

Genetic mutation may play key role in risk of lethal prostate cancer in overweight patients

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Obesity is associated with a worse prostate cancer prognosis among men whose tumors contain a specific genetic mutation, suggest results from a new study led by Harvard School of Public Health (HSPH), Dana-Farber Cancer Institute and Brigham and Women's Hospital researchers. Among prostate cancer patients whose tumors contain the mutation, they had a more than 50% increased risk of dying from prostate cancer if they were overweight or obese compared to healthy-weight men; among men whose tumors did not have the mutation, there was no effect of obesity on cancer survival. It is the first study to link data on obesity, tumor genetics, and cancer-specific survival in prostate cancer patients.

The study was published online November 30, 2013 in the *Journal of the National Cancer Institute*.

"More than 100,000 men in the U.S. are diagnosed with [prostate cancer](#) that harbors this common gene mutation. Given the high prevalence of [obesity](#) among men, this excess risk of lethal prostate cancer associated with obesity is a considerable [public health](#) issue," said senior author Lorelei Mucci, associate professor of epidemiology at HSPH.

Prostate cancer is the second leading cause of cancer deaths in men, after lung cancer. In the United States, some 238,000 men will be diagnosed with prostate cancer in 2013. Previous studies have shown that men who are overweight or obese—about two thirds of the adult male population in the U.S.—were more likely to have a worse [prognosis](#) after being diagnosed with prostate cancer than normal-weight men, but little was known about the mechanisms of how obesity was linked with prostate cancer or whether specific subgroups of patients were more susceptible to the effects of obesity.

The researchers, including lead author Andreas

Pettersson, a former postdoctoral fellow at HSPH and now visiting scholar in the HSPH Department of Epidemiology, Mucci, Massimo Loda at Dana-Farber, and colleagues analyzed data on body mass index (BMI), waist circumference, and a marker for the hormonally regulated genetic mutation TMPRSS2:ERG from 1,243 participants in the Physicians' Health Study and Health Professionals Follow-Up Study who were diagnosed with prostate cancer between 1982 and 2005. Over the course of a follow-up period averaging 13 years, 119 men developed a lethal form of the disease.

One in two men with prostate cancer had tumors that were positive for the common genetic mutation TMPRSS2:ERG. The researchers found that among these men with prostate cancer whose tumors had the mutation, those who were overweight or obese had more than 50% increased risk of dying from cancer after diagnosis than normal-weight men. The effect was even stronger for obesity as measured by waist circumference. In contrast, men whose tumors were negative for the genetic mutation, there was no effect of obesity on cancer survival.

Obesity is associated with higher levels of several hormones, including insulin and growth factors that may fuel the progression of cancer. The authors found for the first time that the men whose tumors contained the TMPRSS2:ERG genetic mutation also had higher levels of the receptors for insulin and growth factor in their tumors. This finding may explain why [men](#) whose prostate tumors contain the genetic mutation would be more susceptible to the effects of obesity.

"The results from this study may help us better understand the mechanisms linking obesity with poorer prostate cancer prognosis. The key public health message is unchanged, however: Prostate [cancer patients](#) who are overweight or obese should lose weight to increase their chance of

survival, regardless of whether their tumors carry this genetic change or not," said Pettersson.

Provided by Harvard School of Public Health

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