 kg/m^2) persons. This might be due to residual confounding

by smoking which can not be completely ruled out even though we additionally adjusted for smoking intensity. For example, depth of inhalation or genetic susceptibility could influence the effect of smoking on weight and mortality and were not accounted for. A further explanation for the higher mortality risk in persons with a low BMI is reverse causation by prevalent chronic disease (6). However, when we excluded people with chronic diseases or excluded the first two years of follow-up, people with a BMI less than 18.5 kg/m^2 still had a significantly higher mortality risk.

For waist circumference, a non-linear pattern was found in former smokers who stopped less than 10 years ago and current smokers, with particularly high mortality rates among people with a very small or a very large waist circumference. This might also be due to a higher prevalence of chronic disease in these groups which may have caused weight loss in these groups. However, a similar pattern was found in people without chronic conditions or after excluding the first two years of follow-up. Information on pre-existing chronic diseases was based on self-report and the comprehensiveness of the panel of diseases considered was limited. In a better-defined healthy group, a stronger linear association with mortality across categories of BMI and waist circumference and mortality may have been found.

The analyses on the combined effects of waist circumference and smoking on mortality were adjusted for BMI. Thus the effect of waist circumference across smoking groups was independent of total adiposity. Previous studies showed that smokers have more central obesity than nonsmokers (16,19,20) and there is some evidence that current smoking is related to visceral fat accumulation (21). In the present study, we did not find a larger waist circumference among current smokers than in never smokers and our data do not suggest that waist circumference has a stronger relation with mortality in current smokers than in never smokers.

Current smokers had the highest mortality rates across all BMI and waist circumference groups. Smoking cessation was associated with significantly lower mortality risk in every BMI or waist circumference group and the longer someone was a former smoker, the lower the mortality risk (34). Losing weight may decrease mortality risk in current smokers; however, smoking cessation will be related to a stronger decrease in risk. Smoking cessation has been associated with weight gain (35) and increase in waist circumference (22) possibly due to decreased metabolic rate and increased caloric intake (18). However, weight gain is not likely to counteract the health benefits of smoking cessation. In the present study we observed lower mortality rates among former smokers with a high BMI or a large waist circumference than in current smokers within the normal BMI range or a normal waist circumference. A recent study, using data from the National Health and Nutrition Examination Survey, showed that a substantial decrease in smoking prevalence had only a small effect on increases in the prevalence of obesity and decreases in the prevalence of healthy weight (36).

This study has some limitations. Height and weight were self-reported, and waist circumference was self-measured by participants. Self reported height and weight are generally known to be accurate, although heavy individuals are more likely to underreport their weight (37). Previous research also shows that the validity of self-measured waist circumference is fairly high (30).

In conclusion, both smoking and adiposity are independent predictors of mortality but the combination of current or recent smoking with a BMI greater or equal to 35 kg/m^2 or a large waist circumference is related to an especially high mortality risk.

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TABLE 1

Baseline characteristics according to BMI, waist circumference, and smoking for men and women [1]

	BMI (kg/m^2)						Waist circumference quintile [2]					Smoking			
	<18.5	**18.5–<23.5**	**23.5–<25**	**25–<30**	**30–<35**	**≥35**	**1**	**2**	**3**	**4**	**5**	**Never**	**Former ≥ 10 yrs**	**Former<10 yrs**	**Current**
MEN															
N	864	23,681	23,877	72,948	22,195	5,937	26,867	30,293	30,411	28,849	33,082	46,905	69,793	18,793	14,011
Age (yrs), Mean (SD)	63.8 (5.1)	63.5 (5.3)	63.5 (5.2)	63.2 (5.2)	62.6 (5.2)	61.6 (5.2)	62.6 (5.4)	63.1 (5.2)	63.3 (5.2)	63.5 (5.2)	63.1 (5.2)	62.7 (5.3)	63.8 (5.1)	62.6 (5.3)	61.9 (5.4)
Non-Hispanic white, %	92.8	93.5	94.2	94.4	94.3	94.1	90.1	93.8	95.0	95.8	95.8	93.8	94.7	93.8	93.7
College or post graduate, %	54.1	55.9	53.3	47.2	40.9	38.2	51.0	50.4	49.2	48.7	43.0	60.1	46.0	38.2	34.0
BMI (kg/m^2), Mean (SD)	17.3 (0.9)	22.1 (1.1)	24.2 (0.4)	27.1 (1.4)	31.9 (1.4)	38.5 (3.6)	23.3 (2.2)	25.1 (2.1)	26.4 (2.4)	27.7 (2.6)	31.6 (4.3)	26.6 (4.0)	27.2 (4.0)	27.7 (4.2)	26.2 (4.1)
Waist circumference (cm) mean (SD)	87.8 (10.5)	87.5 (6.4)	91.7 (6.0)	98.2 (7.4)	108.8 (8.5)	122.2 (11.8)	84.3 (3.4)	90.9 (1.3)	95.9 (1.3)	101.8 (2.0)	113.8 (8.0)	96.7 (10.7)	98.5 (10.9)	100.1 (11.4)	96.1 (11.5)
Current smokers, %	16.8	13.7	10.2	8.3	7.9	6.9	13.7	9.6	8.3	7.6	8.1	-	-	-	-
Physical activity (times/week), Mean (SD)	2.7 (2.0)	3.1 (2.0)	3.0 (1.9)	2.7 (1.9)	2.3 (1.9)	1.8 (1.8)	3.2 (1.9)	3.0 (1.9)	2.8 (1.9)	2.6 (1.9)	2.2 (1.9)	2.8 (1.9)	2.9 (1.9)	2.5 (1.9)	2.0 (1.9)
Alcohol intake ≥15 g/ day, %	29.3	30.1	31.3	29.6	25.5	20.1	28.6	29.8	29.8	29.9	26.9	20.5	32.1	32.0	37.5
WOMEN															
N	1,334	30,788	12,936	27,329	10,545	5,252	17,069	18,077	19,821	15,873	17,344	40,860	24,865	10,986	11,473
Age (yrs), Mean (SD)	63.2 (5.5)	62.6 (5.4)	62.9 (5.3)	62.9 (5.3)	62.7 (5.3)	61.7 (5.3)	61.9 (5.4)	62.5 (5.3)	63.0 (5.2)	63.2 (5.2)	62.9 (5.3)	62.9 (5.3)	63.0 (5.3)	62.3 (5.3)	61.8 (5.4)
Non-Hispanic white, %	94.5	94.4	93.4	91.6	89.6	88.8	93.4	93.4	91.7	92.1	91.8	91.8	93.4	92.4	92.7
College and post graduate, %	41.4	39.0	34.2	31.9	29.4	27.8	39.0	37.4	33.5	31.8	29.7	36.2	37.7	28.4	26.1
BMI (kg/m^2), Mean (SD)	17.7 (0.8)	21.6 (1.3)	24.3 (0.4)	27.2 (1.4)	32.1 (1.4)	39.5 (4.3)	21.5 (2.3)	23.3 (2.4)	25.4 (3.0)	27.5 (3.4)	32.4 (5.6)	26.1 (5.2)	26.1 (5.2)	26.4 (5.2)	24.6 (4.6)
Waist circumference (cm) mean (SD)	69.6 (7.8)	74.8 (7.2)	81.4 (7.5)	88.5 (9.0)	98.2 (10.1)	109.6 (13.4)	68.6 (3.0)	76.3 (1.9)	83.4 (2.1)	91.0 (2.3)	105.5 (9.1)	84.5 (13.2)	85.1 (13.4)	86.9 (13.8)	83.0 (12.8)

	BMI (kg/m^2)						Waist circumference quintile [2]					Smoking			
	<18.5	**18.5–<23.5**	**23.5–<25**	**25–<30**	**30–<35**	**≥35**	**1**	**2**	**3**	**4**	**5**	**Never**	**Former ≥ 10 yrs**	**Former<10 yrs**	**Current**
Current smokers, %	27.4	16.4	13.0	11.3	8.7	7.1	16.0	13.2	13.0	12.4	10.5				
Physical activity (times/week), Mean (SD)	2.5 (2.1)	2.7 (2.0)	2.5 (1.9)	2.3 (1.9)	1.9 (1.8)	1.5 (1.7)	2.9 (2.0)	2.7 (1.9)	2.4 (1.9)	2.2 (1.9)	1.8 (1.8)	2.5 (1.9)	2.6 (1.9)	2.3 (1.9)	1.9 (1.8)
Alcohol intake ≥15 g/ day, %	18.1	16.1	13.5	10.8	7.0	4.6	13.3	14.3	13.0	12.0	8.9	7.3	15.3	16.0	20.4

[1] Differences in baseline characteristics between BMI, waist circumference, or smoking status groups were tested using chi-square tests for categorical and analysis of variance for continuous variables: all p<0.01

[2] Quintile cut-off points men: 88.9, 94.0, 99.1, 106.7 cm; women: 73.7, 80.0, 87.0, 95.9 cm

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TABLE 2

Mortality rates and hazard ratios and 95% confidence intervals of mortality according to the combination of BMI and smoking [1,2]

	BMI																			
	<18.5				18.5–<23.5				23.5–<25				25–<30				30–<35				≥35			
Smoking status	**Rate[3]**	**HR**	**95% CI**		**Rate[3]**	**HR**	**95% CI**		**Rate[3]**	**HR**	**95% CI**		**Rate[3]**	**HR**	**95% CI**		**Rate[3]**	**HR**	**95% CI**		**Rate[3]**	**HR**	**95% CI**	
MEN																								
Never Former	1664	2.11	1.55	2.88	785	1.08	0.96	1.21	741	1.00			844	1.11[4]	1.01	1.22	1137	1.41	1.26	1.59	2055	2.44	2.10	2.82
≥10 yrs Former	1409	2.96	2.18	4.00	1163	2.45	2.16	2.79	1038	2.15	1.89	2.45	1148	2.22	1.97	2.50	1526	2.67	2.35	3.02	2132	3.51	3.05	4.05
<10 yrs	5820	9.64	7.01	13.26	2943	5.46	4.74	6.30	2185	4.09	3.53	4.74	2155	3.92	3.46	4.44	2244	3.79	3.30	4.35	2990	5.00	4.21	5.93
Current	4910	8.36	6.27	11.15	3424	6.48	5.66	7.41	3179	6.15	5.34	7.08	2748	5.21	4.58	5.94	3171	5.87	5.05	6.83	4522	8.13	6.61	10.01
WOMEN																								
Never Former	699	1.51	1.08	2.13	517	1.17	1.02	1.35	454	1.00			531	1.14[3]	0.99	1.31	650	1.33	1.13	1.56	1117	2.18	1.84	2.58
≥10 yrs Former	878	3.01	1.85	4.89	612	2.09	1.52	2.87	563	1.85	1.33	2.57	712	2.20	1.61	3.01	936	2.71	1.96	3.75	1446	3.86	2.77	5.38
<10 yrs	4064	11.98	7.88	18.22	1523	4.66	3.39	6.40	986	2.91	2.06	4.11	1218	3.41	2.48	4.69	1482	3.88	2.78	5.41	2141	5.09	3.59	7.23
Current	3124	9.41	6.54	13.53	1923	5.86	4.28	8.02	1759	5.35	3.85	7.43	1807	5.11	3.71	7.03	2113	5.85	4.14	8.25	2398	6.61	4.48	9.76

[1] Cox proportional hazard models adjusted for age, race, education, smoking intensity, physical activity, and alcohol consumption

[2] The interaction between the combination of BMI and smoking and sex were statistically significant ($p<0.01$)

[3] Age standardized mortality rates per 100,000 person years, standardized to the age distribution of the cohort in men and women

[4] Hazard ratios among never smokers when we further split up the overweight group. Men: BMI 25–<27.5: HR: 1.04, 95%CI: 0.94, 1.15, BMI 27.5–<30: HR: 1.24, 95%CI: 1.11, 1.39; Women: BMI 25–<27.5: HR: 1.09, 95%CI: 0.94, 1.27; BMI 27.5–<30: HR: 1.23, 95% CI: 1.04, 1.45

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TABLE 3

Mortality rates and hazard ratios and 95% confidence intervals of mortality according to the combination of waist circumference and smoking [1,2]

	Waist circumference quintile															
	1				2				3				4				5			
Smoking status	**Rate[3]**	**HR**	**95% CI**		**Rate[3]**	**HR**	**95% CI**		**Rate[3]**	**HR**	**95% CI**		**Rate[3]**	**HR**	**95% CI**		**Rate[3]**	**HR**	**95% CI**	
MEN																				
Never Former	713	0.92	0.83	1.02	799	1.00			829	1.01	0.91	1.12	901	1.06	0.96	1.18	1265	1.35	1.22	1.49
≥10 yrs Former	1066	2.11	1.86	2.38	1070	2.00	1.78	2.26	1075	1.92	1.71	2.16	1229	2.07	1.84	2.33	1624	2.40	2.13	2.71
<10 yrs	2618	4.68	4.08	5.38	2036	3.50	3.06	4.01	2267	3.78	3.31	4.31	2132	3.39	2.98	3.87	2617	3.71	3.27	4.21
Current	3317	6.13	5.39	6.96	2931	5.15	4.50	5.88	2757	4.69	4.08	5.38	2793	4.68	4.06	5.40	3640	5.58	4.87	6.39
WOMEN																				
Never Former	478	1.04	0.90	1.20	477	1.00			513	1.01	0.88	1.15	528	1.00	0.87	1.15	850	1.47	1.28	1.69
≥10 yrs Former	580	1.86	1.34	2.57	611	1.86	1.36	2.56	636	1.84	1.34	2.52	741	2.00	1.46	2.74	1061	2.50	1.83	3.42
<10 yrs	1473	4.19	3.01	5.82	1262	3.50	2.53	4.84	1172	3.11	2.26	4.28	1271	3.11	2.26	4.29	1775	3.89	2.83	5.32
Current	1974	5.73	4.19	7.84	1726	4.87	3.55	6.69	1872	5.01	3.66	6.85	1850	4.78	3.47	6.57	2338	5.27	3.82	7.27

[1] Cox proportional hazard models adjusted for age, race, education, BMI, smoking intensity, physical activity, and alcohol consumption

[2] The interaction between the combination of waist circumference and smoking and sex was borderline significant (p=0.06)

[3] Age standardized mortality rates per 100,000 person years, standardized to the age distribution of the cohort in men and women