Biomarker-Based Visceral Adiposity Score and Incident Type 2 Diabetes in the Multiethnic Cohort

Gertraud Maskarinec[1], **Phyllis Raquinio**[1], **Veronica W. Setiawan**[2], **Thomas Ernst**[3], **Adrian A. Franke**[1], **Steven D. Buchthal**[1], **John A. Shepherd**[1], **Lynne R. Wilkens**[1], **Unhee Lim**[1], **Loïc Le Marchand**[1]

[1]University of Hawaii Cancer Center, Honolulu, HI

[2]Keck School of Medicine, University of Southern California, Los Angeles, CA

[3]University of Maryland School of Medicine, Baltimore, MD

Abstract

Purpose.—Visceral adipose tissue (VAT) may be more important than subcutaneous fat in type 2 diabetes (T2D) etiology. We examined a VAT score developed in reference to MRI measurement of VAT in the Multiethnic Cohort (MEC) as a risk factor for incident T2D.

Methods.—Two nested case-control studies of cancer allowed calculation of the VAT score based on anthropometric measures and eight biomarkers among 2,556 participants without T2D. Incident cases were identified from Medicare linkages and self-reports after blood draws in 2001–2006. Cox regression with age as time metric was applied to estimate the association of the VAT score with T2D.

Results.—During 10.1±2.4 years, 355 incident T2D cases were identified. VAT scores were higher in T2D cases than among those without disease (5.06±0.43 vs. 4.95±0.41; p<0.0001) and significantly associated with T2D (HR=2.70; 95%CI 1.60, 4.58 per unit) with similar values in men (HR=2.99; 95%CI 1.03, 8.73) and women (HR=2.61; 95%CI 1.39, 4.91). A significant association was observed in all five ethnic groups but only statistically significant among Japanese Americans (HR=6.24; 95%CI 2.34, 16.68).

Conclusions.—These findings support that VAT as estimated by a biomarker-based score predicts T2D incidence beyond BMI in particular among older adults of Japanese ancestry.

Introduction

In addition to obesity, the type and location of excess body fat (1) play an important role in the etiology of type 2 diabetes (T2D) (2). Evidence comes from studies in populations with Asian ancestry who experience a higher risk of breast cancer and T2D associated with obesity than Whites (3, 4) and, at the same time, show a high propensity to accumulate visceral adipose tissue (VAT) as opposed to subcutaneous adipose tissue (SAT) (5). The optimal way to investigate this hypothesis is within prospective cohorts that assess body fat through computerized tomography (CT), magnetic resonance imaging (MRI), or Dual X-ray Absorptiometry (DXA) (6, 7). Given the high cost and participant burden, few cohorts have collected imaging results for a sufficient sample size. Both a cohort of Japanese Americans (2, 8) and the Dallas Heart Study (9) have shown a high incidence of T2D associated with image-based VAT.

As an alternative, a Visceral Adiposity Index (VAI) based on anthropometric characteristics and biomarkers has been applied repeatedly. With one exception that included age (10), the VAIs in previous reports were composed of body mass index (BMI), waist circumference, triglycerides, and HDL-cholesterol. Significant associations between the VAI and T2D of similar magnitude were reported by five studies from East/Southeast Asia (10–14), three from the Middle East (15–17), and three from Europe (18–20). Within the Multiethnic Cohort (MEC), a more complex prediction score based on BMI, height and blood biomarkers was developed among a subset of cohort members in five ethnic groups (21). In nested case-control studies of cancer, the top tertile of this score was associated with a 48% higher breast cancer risk independently of BMI but was not associated with colorectal cancer risk. As a higher incidence of T2D in every BMI category among Japanese Americans than Whites was seen in the MEC (4), we tested the hypothesis that the VAT component is responsible for the higher T2D incidence in this group despite their lower obesity rates and examined T2D incidence associated with the VAT prediction score among MEC participants with available biomarker information.

Materials and Methods

Study Population.

The MEC is an on-going prospective study in Hawaii and Los Angeles, California (5) that examines diet, lifestyle, and genetic risk factors for cancer (22). The cohort consists of more than 215,000 men and women from primarily five ethnic groups (Japanese American, Whites, Latino, African American and Native Hawaiian) who completed a 26-page questionnaire by mail in 1993–96, which included self-reported height and weight used to compute BMI; no other measures of adiposity were available for the full cohort. During 2001–06, a biorepository with 68,988 MEC participants was established (23). In

2013–16, the Adiposity Phenotype Study (APS) with close to 2,000 participants examined body fat distribution using MRI and DXA imaging in a subset of the MEC, with similar proportions of normal weight, overweight, and obesity participants aged 60–72 years from the five ethnic groups (5).

VAT Score.

Among 1,801 APS participants with MRI-based VAT measures, a score to predict MRI VAT was developed by LASSO (least absolute shrinkage and selection operator) regression models in a cross-sectional design as published in detail in the Supplemental Material to the original study (21). The final sex-specific models with the same list of predictors included only variables with a standardized coefficient >0.3 in absolute value. These were BMI, height, adiponectin, leptin, total, HDL and LDL cholesterol, triglycerides, insulin, total carotene, and sex hormone-binding protein. This score explained 64% of the variance in VAT among men and 67% among women; the respective areas under the receiver operating curves (AUROC) for VAT 150 cm^2 were 0.90 in men and 0.86 in women (21). As reported previously (21), the AUROCs were of similar size across ethnic groups with ranges of 0.86–0.93 in men and 0.84–0.91 in women; African Americans had the lowest and Japanese Americans the highest values.

For comparison with the VAT score, we computed a VAI score as presented in previous studies (14) among the 1,917 participants who reported waist circumference measurements as part of a repeat questionnaire administered in 2003–2008 (24).

Analysis Population.

Within the MEC biorepository, two nested case-control studies, one for postmenopausal breast and one for colorectal cancer, were conducted using the VAT score as these participants had not undergone MRI imaging (21). The cancer cases were identified through linkage to the Surveillance, Epidemiology and End Results (SEER) registries for Hawaii and California through December 2013. Deaths were ascertained by linkage to state vital statistics reports and the National Death Index. During a mean follow-up of 6 years after blood collection for the biorepository, 950 incident cases of invasive postmenopausal breast cancer and 831 incident cases of invasive adenocarcinoma of the colon or rectum with blood samples, which had all been collected before the cancer diagnosis, were identified. One cancer-free control per case was matched by the incidence density approach using age as the time metric on the following characteristics: geographic location, birth year, sex, ethnicity, year of blood collection, and hours of fasting (21). There was no overlap among participants of the APS and the nested case-control studies. Each case and control in the nested case-control studies was assigned a VAT score by applying the sex-specific VAT prediction model using the analytes uniformly measured in the MEC biorepository using the same assays (21).

Ascertainment of T2D Status.

T2D status in the MEC was determined from three different sources. Self-reports were available from five questionnaires (QX1-QX5) in response to the question "Has your doctor ever told you that you had diabetes?" As part of the biorepository, cohort members who

reported T2D medication at time of blood draw were classified as cases. In addition, administrative data were obtained through linkages with Medicare claims for years 1999 to 2016 (25). The source of information for the T2D diagnosis was Medicare only (80%), Medicare plus self-report (8%), and self-report of T2D or medication (12%). The first report of T2D in a questionnaire or Medicare data was considered as date of onset. Only diagnoses first reported after blood draw and before the end of 2013 were classified as incident cases. T2D cases identified before or at biospecimen collection were categorized as prevalent cases and excluded from the analysis while those diagnosed after 2013 were retained as participants without T2D. To adjust for glucose status at time of blood draw, fasting glucose levels were classified as normal (<100 mg/dL), prediabetes (100-<125 mg/dL), or diabetes (125 mg/dL). The homeostatic model assessment for insulin resistance (HOMA-IR) was computed as fasting insulin x fasting glucose /405.

Statistical Analysis.

Of the 3,562 participants (950 breast cancer cases and controls; 831 CRC cases and controls), 30 were part of both studies and 93 had missing values for the VAT score leaving 3,439 observations. After excluding nine individuals reporting other ethnicity and 874 prevalent T2D cases at blood draw, 2,556 participants remained in the analytic dataset. To evaluate the combined influence of the highly correlated variables of BMI and the VAT score in the model, BMI-adjusted VAT scores were created using the method of residuals (21, 26). Descriptive statistics for all relevant variables were computed by sex and cancer status. Cox regression of T2D with age as time metric was applied to estimate the association with the continuous BMI-adjusted VAT score for the entire study population and separately for cancer cases and controls. Hazard ratios (HR) and 95% confidence intervals (CI) per unit of VAT score were estimated from the Cox regression. All models were adjusted for sex, ethnicity, age, and glucose status at blood draw, BMI at cohort entry, smoking status at blood draw, alcohol intake, and physical activity at MEC baseline; and cancer status (breast or colorectal cancer vs. control). To assess effect modification by ethnicity, an interaction term with the VAT score was introduced into the model and stratified analyses were performed. Risk of T2D was also estimated separately for participants who had normal weight, overweight, and obesity at cohort entry. For comparison with the VAT score, log-transformed HOMA-IR values and the log-transformed VAI score available for 1,917 participants were modeled with the same approach as described above. A C-like (AUROC) statistics called Uno's C-statistic for right-censored data was computed using PROC PHREG (27). The SAS 9.4 (Cary, NC) package was used to perform all data management and analyses.

Results

The mean age of the participants at blood draw was 68.4 ± 8.1years (Table 1) and women comprised the majority of the study population (77%) due to the breast cancer study. As to ethnicity, 19.9% identified as White, 18.1% as African American, 7.9% as Native Hawaiian, 34.3% as Japanese American, and 19.8% as Latino. The mean BMI was 25.8 ± 4.7 kg/m^2 and the mean values of the VAT score after adjustment (by residual method) for BMI were 5.0 ± 0.4 (range: 3.8–6.1). Women had lower VAT scores than men but little difference by

cancer status was seen. The Spearman correlation coefficient of BMI with the adjusted VAT score was $r_s = 0.16$ (p<0.001).

Of the 2,556 eligible participants, 355 were incident T2D cases after a mean of 10.1±2.4 years of follow-up. As to the source of information, 283 incident cases were identified through Medicare files, 43 by self-report in one of the questionnaires and 29 by questionnaire plus Medicare files. Of the incident cases, 118 occurred in Japanese Americans, 93 in Latinos, 76 in African Americans, 43 in Whites, and 25 in Native Hawaiians. Mean VAT scores differed significantly by T2D status (Table 2) with values of 5.06 ± 0.43 among incident T2D cases as compared to 4.95 ± 0.41 in cohort members without a T2D diagnosis (p<0.0001). Cases and controls showed similar scores for participants in both cancer studies. Significant differences were seen by ethnic group, sex, and BMI (p<0.0001). Whites (4.85 ± 0.40) had the lowest values, followed Native Hawaiians (4.94 ± 0.37), African Americans (4.95 ± 0.45) and Japanese Americans (4.99 ± 0.41) while Latinos were highest (5.05 ± 0.41). VAT scores were elevated for individuals with obesity (4.90 ± 0.40) and overweight (5.09 ± 0.43) as compared to those with normal weight (4.90 ± 0.39). Men had higher mean scores (5.61 ± 0.21) than women (4.77 ± 0.22).

For the association of VAT score with T2D (Table 3), significantly higher risk estimates were detected for the combined study population (HR = 2.70; 95% CI 1.60, 4.58), cancer cases (HR = 3.40; 95% CI 1.57, 7.39), and controls (HR = 2.30; 95% CI 1.10, 4.81). The strength of the association was similar in men (HR = 2.99; 95% CI 1.03, 8.73) and women (HR = 2.61; 95% CI 1.39, 4.91). In all models, BMI also remained significantly associated with T2D; the respective HRs for overweight and obesity were 1.61 (95% CI 1.24, 2.08) and 2.06 (95% CI 1.50, 2.83) for all participants combined. The HR values for BMI were in a similar range for separate models by case-control status. Removing the VAT score or BMI from the overall model did not substantially change the risk estimates for the remaining variable (data not shown). In these models, the HR for VAT score was 2.80 (95% CI 1.67, 4.69) and for overweight and obesity, the respective HRs were 1.72 (95% CI 1.33, 2.23) and 2.02 (95% CI 1.47, 2.79).

Although an interaction term between T2D status and ethnicity was not statistically significant (p=0.20), only Japanese Americans showed a significantly higher T2D incidence (HR = 6.24; 95% CI 2.34, 16.68) in ethnic-specific models. The HRs for all ethnic groups except Whites were non-significantly greater than one (range from 1.80 to 5.84). BMI status in these models lost significance among Japanese Americans (HR = 1.18; 95% CI 0.77, 1.80 for overweight and HR = 1.85; 95% CI 0.88, 3.85 for obesity). On the other hand, overweight and obesity were significantly associated with T2D incidence among Whites, Latinos, and Native Hawaiians (overweight only). In African Americans, no significant relation was seen for both the VAT score and BMI.

In stratified models by BMI status, one unit of VAT score predicted an elevated T2D risk among participants with normal weight (HR = 3.31; 95% CI 1.30, 8.44) and overweight (HR = 4.00; 95% CI 1.63, 9.81) but not obesity (HR = 2.08; 95% CI 0.69, 6.28).

The C-statistic for a model that included the VAT score and BMI in addition to glucose status (0.74) was higher than for models with only BMI (0.68) or only the VAT score (0.66) emphasizing the importance of total adiposity as assessed by BMI in combination with VAT. In ethnic-specific models, the respective C-statistics for the full models were 0.81 (Native Hawaiians), 0.76 (Whites), 0.74 (Latinos), 0.71 (Japanese Americans), and 0.69 (African Americans).

In a separate model, HOMA-IR was also associated with T2D incidence (HR = 1.19; 95% CI 1.06, 133) with a C-statistic of 0.70. For the subset of 1,917 participants with waist circumference measurements to calculate the VAI, the mean score was 2.8±4.0. The Spearman correlation coefficient with the VAT score was 0.55 (p<0.0001). The difference by T2D status was not significant (2.73 vs. 3.01, p=0.31). The HR of the VAI overall model was 1.06 (95% CI 0.90, 1.25) with a C-statistic of 0.71.

Discussion

The current findings among older adults indicate that VAT as estimated by a biomarker-based score predicted additional T2D incidence beyond BMI, among participants of previous nested case-control studies of cancer using pre-diagnostic samples. The association was only significant among Japanese Americans although the HRs were greater than one in most other ethnic groups. Interestingly, the association was stronger among those who were also diagnosed with breast or colorectal cancer during the follow-up period than among the controls (HRs 3.40 vs. 2.70). This may be due to similar risk profiles for persons at risk for T2D and the two cancer sites, in particular excess body weight (28). Although the findings of this study are not completely novel, this is the first study that compares the relation of the VAT score across ethnic groups in the same investigation. These comparative findings in a multiethnic population show that the association of the VAT predictor score among Japanese Americans is very strong (6-fold higher T2D risk for each increase in one unit of the VAT score) while BMI lost significance in this group. In contrast, BMI showed a stronger association with T2D risk than the VAT score among Whites, Native Hawaiians, and Latinos. This result offers a better understanding of the previously reported high T2D incidence among Japanese Americans in the MEC despite their low obesity rates (4). The fact that the VAI as computed in previous studies (14) did not show a significant association with T2D confirms the importance of scores based on MRI measures of VAT (21).

These results agree with the limited number of studies that have evaluated T2D incidence in relation to VAT assessed by CT, MRI, or DXA imaging. Second-generation Japanese Americans in a Seattle cohort (2) experienced a 60% higher T2D risk associated with 1 SD increase in intra-abdominal fat area (IAFA) as assessed by CT, a measure of VAT after adjustment for other adiposity measures such as BMI, non–intra-abdominal fat area, or subcutaneous abdominal fat. Similarly, among third-generation Japanese Americans, only IAFA remained significantly associated with higher T2D risk with an odds ratios (OR) of 2.7 (95% CI 1.4–5.4) per one SD increase. In the same cohort, accumulation of IAFA over a 10-year period was an additional predictor of T2D incidence (8). Similarly, the Dallas Heart Study reported an OR of 2.4 (95% CI, 1.6–3.7) for the association between MRI-derived VAT measures and T2D after adjustment for weight gain (9).

Five previous studies conducted in East Asian populations reported significant associations between T2D and VAI composed of BMI, waist circumference, triglycerides, and HDL-cholesterol (10–14). However, their risk estimates were lower than the 6-fold higher incidence per unit VAT score for Japanese Americans in our study. The four Chinese investigations reported the following results: ORs of 3.6 (95% CI 2.5, 5.3) for men and 2.8 (95% CI 1.9, 4.2) for women (11), a 2.55 higher risk of T2D (95% CI 1.58, 4.11) (12) and HRs of 2.72 (95% CI: 1.53, 4.84) (13) and 1.61 (95% C 1.09, 2.36) for a change in one SD of VAI (10). A cohort in Indonesia detected ORs of 2.29 (95% CI 1.15, 4.56) in men and of 1.95 (95% CI 1.49, 2.54) in women (14). In the Korean National Health and Nutrition Examination Survey, the VAI was positively associated with insulin resistance and beta cell function in adults without T2D (29). Among other populations, the age-adjusted risks for incident T2D in the highest vs. lowest VAI category were 4.5 (95% CI 3.0, 6.9) and 2.5 (95% CI 1.56, 3.86) in the Iranian studies (15, 16), and 1.90 (95% CI 1.07, 3.37) in a Polish study (19). Also, 20–50% higher risks per 1-unit increase of the VAI were detected in Greece (18), Qatar (17), and among women and men of European descent in the Rotterdam study (20).

Strengths of the study include the prospective cohort study design, the ethnic diversity with a large proportion of participants with Japanese ancestry, and the substantial follow-up time of 10 years. Compared to previous studies (10, 14, 20, 29), the current analysis developed a more robust VAT score with a greater number of components that was tested in relation to cancer (21) and T2D incidence. The benefit of this approach is visible in the substantial association between the predictor score and T2D risk, which was stronger than for BMI in some ethnic groups. The multiple sources of information to identify T2D cases provide confidence that most incidence cases were identified correctly. However, the fact that HbA1c levels were not available, as indicators of glucose control, may have biased the risk estimates, as fasting glucose levels do not offer a comprehensive assessment of metabolic status. However, despite the lack of glucose and Hb1Ac values, we are confident that Medicare information and self-reports of T2D are quite accurate as shown in multiple investigations (30, 31). Other limitations include the lack of younger individuals in the study population and the underrepresentation of men compared to women due to the inclusion of the breast cancer case-control study although separate HRs by sex were computed. Clearly, actual measured VAT measures would have been preferable, but due to the retrospective design, MRI assessments were not available and had to be estimated based on a subset of the MEC (21). Finally, the high prevalence of T2D in this population (32) resulted in a large number of individuals who had to be excluded from the analysis, thereby reducing the generalizability of the findings to ethnic groups who experience a high incidence of T2D. Hence, the ethnic-specific models suffered from small numbers of incident T2D cases.

The current findings indicate that VAT area is a stronger predictor of T2D incidence than BMI among older adults, in particular among individuals with Japanese American ancestry who are known to have more VAT than other ethnic groups (5). In fact, the ethnic-specific model suggests that BMI plays a less important role in T2D development among this ethnic group than the presence of VAT. These findings provide more insight into T2D etiology among Asian populations. In terms of T2D screening, these findings imply that detecting individuals with a high level of VAT is important, especially among individuals

with normal BMI (1, 33). However, in clinical settings, regular blood tests and weight loss programs remain the main strategies to identify and prevent T2D as glucose and HbA1c are established diagnostic criteria that cannot easily be replaced with repeated VAT assessments at this time.

Funding.

Data Availability.

The data underlying this study cannot be made publicly available because they contain patient identifying information. Data are available from the Multiethnic Cohort study (http://www.uhcancercenter.org/research/the-multiethnic-cohort-study-mec/data-sharing-mec) for researchers who meet the criteria for access to confidential data.

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Highlights

- Differences in body fat distribution, i.e., visceral vs. subcutaneous adipose tissue, may explain the discrepant incidence of type 2 diabetes across populations given the same body mass index.

- If imaging is not an option, the relative proportion of visceral adipose tissue (VAT) can be successfully estimated using a score computed from body mass index and biomarker measurement.

- The risk to develop type 2 diabetes increased nearly three-fold with one unit of VAT score after adjustment for body mass index and other confounders.

- Japanese Americans experienced the strongest association of the VAT with type 2 diabetes incidence as compared to Latinos, African Americans, Native Hawaiians, and Whites.

Table 1.

Characteristics of the study population at blood draw[a]

Characteristic	Categories	All	Men		Women	
			Cancer controls	Cancer cases	Cancer controls	Cancer cases
N		2,556	310	279	1005	962
Previous study	Breast	1,397	0	0	714	683
	Colorectal	1,159	310	279	291	279
Diabetes status	None	2,201	258	227	880	836
	Incident case	355	52	52	125	126
Ethnicity	White	509	46	42	208	213
	African American	462	57	62	173	170
	Native Hawaiian	201	19	16	85	81
	Japanese American	877	116	93	339	329
	Latino	507	72	66	200	169
BMI status at cohort entry (kg/m²)	<18.5	40	0	2	19	19
	18.5–<25	1,211	125	107	534	445
	25–<30	909	141	135	295	338
	30	396	44	35	157	160
Smoking status at blood draw[b]	Never	1,530	158	127	647	598
	Past	818	121	116	273	308
	Current	148	26	21	65	36
Follow-up time, yrs		10.1 ± 2.4	10.1 ± 3.0	9.5 ± 3.2	10.3 ± 2.1	10.0 ± 2.2
Age at blood draw, yrs		68.4 ± 8.1	70.7 ± 8.1	70.0 ± 7.8	67.9 ± 8.1	67.7 ± 8.0
VAT score[c]		5.0 ± 0.4	5.6 ± 0.2	5.6 ± 0.2	4.8 ± 0.2	4.8 ± 0.2
BMI, kg/m²		25.8 ± 4.7	26.3 ± 3.9	26.2 ± 4.0	25.5 ± 5.0	25.8 ± 4.7
Fasting glucose, mg/dL		79.8 (17.9)	86.3 (18.8)	86.6 (16.6)	77.2 (16.3)	78.9 (18.2)
Fasting insulin, μU/mL		6.6 (11.6)	6.4 (9.0)	6.3 (7.1)	6.1 (11.4)	7.5 (12.8)
HOMA-IR		1.3 (2.3)	1.4 (1.9)	1.3 (1.6)	1.2 (2.2)	1.4 (2.6)
Alcohol intake, g/day		0.4 (5.0)	3.5 (16.4)	3.9 (20.4)	0.0 (2.8)	0.0 (2.6)
Physical activity, hrs/day		0.7 (0.9)	0.4 (1.1)	0.4 (1.1)	0.7 (0.9)	0.7 (0.9)

[a] Number of participants, mean ± standard deviation, or median (interquartile range) is shown as appropriate

[b] N=60 with missing information about smoking

[c] VAT score is based on 8 biomarkers plus BMI and height adjusted for BMI at cohort entry by the method of residuals.

Abbreviations: BMI=body mass index, HOMA-IR=homeostatic model assessment for insulin resistance, VAT=visceral adipose tissue

Table 2.

Mean VAT scores by diabetes status and relevant characteristics

Characteristic	N	Categories	Mean ± std	P-value[a]
Diabetes status		No diabetes known	4.95 ± 0.41	
		Incident case	5.06 ± 0.43	<0.0001
Cancer status		Breast cancer case	4.75 ± 0.23	
		Breast cancer control	4.77 ± 0.23	0.02
		Colorectal cancer case	5.22 ± 0.46	
		Colorectal cancer control	5.20 ± 0.46	0.54
Ethnicity		White	4.85 ± 0.40	
		African American	4.95 ± 0.45	
		Native Hawaiian	4.94 ± 0.37	
		Japanese American	4.99 ± 0.41	
		Latino	5.05 ± 0.41	<0.0001
BMI status		<18.5 kg/m^2	4.62 ± 0.19	
		18.5–<25 kg/m^2	4.90 ± 0.39	
		25–<30 kg/m^2	5.09 ± 0.43	
		30 kg/m^2	4.90 ± 0.40	<0.0001
Sex		Men	5.61 ± 0.21	
		Women	4.77 ± 0.22	<0.0001

[a]P-values obtained through general linear regression using the unadjusted VAT score based on 8 biomarkers plus BMI and height adjusted for BMI at cohort entry by the method of residuals

Abbreviations: BMI=body mass index; VAT=visceral adipose tissue

Table 3.

Association of biomarker-based VAT score and BMI with incidence of type 2 diabetes[a]

Characteristic	Incident T2D cases	Sample size	Person-years	VAT Score		BMI[b]		
				HR[a]	95% CI	Category	HR	95% CI
All	355	2,556	34,213	2.70	1.60, 4.58	18–<25 kg/m²	1.00	
						25–30 kg/m²	1.61	1.24, 2.08
						30 kg/m²	2.06	1.50, 2.83
Cancer Status						18–<25 kg/m²	1.00	
Cases	178	1,241	16,726	3.40	1.57, 7.39	25–30 kg/m²	1.71	1.17, 2.50
						30 kg/m²	2.16	1.37, 3.40
Controls	177	1,315	17,487	2.30	1.10, 4.81	25–30 kg/m²	1.52	1.05, 2.21
						30 kg/m²	1.91	1.20, 3.04
Sex						18–<25 kg/m²	1.00	
Men	104	589	5,782	2.99	1.03, 8.73	25–30 kg/m²	1.78	1.07, 2.98
						30 kg/m²	1.96	0.93, 3.99
Women	251	1,967	19,952	2.61	1.39, 4.91	25–30 kg/m²	1.53	1.12, 2.08
						30 kg/m²	2.07	1.43, 2.99
Ethnicity						18–<25 kg/m²	1.00	
White	43	509	5,629	1.07	0.20, 5.72	25–30 kg/m²	2.46	1.10, 5.46
						30 kg/m²	2.96	1.17, 7.49
African American	76	462	6,788	2.24	0.68, 7.34	25–30 kg/m²	1.16	0.57, 2.20
						30 kg/m²	1.10	0.53, 2.28
Native Hawaiian	25	201	2,979	5.84	0.47, 72.3	25–30 kg/m²	7.39	1.50, 36.4
						30 kg/m²	4.45	0.75, 26.6
Japanese American	118	877	10,957	6.24	2.34, 16.7	25–30 kg/m²	1.18	0.77, 1.80
						30 kg/m²	1.85	0.88, 3.85
Latino	93	507	7,859	1.80	0.58, 5.58	25–30 kg/m²	2.24	1.22, 4.11
						30 kg/m²	2.41	1.22, 4.77
BMI[c]								
Normal weight	115	1,413	14,025	3.31	1.30, 8.44		NA	
Overweight	155	1,235	12,356	4.00	1.63, 9.81		NA	
Obesity	80	728	7,374	2.08	0.69, 6.28		NA	

[a] Hazard ratios and 95% confidence intervals for continuous VAT score obtained by Cox regression with age as time metric and adjusted for sex, ethnicity, BMI, alcohol intake, physical activity (at cohort entry), age, glucose control, smoking history (at blood draw), and cancer status where applicable

[b] HRs are for BMI as covariate in model with VAT score

*c*Models for continuous VAT score stratified by BMI; N=40 (5 incident T2D cases) with underweight are not shown

Abbreviations: BMI=body mass index, T2D=type 2 diabetes, VAT=visceral adipose tissue