Title

Association of total adiposity and computed tomographic measures of regional adiposity with incident cancer risk: a prospective population-based study of older adults1

Journal

Applied Physiology Nutrition and Metabolism, 39(6)

ISSN

1715-5312

Authors

Murphy, Rachel A
Bureyko, Taylor F
Miljkovic, Iva
et al.

Publication Date

2014-06-01

DOI

10.1139/apnm-2013-0360

Peer reviewed

Published in final edited form as:
Appl Physiol Nutr Metab. 2014 June ; 39(6): 687–692. doi:10.1139/apnm-2013-0360.

Association of total and computed tomographic measures of regional adiposity with incident cancer risk: a prospective population-based study of older adults

Rachel A. Murphy[1], **Taylor F. Bureyko**[2], **Iva Miljkovic**[3], **Jane A. Cauley**[3], **Suzanne Satterfield**[4], **Trisha F. Hue**[5], **Heidi D. Klepin**[6], **Steven R. Cummings**[5], **Anne B. Newman**[3], **Tamara B. Harris**[1], and **Health, Aging, and Body Composition Study**

[1]Laboratory of Epidemiology, and Population Sciences, Intramural Research Program, National Institute on Aging, 7201 Wisconsin Ave, 3C-309, Bethesda, MD, 20814, USA

[2]Department of Agricultural, Food and Nutritional Science, University of Alberta, 4-126 Li Ka Shing Center, Edmonton, AB, Canada T6G 2E1

[3]Center for Aging and Population Health, Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA, 15261, USA

[4]Department of Preventive Medicine, University of Tennessee, Health Science Center, Memphis, TN, 38163, USA

[5]California Pacific Medical Center Research Institute, PO Box 7999, San Francisco, CA, 94120, USA

[6]Comprehensive Cancer Center, Wake Forest School of Medicine, Winston-Salem, NC, 27157, USA

Abstract

Obesity is associated with increased risk of many types of cancer. Less is known regarding associations between adipose depots and cancer risk. We aimed to explore relationships between adipose depots, risk of cancer and obesity-related cancer (per NCI definition) in participants initially aged 70–79 without prevalent cancer (1,179 men, 1,340 women), and followed for incident cancer for 13 years. Measures included body mass index (BMI), total adipose tissue from dual-energy X-ray absorptiometry and computed tomography measures: visceral adipose tissue (VAT), abdominal subcutaneous adipose tissue (SAT), thigh intermuscular adipose tissue and thigh muscle attenuation (Hounsfield Unit, HU), low HU indicates fatty infiltration. Hazard ratios (HR) and 95% confidence intervals (CIs) were estimated by Cox proportional hazards regression adjusted for demographics, lifestyle variables and medical conditions. During follow-up 617 participants developed cancer of which 224 were obesity-related cancers. Total adipose tissue and VAT were positively associated with cancer risk among women (HR 1.14, 95% CI 1.01–1.30 per SD increase, HR 1.15, 95% CI 1.02–1.30 per SD increase). There were no associations with cancer risk among men. Total adipose tissue was positively associated with obesity-related cancer

Correspondence: Rachel A Murphy, PhD Laboratory of Population Science National Institute on Aging 7201 Wisconsin Ave, 3C-309 Bethesda, MD 20814 Telephone: 301.496.6524, Rachel.murphy@nih.gov.

risk among women (HR 1.23, 95% CI 1.03–1.46 per SD increase). VAT was positively associated with obesity-related cancer risk among men (HR 1.30, 95% CI 1.06–1.60 per SD increase) and remained associated even with adjustment for BMI (HR 1.40, 95% CI 1.08–1.82 per SD increase). These findings provide insight into relationships between specific adipose depots and cancer risk and suggest differential relationships among men and women.

Keywords

Obesity; weight; adipose; body fat; cancer incidence; cancer risk; aging

Introduction

Excess body weight is a strong risk factor for cancer development. A large meta-analysis of over 280,000 cancer cases showed greater body mass index (BMI) was associated with increased risk of many types of cancer (Renehan et al. 2008). Evidence is particularly strong for cancers of the breast, endometrium, esophagus, pancreas, colon and rectum, kidney, thyroid, and gallbladder (Bianchini et al. 2002; Pan et al. 2004; National Cancer Institute, 2012). However, there are limitations to using BMI as a proxy for adiposity, including that it does not provide information on adipose tissue distribution.

Knowledge of cancer risk in relation to specific adipose tissue depots may be of particular importance in old age when there is a propensity for adipose tissue redistribution. In general, visceral adipose tissue (VAT) and intermuscular adipose tissue (IMAT, adipose between muscle bundles) increase, while the amount of subcutaneous adipose tissue (SAT) decreases (Kuk et al. 2009). As a result, there is controversy over the clinical utility of BMI as an indicator of obesity in older adults (Zamboni et al. 2005). It is unclear if age-related changes in body composition impact estimation of obesity and cancer risk.

The purpose of this study was to provide a new perspective on obesity and cancer risk by examining radiographically derived measures of adiposity and incident cancer in a prospective study of older adults. We aimed to 1) determine associations between total body adipose tissue, VAT, SAT, and thigh IMAT with obesity-related cancer risk, 2) explore adiposity measures in relation to risk of all incident cancer as several studies have reported associations between BMI and risk of non-obesity-related cancers (Olson et al. 2002; Pan et al. 2004; Kabat et al. 2008), and 3) determine if adipose depots convey risk beyond that attributable to BMI. We hypothesized that metabolically active adipose tissue, specifically VAT and thigh IMAT would be independently and positively associated with risk of cancer and obesity-related cancer.

Methods

Study population

The Health, Aging, and Body Composition Study (Health ABC) is a prospective, population study that was designed to examine effects of body composition and weight-related health conditions on functional limitation in older adults. Between April 1997 and June 1998, 3,075 community-dwelling black and white men and women aged 70–79 years were

enrolled. Participants were drawn from a random sample of white Medicare beneficiaries and all black Medicare eligible residents in the areas surrounding Memphis, TN, and Pittsburgh, PA. Eligibility criteria included: 1) no reported difficulty walking one-quarter mile, climbing 10 steps or performing activities of daily living, 2) no history of active cancer treatment in the prior 3 years, 3) no plans to leave the study area for 3 years, and 4) no active participation in a lifestyle intervention trial. All participants provided informed consent; protocols were approved by the institutional review boards of the clinic sites.

Cancer ascertainment

Participants or their proxies were contacted every 6 months in person or by telephone and queried about any hospitalization and health conditions including new cancer diagnoses. Incident cancers were determined directly from hospital records or from the underlying cause of death from death certificates. Diagnoses were confirmed by review of imaging and biopsy reports. Cancer cases excluding non-melanoma skin cancer were determined over 13 years of follow-up. Obesity-related cancer was defined according to the National Cancer Institute Obesity and Cancer Fact Sheet (National Cancer Institute, 2012) which includes cancer of the breast, endometrium, esophagus, pancreas, colon and rectum, kidney, thyroid, and gallbladder. Follow-up time was calculated as the difference between baseline and date of diagnosis for cancer cases or the difference between baseline and date of last contact or death for non-cancer cases.

Anthropometric measures

This study utilizes year 1 data on BMI, total fat from dual-energy X-ray absorptiometry (DXA), VAT and SAT area from abdominal computed tomography (CT), IMAT area and muscle attenuation (Hounsfield Units, HU) from thigh CT. BMI was calculated from height and weight measured by stadiometer and calibrated scale. Total adipose tissue was determined by DXA using a Hologic QDR4500A as previously reported (Visser et al. 1999; Salamone et al. 2000). CT imaging of the abdomen at the L4/L5 vertebrae and the thigh were performed with a Siemens Somatom or Picker PQ200S in Memphis and a General Electric 9800 Advantage in Pittsburgh. CT data were analyzed at the University of Colorado Health Sciences Center according to standardized protocols (Hill et al. 1999). Briefly, adipose areas in centimeters squared were calculated by multiplying the number of pixels by the pixel area using Interactive Data Language software (ITT Visualization Solutions, Boulder, CO, USA). Abdominal VAT was manually distinguished from SAT by tracing along the facial plane. The number of participants with each measure varies from 2,505 to 2,349 due to missing data. The mean attenuation of thigh muscle was recorded. Lower attenuation indicates greater fat infiltration of muscle.

Covariates

Demographic, lifestyle and other risk factors were determined from baseline questionnaire and the clinic visit. Variables included age, gender, race, study site and education (<high school, high school graduate or >high school). Lifestyle factors included smoking history (never, former or current), smoking duration (pack-years), alcohol consumption, and physical activity. Physical activity was assessed as kilocalories expended walking and climbing stairs in the week prior to baseline as described previously (Brach et al. 2004).

Comorbid conditions (diabetes, chronic obstructive pulmonary disease and other pulmonary disease, cardiovascular disease including coronary heart disease, congestive heart failure, and cerebrovascular disease) were determined from self-report, medications and clinical assessments.

Statistical Analysis

Differences in the distributions of baseline characteristics between participants with and without incident cancer were assessed using two-sided t-tests for continuous variables and chi-square test for categorical variables. Risk analyses were conducted per standard deviation (SD) increase in continuous adipose measures. Analyses were also conducted with adipose measures categorized into race and gender specific quartiles (Q, all cancers) or tertiles (T, obesity-related cancers due to fewer events) with P for linear trend across groups reported from the Wald statistic. Associations between baseline adiposity measures and time to diagnosis or date of last contact were estimated by hazard ratios (HR) and 95% confidence intervals (CI) using Cox proportional hazards models. Examination of Schoenfeld residuals and Kaplan Meier plots indicated that the proportional hazards assumption was met. Cox models were initially unadjusted (Model 1). Models were subsequently adjusted for demographics, lifestyle factors and co-morbid conditions (Model 2). Although BMI and adipose measures were correlated (Pearson correlation $r=-0.45$ for thigh HU to $r=0.89$ for total fat), we adjusted Model 2 for BMI to test the strength of associations of adipose measures and cancer risk beyond BMI. The variance inflation factor was <5 for all adipose measures except total adipose tissue in women (variance inflation=7.69). Sensitivity analyses were conducted excluding cancers diagnosed <2 years after baseline (N=118) to account for cancers that may have been clinically undetected at baseline. All analyses were performed with STATA version 12.1 (StataCorp, College Station, TX) with significance set at $P<0.05$.

Results

At baseline, 527 participants had prevalent cancer (cancer diagnosis within the previous 3 years) and were excluded. Over a mean (SD) and median follow-up of 9.74 (4.26) years and 11.7 years, 643 incident cancer were identified. Of this, 24 participants had unconfirmed cancer and were excluded. A further 5 participants were excluded due to incomplete smoking history resulting in an analytical sample of 1902 participants without incident cancer and 617 participants with incident cancer: 268 women (rate 19.2/1000 person years) and 349 men (33.1/1000 person years). During a mean (SD) and median follow-up of 10.3 (3.96) years and 12.4 years, 142 women (rate 10.0/1000 person years) and 82 men developed obesity-related cancer (7.03/1000 person years).

The mean age of the analytic sample was 74 years, 47% were male and 57% were white. Baseline characteristics for participants without and with incident cancer are presented in Table 1. Participants with incident cancer were predominately men and were more likely to report current or former smoking and longer smoking duration. Other characteristics including race/ethnicity, study site, education and BMI were similar between participants

with and without incident cancer. Cancers were predominately of the prostate (N=126), lung (N=110), colon and rectum (N=82), and breast (N=74).

The distribution of adipose tissue measures are shown in Table 2. Measures were stratified by race and gender due to significant interactions with adipose measures ($P<0.05$). There was a wide range for all measures reflecting a spectrum from underweight ($BMI<18.5 kg/m^2$) to class III obesity ($BMI \geq 40 kg/m^2$).

Risks of incident cancer per SD increase in continuous adipose measures are shown in Table 3. In unadjusted models (Model 1), greater total adipose tissue and SAT were associated with lower cancer risk in men while greater total adipose tissue and VAT were associated with increased cancer risk among women. All associations were attenuated with adjustment for risk factors (Model 2). Total adipose tissue and VAT remained positively associated with cancer risk among women in Model 2. However, additional adjustment for BMI attenuated risk for total adipose tissue (HR 1.18, 95% CI 0.87–1.61) and VAT (HR 1.09, 95% CI 0.94–1.28). Similar associations were observed in sensitivity analyses excluding cancers identified within the first 2 years, with the exception that SAT became positively associated with risk among women in sensitivity analyses (Supplementary Table 1).

Table 3 depicts associations between quartiles of adipose measures and risk of incident cancer (reference category Q1). Among men, Q2 and Q4 of total adiposity were associated with a lower risk of cancer in Model 1 but was attenuated in Model 2. Q2 and Q4 of SAT were both associated with lower risk of cancer in Model 1 and associations persisted for Q4 independent of risk factors (Model 2). Among women, Q4 of SAT was positively associated with cancer risk in Model 1 but was no longer significant with adjustment for risk factors. Q2 and Q4 of IMAT were associated with increased cancer risk (Model 1) but only Q2 remained associated in Model 2. Q3 of thigh HU was associated with lower risk of cancer in Model 1 only. There were no other significant associations.

Obesity-related cancer risks per SD increase in adipose measures are shown in Table 4. Among men, greater VAT was associated with increased obesity-related cancer risk (Models 1 and 2). Associations for VAT among men remained with adjustment for BMI (HR 1.40, 95% CI 1.08–1.82). Among women total adipose tissue was positively associated with obesity-related cancer risk but not independently of BMI (HR 1.06, 95% CI 0.70–1.61). Sensitivity analyses excluding obesity-related cancers identified within the first 2 years of study baseline showed comparable associations between adipose measures and obesity-related cancer risk (Supplementary Table 1).

Table 4 depicts associations between tertiles of adipose measurements (reference category T1) and obesity-related cancer. Among men T3 of total adipose tissue was marginally associated with increased obesity-related cancer risk in unadjusted and adjusted models while T2 and T3 of VAT were strongly associated with obesity-related cancer risk in both models. T2 and T3 of VAT remained associated with obesity-related cancer risk even following adjustment for BMI (HR 3.06, 95% CI 1.54–6.10, HR 3.31, 95% CI 1.53–7.16). Among women only T2 of IMAT was associated with obesity-related cancer risk among women and was not associated independent of BMI (HR 1.39, 95% CI 0.88–2.20).

Discussion

This study extends our understanding of relationships between obesity and cancer risk by investigating relationships in a well-characterized population of older adults with radiographic imaging of adipose depots. Our results suggest that adiposity may carry risk for cancers beyond those identified as obesity-related by the National Cancer Institute and further suggest a possible sex differential with respect to adipose and cancer risk. Among men, incident cancers were weighted toward non-obesity related cancer while women tended to develop obesity-related cancer. For all incident cancers there were largely null associations among men whereas there were positive associations for continuous measures of total adipose tissue, VAT and in sensitivity analyses, SAT among women. For every SD increase in total adipose tissue there was a 14% increase in cancer risk and for every SD increase in VAT there was a 15% increase in cancer risk. Total adipose tissue carried a slight increased risk of obesity-related cancer in both men and women. However, VAT was associated with risk of obesity-related cancer only among men and was a particularly strong risk factor: 30% increased risk for every SD increase and nearly a 3-fold greater risk for the second and top tertile versus the lowest tertile of VAT. VAT was the only adipose depot that remained associated with cancer risk independent of BMI, suggesting that among men VAT may provide prognostic information beyond risk captured by BMI.

Previous studies have reported different associations between obesity and risk of cancer by sex, with men generally having a greater risk than women (Moore et al. 2004; Renehan et al. 2008). It was hypothesized that a sex differential may be due to BMI reflecting central adiposity more strongly among men than women. However our results suggest that sex differences extend beyond the limitations of BMI as an indicator of central adiposity as even with directly assessed adipose depots, associations between adipose and cancer risk were not consistent across men and women. Sex differences may reflect hormonal variation between men in women. For example, the oestrogenic effects of adiposity are thought to increase the risk of cancers of the breast, endometrium and possibly ovaries, whereas there are inconsistent associations between testosterone and androgens and cancer risk among men (Calle et al. 2003). Differential relationships may also reflect age-related hormonal milieu in women. Several studies suggest that among women relationships between obesity, breast cancer risk (Morimoto et al. 2002) and colorectal cancer risk (Terry et al. 2001) vary by age and may be attenuated among older postmenopausal women.

Several studies have reported that waist circumference, an indicator of VAT is more strongly associated with cancer risk than BMI (Moore et al. 2004; Kabat et al. 2013). IMAT has metabolic properties similar to VAT, and thus we originally hypothesized that both depots would be associated with increased risk of cancer and obesity-related cancer. However, our results showed inconsistent associations with VAT and generally no associations with either thigh IMAT or thigh HU. There are a limited number of studies with computed tomography assessment of adipose tissue in relation to cancer risk to which we can draw parallels. A case control study reported greater VAT and SAT in men with prostate cancer compared to controls despite similar BMI (von Hafe et al. 2004). Another study reported a positive association between VAT and risk of recurrent rectal cancer among men and women with locally advanced rectal cancer (Clark et al. 2013). These studies align with

our finding of positive associations between VAT and obesity-related cancer risk among men but do not explain our null results with VAT and obesity-related cancer risk among women. Our results may reflect factors not captured by the cross-sectional measures of adiposity in this analysis, including potentially cumulative effects of life-long obesity on cancer risk and effects of fluctuation in weight and adipose depots on estimation of cancer risk. Longitudinal analyses may help to answer these important questions.

The strength of this study is in the detailed measures of adipose depots from high precision imaging rather than relying on estimates of adiposity from BMI or waist circumference. The use of radiographic imaging also made it possible to assess relationships between cancer risk and IMAT, which is a novel contribution. A further strength is the bi-racial participant population that includes white and black participants. There are also study limitations. These results may not be generalizable to younger populations. We were also limited by the number of cancer cases, there were too few to examine relationships by cancer type (ie. colon and rectal or breast). Additional larger studies with similar imaging would help to clarify cancer specific relationships with adipose tissue depots.

It is reassuring that many of the associations we observed between adipose measures and cancer risk (all cancer and obesity-related cancer) were attenuated by BMI which is an overall measure of obesity. BMI is a simple measure that is routinely assessed whereas radiographic imaging of adipose depots is not feasible in most clinical settings. However, the strong association of VAT and obesity-related cancer risk independent of BMI in men suggests that this may be an important depot for prognostication among men.

Conclusions

Although the reasons are unclear, the results of this study suggest that adiposity may confer risks for cancer and obesity-related cancer in older men and women, although only VAT appears to provide information beyond that attributed to BMI. This study further suggests differential associations between adiposity and risk among men and women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research was supported by National Institute on Aging (NIA) Contracts N01-AG-6-2101; N01-AG-6-2103, N01-AG-6-2106; NIA grant R01-AG028050, and NINR grant R01-NR-012459. This research was supported in part by the Intramural Research Program of the NIH, National Institute on Aging. RAM is supported by a Banting Postdoctoral Fellowship.

References

Bianchini F, Kaaks R, Vainio H. Overweight, obesity, and cancer risk. Lancet Oncol. 2002; 3(9):565–74. [PubMed: 12217794]

Brach JS, Simonsick EM, Kritchevsky S, Yaffe K, Newman AB. The association between physical function and lifestyle activity and exercise in the health, aging and body composition study. J Am Geriatr Soc. 2004; 52(4):502–9. [PubMed: 15066063]

Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med. 2003; 348(17):1625–38. [PubMed: 12711737]

Clark W, Siegel EM, Chen YA, Zhao X, Parsons CM, Hernandez JM, Weber J, Thareja S, Choi J, Shibata D. Quantitative Measures of Visceral Adiposity and Body Mass Index in Predicting Rectal Cancer Outcomes after Neoadjuvant Chemoradiation. J Am Coll Surg. 2013; 216(6):1070–81. [PubMed: 23523147]

Hill JO, Sidney S, Lewis CE, Tolan K, Scherzinger AL, Stamm ER. Racial differences in amounts of visceral adipose tissue in young adults: the CARDIA (Coronary Artery Risk Development in Young Adults) study. Am J Clin Nutr. 1999; 69(3):381–7. [PubMed: 10075320]

Kabat GC, Heo M, Miller AB, Rohan TE. Scaling of weight for height in relation to risk of cancer at different sites in a cohort of Canadian women. Am J Epidemiol. 2013; 177(1):93–101. [PubMed: 23139246]

Kabat GC, Kim M, Hunt JR, Chlebowski RT, Rohan TE. Body mass index and waist circumference in relation to lung cancer risk in the Women's Health Initiative. Am J Epidemiol. 2008; 168(2):158–69. [PubMed: 18483121]

Kuk JL, Saunders TJ, Davidson LE, Ross R. Age-related changes in total and regional fat distribution. Ageing Res Rev. 2009; 8(4):339–48. [PubMed: 19576300]

Moore LL, Bradlee ML, Singer MR, Splansky GL, Proctor MH, Ellison RC, Kreger BE. BMI and waist circumference as predictors of lifetime colon cancer risk in Framingham Study adults. Int J Obes Relat Metab Disord. 2004; 28(4):559–67. [PubMed: 14770200]

Morimoto LM, White E, Chen Z, Chlebowski RT, Hays J, Kuller L, Lopez AM, Manson J, Margolis KL, Muti PC, Stefanick ML, McTiernan A. Obesity, body size, and risk of postmenopausal breast cancer: the Women's Health Initiative (United States). Cancer Causes Control. 2002; 13(8):741–51. [PubMed: 12420953]

National Cancer Institute. [Accessed April 10, 2013] Obesity and Cancer Risk. Jan 3. 2012 www.cancer.gov/cancertopics/factsheet/Risk/obesity

Olson JE, Yang P, Schmitz K, Vierkant RA, Cerhan JR, Sellers TA. Differential association of body mass index and fat distribution with three major histologic types of lung cancer: evidence from a cohort of older women. Am J Epidemiol. 2002; 156(7):606–15. [PubMed: 12244029]

Pan SY, Johnson KC, Ugnat AM, Wen SW, Mao Y. Association of obesity and cancer risk in Canada. Am J Epidemiol. 2004; 159(3):259–68. [PubMed: 14742286]

Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008; 371(9612):569–78. [PubMed: 18280327]

Salamone LM, Fuerst T, Visser M, Kern M, Lang T, Dockrell M, Cauley JA, Nevitt M, Tylavsky F, Lohman TG. Measurement of fat mass using DEXA: a validation study in elderly adults. J Appl Physiol. 2000; 89(1):345–52. [PubMed: 10904070]

Terry P, Giovannucci E, Bergkvist L, Holmberg L, Wolk A. Body weight and colorectal cancer risk in a cohort of Swedish women: relation varies by age and cancer site. Br J Cancer. 2001; 85(3):346–9. [PubMed: 11487263]

Visser M, Fuerst T, Lang T, Salamone L, Harris TB. Validity of fan-beam dual-energy X-ray absorptiometry for measuring fat-free mass and leg muscle mass. Health, Aging, and Body Composition Study--Dual-Energy X-ray Absorptiometry and Body Composition Working Group. J Appl Physiol. 1999; 87(4):1513–20. [PubMed: 10517786]

von Hafe P, Pina F, Perez A, Tavares M, Barros H. Visceral fat accumulation as a risk factor for prostate cancer. Obes Res. 2004; 12(12):1930–5. [PubMed: 15687393]

Zamboni M, Mazzali G, Zoico E, Harris TB, Meigs JB, Di Francesco V, Fantin F, Bissoli L, Bosello O. Health consequences of obesity in the elderly: a review of four unresolved questions. Int J Obes (Lond). 2005; 29(9):1011–29. [PubMed: 15925957]

Table 1

Baseline characteristics of participants with and without incident cancer in the Health ABC Study

	No incident cancer N=1902	Incident cancer N=617	P
Follow-up time in years, mean (SD)	10.9 (3.63)	6.05 (3.94)	<0.001
Age in years, mean (SD)	74.1 (2.87)	74.1 (2.90)	0.73
Women, n (%)	1072 (56.4)	268 (43.4)	<0.001
White, n (%)	1097 (57.7)	344 (55.8)	0.40
Memphis site, n (%)	971 (51.1)	303 (49.1)	0.40
Education, n (%)			
<High school	509 (26.8)	145 (23.6)	0.10
High school	624 (32.9)	193 (31.4)	
Postsecondary	765 (40.3)	277 (45.0)	
Smoking status, n (%)			<0.001
Never	900 (47.3)	218 (35.3)	
Current	184 (9.67)	87 (14.1)	
Former	818 (43.0)	312 (50.6)	
Pack-years, mean (SD)	17.4 (27.3)	22.9 (28.8)	<0.001
Comorbid conditions, n (%)			
Cardiovascular disease	469 (25.3)	135 (22.3)	0.19
Diabetes	354 (18.6)	113 (18.3)	0.87
Pulmonary disease	219 (11.5)	82 (13.3)	0.24
BMI in kg/m^2, mean (SD)	27.4 (4.85)	27.5 (4.74)	0.56
Physical activity in kcal/week, n (%)			0.87
0–499.9	1010 (53.1)	321 (52.0)	
500–999.9	315 (16.6)	107 (17.3)	
≥1,000	577 (30.3)	189 (30.6)	
Cancer diagnosis			
Lung, n (%)		110 (17.8)	
Breast, n (%)		74 (12.0)	
Colon and rectum, n (%)		82 (13.3)	
Prostate, n (%)		126 (20.4)	

Notes: Presence or absence of incident cancer determined over 13 years of follow-up. BMI: body mass index, kcal: kilocalorie, SD: standard deviation. Two sample t-tests for continuous variables, chi-square tests for categorical variables.

Table 2

Distribution of baseline adipose tissue measures in the Health ABC Study

	White						Black					
	N	**Range**	**Mean (SD)**	**25%**	**50%**	**75%**	**N**	**Range**	**Mean (SD)**	**25%**	**50%**	**75%**
					Men							
BMI, kg/m^2	735	17.6–44.2	27.0 (3.69)	24.4	26.5	29.2	444	15.7–43.2	27.1 (4.25)	24.3	26.9	29.9
Total AT, kg	731	9.72–44.4	24.6 (6.92)	19.8	23.5	28.6	440	6.69–43.3	23.0 (7.47)	17.9	22.8	27.6
VAT, cm^2	704	35.6–454	168 (71.6)	120	152	208	426	8.37–504	131 (65.9)	82.8	122	167
SAT, cm^2	685	23.9–418	133 (61.2)	89.0	124	165	414	11.0–585	230 (97.8)	165	223	283
Thigh IMAT, cm^2	716	0.86–183	18.9 (12.4)	11.5	16.1	23.5	435	1.99–162	22.1 (16.4)	12.2	18.2	28.2
Thigh HU	716	7.94–55.1	37.4 (6.35)	33.4	37.6	41.9	435	8.55–54.5	37.1 (6.54)	33.0	37.1	41.8
					Women							
BMI, kg/m^2	706	16.8–43.6	26.0 (4.39)	22.7	25.6	28.6	634	14.6–52.0	29.7 (5.93)	25.3	29.1	33.7
Total AT, kg	703	8.72–55.2	27.0 (7.74)	21.5	26.4	31.8	631	8.30–69.5	31.9 (10.4)	24.6	30.8	38.0
VAT, cm^2	694	32.9–608	224 (80.6)	169	211	266	605	20.8–345	129 (56.5)	88.1	122	166
SAT, cm^2	671	30.1–669	309 (104)	243	300	371	579	25.3–787	376 (137)	278	366	462
Thigh IMAT, cm^2	697	2.03–61.4	17.4 (8.63)	11.1	15.9	21.9	613	3.15–104	25.5 (13.9)	15.6	22.0	32.5
Thigh HU	697	8.37–70.1	34.8 (6.71)	30.7	35.1	39.4	613	2.43–48.7	32.4 (7.05)	28.1	32.6	37.5

Notes: AT: adipose tissue, BMI: body mass index, VAT: visceral adipose tissue, SAT: subcutaneous adipose tissue, IMAT: intermuscular adipose tissue

Appl Physiol Nutr Metab. Author manuscript; available in PMC 2014 June 26.

Table 3

Associations between continuous adipose measures (per standard deviation increase) and quartiles of adipose measures with risk of all incident cancer in the Health ABC Study

	Men					Women				
	N. of people	N. cases	Event rate	Model 1 HR (95% CI)	Model 2 HR (95% CI)	N. of people	N. cases	Event rate	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Total AT										
Per SD	1171	349	33.3	0.88 (0.79–0.98)	0.93 (0.83–1.05)	1334	268	19.3	1.12 (1.00–1.26)	1.14 (1.01–1.30)
Q1	292	100	42.2	1.00	1.00	332	54	16.0	1.00	1.00
Q2	293	77	28.9	0.69 (0.51–0.92)	0.75 (0.55–1.02)	334	71	20.9	1.31 (0.92–1.87)	1.32 (0.91–1.91)
Q3	293	89	33.0	0.78 (0.59–1.04)	0.78 (0.58–1.05)	334	64	18.0	1.22 (0.78–1.61)	1.21 (0.82–1.77)
Q4	293	83	30.3	0.71 (0.53–0.96)	0.77 (0.56–1.06)	334	79	22.1	1.37 (0.97–1.93)	1.44 (0.99–2.10)
P for linear trend				0.20	0.30				0.07	0.03
VAT										
Per SD	1130	336	33.1	0.96 (0.86–1.07)	1.01 (0.90–1.13)	1290	260	19.3	1.16 (1.04–1.30)	1.15 (1.02–1.30)
Q1	282	81	33.5	1.00	1.00	322	58	16.8	1.00	1.00
Q2	283	87	33.0	0.98 (0.73–1.33)	0.94 (0.69–1.29)	322	53	15.6	0.92 (0.63–1.33)	0.89 (0.61–1.32)
Q3	282	88	34.0	1.01 (0.75–1.37)	1.00 (0.73–1.37)	322	67	20.5	1.23 (0.87–1.75)	1.29 (0.89–1.85)
Q4	283	80	31.7	0.94 (0.69–1.28)	0.94 (0.68–1.31)	324	82	24.5	1.47 (1.05–2.06)	1.40 (0.98–2.02)
P for linear trend				0.90	0.92				0.007	0.01
SAT										
Per SD	1109	330	33.0	0.85 (0.76–0.95)	0.90 (0.80–1.02)	1250	249	19.1	1.07 (0.95–1.21)	1.10 (0.97–1.25)
Q1	276	94	42.1	1.00	1.00	311	54	17.3	1.00	1.00
Q2	278	74	29.4	0.70 (0.52–0.95)	0.75 (0.55–1.03)	313	64	19.4	1.11 (0.77–1.60)	1.22 (0.83–1.80)
Q3	276	94	37.1	0.88 (0.66–1.17)	0.89 (0.66–1.19)	313	57	17.0	0.97 (0.67–1.41)	1.03 (0.69–1.52)
Q4	279	68	25.1	0.59 (0.43–0.81)	0.62 (0.45–0.87)	313	74	22.5	1.28 (0.90–1.81)	1.44 (0.99–2.11)
P for linear trend				0.08	0.15				0.09	0.03
Thigh IMAT										
Per SD	1151	343	33.2	0.89 (0.78–1.01)	0.91 (0.80–1.05)	1310	264	19.3	1.10 (0.98–1.23)	1.09 (0.97–1.23)
Q1	287	95	39.6	1.00	1.00	327	50	14.5	1.00	1.00
Q2	288	90	33.2	0.84 (0.63–1.12)	0.84 (0.62–1.13)	326	75	22.5	1.56 (1.09–2.23)	1.51 (1.04–2.20)
Q3	288	79	29.6	0.74 (0.55–1.00)	0.74 (0.54–1.01)	328	67	19.5	1.36 (0.94–1.96)	1.45 (0.99–2.11)

	Men					Women				
	N. of people	**N. cases**	**Event rate**	**Model 1 HR (95% CI)**	**Model 2 HR (95% CI)**	**N. of people**	**N. cases**	**Event rate**	**Model 1 HR (95% CI)**	**Model 2 HR (95% CI)**
Q4	288	79	31.2	0.78 (0.58–1.06)	0.76 (0.55–1.06)	329	72	20.9	1.44 (1.01–2.07)	1.41 (0.96–2.06)
P for linear trend				0.17	0.12				0.09	0.09
Thigh HU										
Per SD	1151	343	33.2	1.10 (0.98–1.23)	1.10 (0.98–1.25)	1310	264	19.3	0.90 (0.80–1.01)	0.91 (0.80–1.04)
Q1	287	73	28.6	1.00	1.00	327	76	22.9	1.00	1.00
Q2	288	90	34.9	1.23 (0.90–1.67)	1.22 (0.88–1.68)	327	71	20.5	0.89 (0.64–1.23)	0.89 (0.64–1.23)
Q3	288	95	37.5	1.32 (0.97–1.79)	1.34 (0.97–1.84)	327	53	15.6	0.69 (0.48–0.97)	0.72 (0.50–1.04)
Q4	288	85	32.1	1.13 (0.83–1.55)	1.15 (0.83–1.61)	329	64	18.4	0.81 (0.58–1.14)	0.84 (0.59–1.21)
P for linear trend				0.48	0.35				0.10	0.18

Notes: Model 1 unadjusted; Model 2 adjusted for age, race, study site, education, height, smoking status and smoking duration, comorbid conditions (cardiovascular disease, diabetes, and pulmonary disease), and physical activity. P for linear trend across quartiles from Wald statistic. AT: adipose tissue, CI: confidence interval, HR: hazard ratio, HU: Hounsfield Unit, IMAT: intermuscular adipose tissue, Q: quintile SAT: subcutaneous adipose tissue, SD: standard deviation, VAT: visceral adipose tissue

Table 4

Associations between continuous adipose measures (per standard deviation increase) and tertiles of adipose measures with incident obesity-related cancer in the Health ABC Study

	Men					Women				
	N. of people	N. cases	Event rate	Model 1 HR (95% CI)	Model 2 HR (95% CI)	N. of people	N. cases	Event rate	Model 1 HR (95% CI)	Model 2 HR (95% CI)
Total AT										
Per SD	1171	82	7.03	1.11 (0.91–1.36)	1.16 (0.93–1.44)	1334	142	10.0	1.22 (1.05–1.43)	1.23 (1.03–1.46)
T1	389	18	4.84	1.00	1.00	444	38	8.29	1.00	1.00
T2	391	30	7.55	1.57 (0.87–2.81)	1.61 (0.88–2.93)	444	46	9.60	1.16 (0.75–1.78)	1.06 (0.68–1.66)
T3	391	34	8.58	1.78 (1.01–3.14)	1.83 (1.00–3.36)	446	58	12.1	1.44 (0.96–2.17)	1.41 (0.91–2.19)
P for linear trend				0.05	0.06				0.08	0.11
VAT										
Per SD	1130	78	6.90	1.25 (1.02–1.52)	1.30 (1.06–1.60)	1290	138	10.1	1.12 (0.96–1.32)	1.12 (0.94–1.32)
T1	376	13	3.43	1.00	1.00	429	40	8.64	1.00	1.00
T2	377	33	8.75	2.55 (1.34–4.84)	2.86 (1.47–5.57)	430	49	10.8	1.24 (0.82–1.89)	1.29 (0.84–1.98)
T3	377	32	8.55	2.49 (1.31–4.75)	2.85 (1.45–5.62)	431	49	10.8	1.25 (0.82–1.90)	1.24 (0.79–1.93)
P for linear trend				0.008	0.004				0.31	0.36
SAT										
Per SD	1109	75	6.73	0.97 (0.78–1.22)	1.01 (0.80–1.27)	1250	129	9.68	1.16 (0.98–1.37)	1.16 (0.97–1.38)
T1	369	25	7.13	1.00	1.00	416	36	8.40	1.00	1.00
T2	369	28	7.36	1.04 (0.61–1.78)	1.01 (0.58–1.76)	417	43	9.49	1.13 (0.72–1.76)	1.13 (0.71–1.79)
T3	370	22	5.74	0.81 (0.46–1.44)	0.82 (0.46–1.49)	417	50	11.1	1.31 (0.85–2.00)	1.38 (0.88–2.17)
P for linear trend				0.48	0.52				0.22	0.16
Thigh IMAT										
Per SD	1151	81	7.06	1.04 (0.83–1.28)	0.96 (0.70–1.32)	1310	139	9.97	1.12 (0.96–1.31)	1.12 (0.95–1.31)
T1	383	26	6.90	1.00	1.00	436	36	7.76	1.00	1.00
T2	384	23	5.70	0.83 (0.48–1.46)	0.85 (0.48–1.51)	436	53	11.6	1.51 (0.99–2.31)	1.59 (1.02–2.47)
T3	384	32	8.71	1.26 (0.75–2.11)	1.27 (0.73–2.19)	438	50	10.5	1.36 (0.88–2.08)	1.38 (0.88–2.17)
P for linear trend				0.36	0.38				0.19	0.19
Thigh HU										
Per SD	1151	81	7.06	0.96 (0.76–1.21)	0.95 (0.75–1.21)	1310	139	9.97	0.95 (0.80–1.12)	0.94 (0.79–1.13)

	Men					Women				
	N. of people	**N. cases**	**Event rate**	**Model 1 HR (95% CI)**	**Model 2 HR (95% CI)**	**N. of people**	**N. cases**	**Event rate**	**Model 1 HR (95% CI)**	**Model 2 HR (95% CI)**
T1	383	32	8.74	1.00	1.00	436	49	10.8	1.00	1.00
T2	384	21	5.35	0.62 (0.36–1.07)	0.62 (0.35–1.08)	436	51	10.9	1.03 (0.70–1.53)	0.99 (0.66–1.48)
T3	384	28	7.20	0.83 (0.50–1.38)	0.81 (0.50–1.38)	438	39	8.24	0.78 (0.51–1.19)	0.78 (0.50–1.22)
P for linear trend				0.46	0.42				0.26	0.28

Notes: Model 1 unadjusted; Model 2 adjusted for age, race, study site, education, height, smoking status, and smoking duration, comorbid conditions (cardiovascular disease, diabetes, and pulmonary disease), and physical activity. P for linear trend across tertiles from Wald statistic. AT: adipose tissue, CI: confidence interval, HR: hazard ratio, HU: Hounsfield Unit, IMAT: intermuscular adipose tissue, SAT: subcutaneous adipose tissue, SD: standard deviation, T: tertile, VAT: visceral adipose tissue