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Hormone therapy for prostate cancer does not appear to increase cardiac deaths

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Treating prostate cancer patients with drugs that block hormonal activity does not appear to increase the risk of death from cardiovascular disease, according to a study led by Massachusetts General Hospital (MGH) researchers. While a 2006 report from members of the same study team found that treatment with gonadotropin-releasing hormone (GnRH) agonists increased the risk of diabetes and heart disease, the current study is the first to examine whether treatment actually increased heart-disease-related deaths. In their *Journal of Clinical Oncology* report, which has been released online, the researchers note that GnRH agonist treatment has a number of adverse side effects, which should be kept in mind when determining treatment strategies.

"Hormonal therapy for prostate cancer has become routine for many patients, so it's even more important to understand the potential adverse effects of treatment," says lead author Jason Efstathiou, MD, PhD, of the MGH Cancer Center. "Given recent concerns about the safety and impact on cardiac health of hormonal therapies – particularly GnRN agonists – our study is quite timely."

Since the male hormones called androgens can accelerate the development of prostate cancer, reducing their activity is a standard part of treating the disease. Most commonly this is done with GnRH agonists that block the production of all sex hormones. GnRH agonist therapy is routinely administered to men whose cancer has spread beyond the prostate gland, and its use in patients whose tumors appear confined to the prostate is becoming more common. It is estimated that one-third of

the two million prostate cancer survivors in the U.S. are currently receiving this therapy, making understanding the potential adverse effects of treatment particularly important.

The earlier report from a Harvard Medical School team – including Matthew Smith, MD, PhD, of the MGH Cancer Center, who is corresponding author of the current study – found that men with localized prostate cancer who received GnRH agonist therapy had a greater risk of developing diabetes or cardiovascular disease than patients not receiving hormonal treatment. To specifically investigate the relationship between GnRH agonist therapy and death from cardiovascular disease, the current study analyzed data from a 1987-92 clinical trial in which almost 1,000 patients were treated for locally advanced prostate cancer with either the GnRH agonist goserelin plus radiation therapy or radiation therapy alone.

During the decade following completion of the clinical trial, more than half the participants died from various causes. Of the 574 deaths, 117 were from cardiovascular disease, but whether or not patients had received the GnRH agonist apparently had no effect on the risk of cardiovascular death. Instead, it was established cardiac risk factors – including heart disease or diabetes that existed prior to GnRH agonist treatment – that appeared to increase the risk of dying from cardiovascular disease.

"The absence of an increase in cardiovascular mortality does not exclude the possibility that GnRH agonists increase non-cancer deaths through other mechanisms," Efstathiou stresses. "In addition to the increased risk for diabetes identified in the 2006 study, we know they can raise the risk of fractures and anemia – both of which can reduce survival – and can have adverse effects on weight gain, cholesterol levels, mood and sexual function.

"While our study supports the continued use of GnRH agonists in situations where the benefit for cancer control has been established – typically the treatment of advanced or more aggressive prostate cancer – clinicians should keep in mind the risks of diabetes and cardiovascular disease and help their patients adopt strategies to reduce those risks," he adds. "Further studies are needed to evaluate potential risks for men with earlier stage prostate cancer, for whom the role of GnRH agonists is not as well defined, and treatment decisions need to carefully weigh potential risks and benefits." Efstathiou is an instructor in Radiation Oncology at Harvard Medical School.

Source: Massachusetts General Hospital