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## More Evidence Links Body Fat With Prostate Cancer

— Risk of advanced, fatal disease rises with abdominal visceral fat

by Charles Bankhead, Senior Editor, MedPage Today June 12, 2019

Increasing body fat accumulation significantly raised men's odds of developing advanced and fatal prostate cancer, data from a large prospective study of men in Iceland showed.

Higher concentrations of visceral and thigh fat increased the odds of aggressive or fatal prostate cancer by 30%-40% as compared with leaner men. The prostate cancer risk associated with increased visceral fat accumulation carried over to men who had a lower BMI, reported Barbra A. Dickerman, PhD, of the Harvard T. H. Chan School of Public Health in Boston, and colleagues.

Higher BMI and waist circumference also were associated with an increased risk of aggressive and fatal prostate cancer. None of the measured parameters had significant associations with total prostate cancer or cancer grade, they stated in *Cancer*.

"To our knowledge, this is the first prospective study of directly measured fat distribution and the risk of advanced prostate cancer," the authors wrote. "Previous retrospective and cross-sectional studies incorporating CT measures of adiposity have reported mixed findings."

The findings relative to BMI were consistent with prior studies, whereas previous evaluations of waist circumference and prostate cancer yielded mixed results, they added.

The findings added to and extended knowledge about the relationship between obesity and prostate cancer, according to authors of a related editorial. However, Celina H. Shirazipour, PhD, and Stephen J. Freedland, MD, of Cedars-Sinai Medical Center in Los

Angeles, noted a couple of factors that might limit the generalizability of the results: use of a median BMI of 27, which encompassed both normal-weight and overweight men; and the observation that fat accumulation in more than one body area was associated with advanced prostate cancer, supporting existing evidence linking body fatness, irrespective of location, to the risk of advanced prostate cancer.

"The findings from [the] research, in addition to existing evidence on obesity and prostate cancer, highlight the need to examine lifestyle interventions that target fat loss in promoting optimal prostate cancer outcomes," they wrote.

"In light of the strong emphasis in the article on the findings associated with visceral fat and advanced prostate cancer among men with lower BMIs, and in light of existing knowledge on the detrimental impact of visceral fat, there is also a need to determine what behavior may be most effective in targeting this regional fat distribution," they added.

Multiple studies have shown a consistent association between obesity (as measured by BMI or waist circumference) and an increased risk of advanced prostate cancer, as well as a poorer prognosis after cancer diagnosis. More recently, studies have suggested that specific patterns of body fat distribution may have prognostic importance for prostate cancer.

Body fat distribution has attracted interest as a research subject because of its potential as a marker for different metabolic, hormonal, and inflammatory processes that may contribute to prostate carcinogenesis, Dickerman and colleagues noted. Visceral fat, for example, has an inverse association with bioavailable testosterone and strong associations with insulin resistance and proinflammatory cytokines. Increased intramuscular thigh fat has a strong association with poorer glucose tolerance, whereas subcutaneous thigh fat is associated with a more favorable metabolic profile.

Few studies examined associations between directly measured body fat distribution and prostate cancer risk, the authors continued. Some cross-sectional studies showed associations between CT measures of visceral fat and both total and high-grade prostate cancer. However, prior studies were limited by small sample sizes and did not account for the potential effects of the cancer or treatment on adiposity.

Dickerman and colleagues reported findings from 1,832 men participating in the Age, Gene/Environment Susceptibility-Reykjavik study. At enrollment during 2002 to 2006, study participants had baseline CT imaging of fat distribution, bioimpedance analysis, and measurements of BMI and waist circumference. Investigators calculated accumulation of

abdominal visceral fat, abdominal subcutaneous fat, thigh intramuscular fat, and thigh subcutaneous fat.

The 1,832 men had a mean age of 75-76 at enrollment, median BMI of 27, and median waist circumference of 102 cm. Follow-up for prostate cancer endpoints continued through 2015, during which time 172 of the men had prostate cancer diagnoses, 43 had high-grade prostate cancer (Gleason ≥8), and 41 had advanced disease at diagnosis or died of prostate cancer (31 prostate cancer deaths). BMI correlated with waist circumference and total body fat. Abdominal subcutaneous fat had a strong correlation with both BMI and waist circumference. Abdominal visceral fat had a lesser correlation with BMI and waist circumference.

The data showed that the risk of having advanced prostate cancer at diagnosis increased by 31% for each standard deviation increase in visceral fat. The risk of dying of prostate cancer increased by 37% for each standard-deviation increase in subcutaneous thigh fat. Visceral fat accumulation increased the risk of both advanced and fatal prostate cancer among with a BMI <27 (HR 1.95, 95% CI 1.07-3.54; HR 2.13, 95% CI 1.12-4.05) but did not significantly increase the risk of total, high-grade, advanced, or fatal prostate cancer among men with a BMI ≥27.

Each 5 kg/m<sup>2</sup> increase in BMI was associated with a 50% increase in the hazard for advanced prostate cancer and fatal prostate cancer. Each standard-deviation increase in waist circumference led to a 40% rise in the hazard for advanced and fatal prostate cancer.

Study limitations included the fact that exposures were measured once at cohort entry, so the authors were unable to assess changes in fat depots over time. Also, the study population was predominantly older white men, so the results may not be generalizable to younger, more diverse groups of men.

The study was supported by the National Cancer Institute, Harvard University, and the Icelandic Cancer Society. The AGES-Reykjavik study is supported by the National Institute on Aging, the Icelandic Heart Association, and the Icelandic Parliament.

Dickerman and co-authors, as well as Shirazipour and Freedland, disclosed no relevant relationships with industry.

## Cancer

Source Reference: Dickerman BA, et al "Body fat distribution on computed tomography imaging and prostate cancer risk and mortality in the AGES-Reykjavik Study" Cancer 2019; DOI:10.1002/cncr.32167.

## **Secondary Source**

Cancer

Source Reference: Shirazipour CH and Freedland SJ "Obesity, visceral adiposity, and prostate cancer: What is the role of lifestyle interventions?" Cancer 2019; DOI:10.1002/cncr.32165.