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Prostate cancer patients on hormone therapy at increased risk for various heart diseases

Berlin, Germany: New research has found that hormone therapy used to treat men with advanced prostate cancer is associated with an increased chance of developing various heart problems. Some choices of therapy appear, however, to be less risky than others.

Researchers told Europe's biggest cancer congress, ECCO 15 – ESMO 34 [1], in Berlin today (Tuesday 22 September) that the findings of their study, the largest and most comprehensive to date on the issue, indicate that doctors need to start considering heart-related side effects when they prescribe endocrine therapy for prostate cancer and might want to refer patients to a cardiologist before starting treatment.

A few smaller studies have indicated that some types of hormone therapy increase the risk of coronary heart disease and heart attacks in prostate cancer patients, but others have found no increased risk. This is the first large study to investigate how the broader range of hormone therapies affect a wider range of heart problems and provides for the first time a detailed picture of the impact of each sort of hormone therapy on individual types of heart trouble.

"If we have observed a causative effect, then for all hormone therapies put together, we estimate that compared with what's normal in the general population, about 10 extra ischaemic heart disease events a year will appear for every 1,000 prostate cancer patients treated with such drugs," said the study's leader, Ms Mieke Van Hemelrijck, a cancer epidemiologist at King's College in London. "However, not all types of therapy were associated with the risk of heart problems to the same degree. We found that drugs which block testosterone from binding to the prostate cells were associated with the least heart risk, while those that reduce the production of testosterone were associated with a higher risk. This may have implications for treatment choice."

Prostate cancer is diagnosed in more than 670,000 men each year worldwide, making it the second most common cancer among men worldwide, after lung cancer. Hormone therapy is a mainstay of treatment when the cancer is locally advanced and when it has spread to more

distant parts of the body, but is increasingly being used in earlier stages of the disease. It involves either removing the testicles to eliminate the main source of testosterone production, injections of gonadotropin releasing hormone agonists to dramatically reduce the production of testosterone from the testicles or anti-androgen pills, which do not reduce the amount of testosterone produced but block it from attaching the prostate cells. Doctors sometimes use a combination of those approaches.

In the study, researchers analysed the link in 30,642 Swedish men with locally advanced or metastatic prostate cancer who had received hormone therapy as primary treatment for their disease between 1997 and 2006. The men were followed for an average of three years. The researchers calculated the risk of developing ischaemic heart disease, heart attacks, arrhythmia and heart failure requiring hospitalisation as well as the risk of dying from these heart diseases by comparing the rates among the cancer patients with what's normal in the general Swedish population. Most patients got one of the three hormone treatment choices, but 38% got a combination of the two types of drugs.

"We found that prostate cancer patients treated with hormone therapy had an elevated risk of developing all of the individual types of heart problems and that they were more likely than normal to die from those causes," Ms Van Hemelrijck said, adding that the problems started happening within a few months of initiating treatment.

Overall, prostate cancer patients treated with hormone therapy had a 24% increased risk of a non-fatal heart attack, a 19% increased risk of arrhythmia, a 31% increased risk of ischaemic heart disease and a 26% increased risk of heart failure. The risk of a fatal heart attack was increased by 28%, the risk of dying from heart disease by 21%, the risk of heart failure death was increased by 26% and the risk of fatal arrhythmia was increased by 5%.

"In a more detailed analysis by type of hormone therapy, the lowest increase in risk for ischaemic heart disease, heart attack and heart failure was seen in the group taking anti-androgen therapy, and we saw no increase in risk of death from heart disease in this group," Ms Van Hemelrijck said. "Patients on gonadotropin releasing hormone agonist therapy had the highest risk of these problems."

For instance, the increased heart failure risk for anti-androgens was 5%, compared with 34% for gonadotropin releasing hormone agonists and the increased ischaemic heart disease risk was 13% in the anti-androgen group, compared with 30% in the gonadotropin releasing hormone agonist therapy group.

"The finding that anti-androgens carry the least heart risk supports the view that circulating testosterone may protect the heart," she said.

The association with heart risk when the testicles were removed was close to that seen with the gonadotropin releasing hormone agonist therapy, Ms Van Hemelrijck added.

The increased risk of heart events requiring hospitalisation was less pronounced in patients who already had heart disease before hormone treatment, with a 17% risk increase for a new ischaemic heart disease event among those with a history of heart disease, compared with a 41% increase among men who didn't have any heart trouble before hormone treatment, for instance. Ms Van Hemelrijck said that could be because the men who already had heart disease were likely to be taking heart medications that protected them from further heart risk imposed by the endocrine treatment.

"We now need studies verifying the association and exploring plausible biological mechanisms. Then we would know how to best use these treatments according to a patient's history of various types of heart disease and whether it would be a good idea to give patients heart medicines to counteract these side effects," Ms Van Hemelrijck concluded.

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