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Free testosterone drives cancer aggressiveness, study finds

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What is the reason for the widely reported fact that men are more likely than women to die of cancer? New evidence from population studies suggests that free testosterone could be a key driver of cancer aggressiveness in a broad range of solid tumors and sarcomas, not just gender-specific cancers, according to researchers at the Danbury Hospital Research Institute. The conclusions, published in *PLOS One*, are based on analyses of about 1.2 million cases from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) database.

"Although we live in the era of personalized medicine, gender is not taken into consideration when selecting treatment options for cancer patients. Our study emphasizes that gender has an important role to play in oncology," said Dr. Christiano Ferlini, one of the researchers. "Thus far, anti-cancer strategies targeting sex hormones have been confined to prostate and breast cancer, and we generally give men and women the same treatments for many malignancies. Our findings, obtained in the largest available public database, suggest that a much broader use of anti-androgen therapies in men under the age of 61 should be studied."

First, the researchers studied gender differences in cancer outcomes five years after diagnosis—the so-called "gender effect"—across the age range in the SEER database, excluding gender-specific cancers and cases lacking enough information. It is believed to be the first study to analyze the gender effect in the US population that included age as one of the consistent variables. After calculating the hazard ratio—a statistical tool used to compare survival rates—between men and women, they found

that "gender differences in cancer outcomes are most significant between the ages of 17-61, when males and females exhibit the most dramatic differences in circulating levels of sex hormones," said Dr. Shohreh Shahabi, another author of the study. "The differences peak at age 27."

The analysis also showed that the risk of death from cancer 5 years after diagnosis in males was about 30% higher than that of females of the same age, in the age range 17-61. The gender effect was evident only in patients with epithelial solid tumors and sarcomas, not hematological malignancies, and the effect was more prominent in African Americans than Caucasians.

To identify possible biological causes of the gender effect, the researchers then turned to the NHANES III survey, which examines the health of the U.S. population based on different variables. In a population sample of about 29,000, they tracked the distribution of 65 health-related variables across the age range. They discovered that the distribution of free testosterone almost exactly matched the distribution of the hazard ratio that compared cancer outcomes in men and women in the SEER database. None of the other 64 physiological variables they analyzed were so closely correlated with the gender effect.

One potential therapeutic application involves colorectal cancer, said Dr. Ferlini. "Recently, androgens have been reported in several studies to activate a pro-survival pathway in colorectal cancer. Our population study gives further impetus to the idea of testing anti-androgen therapies when a young male patient is diagnosed with a solid tumor."

More information: Shahabi S, He S, Kopf M, Mariani M, Petrini J, et al. (2013) Free Testosterone Drives Cancer Aggressiveness: Evidence from US Population Studies. *PLoS ONE* 8(4): e61955. doi:10.1371/journal.pone.0061955

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