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An Analysis of Individual Body Fat Depots and Risk of Developing Cancer: Insights From the Dallas Heart Study

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Abstract

Objective: To examine the association between specific adipose tissue depots and the risk of incident cancer in the Dallas Heart Study.

Patients and Methods: Individuals without prevalent cancer in the Dallas Heart Study underwent quantification of adipose depots: visceral adipose tissue (VAT), abdominal subcutaneous adipose tissue, and liver fat by magnetic resonance imaging, and subcutaneous lower-body fat (LBF) by dual-energy X-ray absorptiometry from January 1, 2000, through December 31, 2002, and were observed for the development of cancer for up to 12 years. Multivariable Cox proportional hazards modeling was performed to examine the association between fat depots and cancer.

Results: Of 2627 participants (median age, 43 years; 69% nonwhite race), 167 (6.4%) developed cancer. The most common primary sites of cancer were the breast (in women) and the prostate (in men). In multivariable models adjusted for age, sex, race, smoking, alcohol use, family history of malignancy, and body mass index, a 1-SD increase in VAT was not associated with increased risk of cancer (hazard ratio [HR], 0.94; 95% CI, 0.77-1.14). In contrast, each 1-SD increase in LBF was associated with a reduced incidence of cancer (HR, 0.69; 95% CI, 0.52-0.92) in the fully adjusted model.

Conclusions: In this study, adiposity-associated cancer risk was heterogeneous and varied by fat depot: VAT was not independently associated with incident cancer, and LBF seemed to protect against cancer development. Further studies of the adiposity-cancer relationship, including serial assessments, are needed to better elucidate this relationship.

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Obesity, as defined by a body mass index (BMI) of at least 30, is associated with an increased incidence of, and mortality from, cancer.[1,2] This association may be stronger for certain obesity-associated cancers, such as those of the breast, endometrium, colon, and kidneys.[3] However, BMI is not a completely representative measure of body fat risk because distinct fat depots, such as visceral adipose tissue (VAT), abdominal subcutaneous adipose tissue (SAT), and liver fat (LF), have been associated with differing effects on metabolic and cardiovascular disease risk.[4-8] The relation of these adipose depots with the risk of noncardiovascular chronic conditions, particularly cancer, is not well understood. Studies reporting the risk of cancer in patients who have undergone image-guided measurements of VAT are limited and have focused on predominantly white or elderly populations, with inconsistent results.[4,9] Although SAT has been shown to have a neutral association with cancer, LF and lower-body fat (LBF) have not been studied in this regard. We aimed to study the relationship between specific fat depots and the risk of incident cancer in relatively young, multiethnic participants in the Dallas Heart Study (DHS).

MATERIALS AND METHODS

Study Population

Details about the design of the DHS have been previously described.[10] Briefly, the DHS is a

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single-site, multiethnic, population-based probability sample of Dallas County (Texas) residents (aged 18-65 years), with deliberate oversampling of the black population. The present study population was drawn from 3072 participants who completed DHS phase 1 visits from January 1, 2000, through December 31, 2002, which included a computer-assisted survey, anthropometric and blood pressure measurements, laboratory testing, and imaging assessments. Participants without imaging assessment of VAT were excluded. Because cancer diagnoses were made through linkage to the state cancer registry, participants who had moved out of Texas before 2012 were censored at the date they were last known to be a Texas resident. Of the remaining participants, those with a history of or a present diagnosis of malignancy were also excluded. To account for cancers that may have been undetected at baseline, new cases of cancer diagnosed within 1 year after the DHS enrollment date were excluded from the analysis (blanking period). After these exclusions, 2627 participants were eligible for follow-up (Supplemental Figure, available online at http://www.mayoclinicproceedings.org). All the participants provided written informed consent, and the University of Texas Southwestern Medical Center institutional review board approved the protocol.

Demographic characteristics, lifestyle, and other risk factors were determined from a baseline questionnaire. The BMI was calculated as the weight in kilograms divided by the height in meters squared. Waist circumference (WC) and hip circumference (HC) were measured in centimeters, and waist-hip ratio (WHR) was calculated as the ratio of WC:HC. The hypertriglyceridemic waist phenotype was defined by a WC of at least 90 cm and with serum triglyceride levels of at least 177 mg/dL (to convert to mmol/L, multiply by 0.0113).[11] Hypertension was defined as blood pressure of at least 140/90 mm Hg or taking antihypertensive medication(s). Diabetes mellitus was defined as a fasting serum glucose level of at least 126 mg/dL (to convert to mmol/L, multiply by 0.0555), self-reported diabetes, or taking hypoglycemic medication. Smoking was defined as cigarette use within the previous 30 days or a lifetime history of having smoked at least 100 cigarettes. Alcohol use was determined in grams per week by self-report. Comorbid conditions were determined from self-report, medication history, and clinical assessment. Fasting blood samples were obtained from participants, collected in EDTA-containing tubes, and stored at −80°C. Samples were analyzed for high-sensitivity C-reactive protein, interleukin-6, adiponectin, leptin, and insulin levels.[5,8]

Body Fat Distribution Measurements

Participants were scanned using a 1.5-T magnetic resonance imaging (MRI) scanner (Intera; Philips Healthcare). Retroperitoneal, intraperitoneal, and SAT abdominal fat masses were quantified by a single MRI slice taken at the L2-L3 level using manual contours, as previously validated against cadaveric samples.[12] Areas were converted to mass using previously determined regression equations.[13] VAT was defined as the combination of retroperitoneal and intraperitoneal fat masses.[8] Participants also underwent ^{1}H-magnetic resonance spectroscopy for hepatic triglyceride quantification (LF) as previously described.[14] Participants were also scanned by dual-energy X-ray absorptiometry, which was performed using a Delphi W scanner (Hologic) with a fan beam to determine fat and lean mass.[15] Lower-body fat was quantified from the total fat mass from the lower extremities.

Cancer Outcomes

The DHS was systematically linked to the Texas Cancer Registry (TCR) to determine cancer cases in the cohort.[16] The TCR is a population-based registry of Texas that meets the quality data standards of the National Program of Cancer Registries (Centers for Disease Control and Prevention) and the North American Association of Central Cancer Registries. The Texas Cancer Incidence Reporting Act mandates that health care facilities, including hospitals, ambulatory surgical centers, and cancer treatment centers, report to the TCR. All cancer cases identified by the TCR were classified as prevalent or incident based on date of cancer diagnosis in relation to date of enrollment in the DHS. In cases with more than 1 known cancer, only the first cancer was included. Carcinoma in situ and skin cancers were not included. Cancers of the gastrointestinal tract in close proximity to visceral fat depots were classified as visceral cancers and