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Androgen deprivation therapy associated with increased risk for fatal heart attack

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Long term follow up indicates that men with comorbidity, predominately a prior heart attack, who received androgen deprivation therapy (ADT) died earlier, due to a fatal heart attack.

Androgen deprivation therapy (ADT) and radiation therapy (RT) is known to prolong survival in men with unfavorable-risk prostate cancer and is considered a standard of care. However, in 2008, the FDA implemented a black box warning about ADT use for prostate cancer due to evidence that suggested an increased risk in non-fatal cardiovascular events. The association of ADT use and fatal heart attacks has remained uncertain until now. Specifically, long term follow up of a randomized clinical trial that compared ADT and radiation therapy (RT) to RT alone finds that men with significant comorbidity; most commonly prior heart attack, who received ADT died earlier, due to a fatal heart attack, compared to men who did not receive ADT.

These findings are published in a research letter in the September 22/29, 2015 issue of the *Journal of the American Medical Association*.

"These findings give us reason to rethink how we manage prostate cancer in men with known heart disease," said Anthony D'Amico, MD, lead author of the research paper and chief of genitourinary radiation oncology at Brigham and Women's Hospital.. "Specifically, we should be cautious in prescribing ADT in all men who have had a prior heart attack. Men with significant heart disease that is not amenable to medical or surgical correction may be best served with RT alone."

Researchers compared overall survival and death due to prostate cancer, fatal heart attack and all other causes in a group of 206 men with unfavorable risk prostate cancer who were randomized to receive RT alone or RT and six months of ADT. They also categorized the men into subgroups based on extent of prior comorbidity, including prior heart attack. After a median follow up exceeding 16 years, researchers found that overall, survival did not differ between the two groups of men. When analyzing the subgroups of men by differing extent of comorbidity, researchers found that among men whose comorbidity included prior heart attack, treatment with RT and ADT shortened survival due to higher rates of fatal heart attacks, while prolonging survival in men with no or minimal comorbidity.

"While there is a growing body of evidence to support active surveillance for men with low risk prostate cancer, men who have unfavorable-risk cancer and significant comorbidity, notably heart disease, may be best served by considering RT alone or possibly active surveillance. For these men, the side effects of ADT may be life threatening. More research is needed to better understand the newer forms of hormone therapy that do not lower testosterone and how they impact survival," D'Amico said.

More information: *Journal of the American Medical Association*, DOI: 10.1001/jama.2015.8577

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