No Early Cardiovascular Risks With Testosterone Treatment

— Data on long-term safety needed, however

by Michal Ruprecht, Editorial Intern, MedPage Today
June 13, 2022

Testosterone treatment for hypogonadism did not increase short- or medium-term risks for cardiovascular events, according to a systematic review and meta-analysis.

Cardiovascular risks were similar between men in the testosterone group and those in the placebo group (7.5% vs 7.2%; OR 1.07, 95% CI 0.81-1.42, *P*=0.62), reported Channa Jayasena, PhD, of Imperial College London, at ENDO 2022, the annual meeting of the Endocrine Society.

The findings were also recently published in *Lancet Healthy Longevity.*

The mortality rate among those on testosterone treatment was 0.4 percentage points lower than the control group, but this difference was not statistically significant (0.4% vs 0.8%; OR 0.46, 95% CI 0.17-1.24, *P*=0.13).

"While there were a few deaths that happened so far, there's no current evidence that we could find that testosterone would elevate cardiovascular or cerebrovascular risk," Jayasena pointed out during a presentation of the findings.

However, he noted that the meta-analysis drew upon short-term studies -- some as short as 3 months -- that weren't designed to fully assess this risk.

"Prescribing of testosterone for hypogonadism is increasing globally, but conflicting messages about its safety may have led to many patients not receiving the treatment," said co-investigator Jemma Hudson, MSc, of the University of Aberdeen in Scotland, in a press release. "Ongoing studies should help to determine the longer-term safety of testosterone but, in the meantime, our results provide much-needed reassurance about its short- to medium-term safety. Our findings could have important implications for the treatment of men with hypogonadism worldwide."

The most common cardiovascular events in the testosterone and placebo groups included arrhythmia (31.3% vs 26.7%), coronary heart disease (19.9% vs 18.8%), heart failure (13.3% vs 15.9%), and myocardial infarction (6.0% vs 9.1%).

Testosterone treatment did lead to decreased high-density lipoprotein (HDL) cholesterol compared with the placebo group (mean difference -0.06 nmol/L, 95% CI -0.08 to -0.04, $P<0.0001$). Both serum total cholesterol and triglycerides were also significantly lower in the testosterone group versus the placebo group (total cholesterol: mean difference -0.15 mmol/L, 95% CI -0.20 to -0.10, $P<0.001$; triglycerides: mean difference -0.09 nmol/L, 95% CI -0.18 to -0.00, $P=0.04$).

However, serum levels of low-density lipoprotein cholesterol, blood pressure, glycemic parameters, diabetes incidence, and prostate adverse outcomes were not significantly different. And this held true when the researchers performed a sensitivity analysis that looked at outcomes between men with different reasons for starting testosterone, Jayasena said, including, for example, men presenting with normal baseline levels who started treatment for sexual symptoms.

"What we don't want is to be kind of a green flag to say, 'It's open season for giving testosterone,'" he added. "Because any drug that is not needed is unsafe. But we could not find a trend for increased harm when you became looser in your definition."

Previous studies have suggested that testosterone may negatively impact cardiovascular risk. As a result, the FDA required companies to include a cardiovascular risk warning on all testosterone products. The agency also restricted testosterone treatment to hypogonadism caused by documented pituitary or testicular disease, excluding treatment for age-related hypogonadism.

For this systematic review, the researchers included data from 35 studies in 109 peer-reviewed publications, involving 5,601 participants (mean age 65). They also looked at individual patient data in 17 of those studies (3,400 hypogonadism patients). Of these men, 1,750 received testosterone treatment and 1,681 were given placebo. On average, treatment lasted for 9.5 months. Over 87% of participants were white, the majority were non-smokers, and mean BMI was 30.

Patient age (interaction 0.97, 99% CI 0.92-1.03, *P*=0.17), baseline testosterone (interaction 0.97, 99% CI 0.82-1.15, *P*=0.69), smoking status (interaction 1.68, 99% CI 0.41-6.88, *P*=0.35), and diabetes status (interaction 2.08, 99% CI 0.89-4.82, *P*=0.025) were not associated with cardiovascular risk.

"An important strength of this IPD [individual participant dataset] meta-analysis is its large size compared with individual testosterone trials, which have provided limited and situation-dependent information on cardiovascular safety," the authors wrote. "This study has allowed us to more precisely estimate the incidence of cardiovascular events associated with testosterone treatment, which might be generalizable to patients worldwide."

The lack of data beyond 12 months was a limitation to the study, they noted, adding that the low number of deaths that occurred during treatment made it difficult to determine why those deaths occurred.

Jayasena said he is eagerly awaiting findings of AbbVie's randomized TRAVERSE trial, testing topical testosterone replacement therapy in symptomatic hypogonadal men with increased risk for cardiovascular disease, which is expected to be completed in the next few weeks.

Kristen Monaco contributed to this article.

Michal Ruprecht is a medical student based in Michigan. He is a former reporting intern for MedPage Today. Follow

---

Disclosures

The study was funded by a grant from the National Institute for Health Research Health Technology Assessment Programme.

Jayasena reported relationships with LogixX Pharma, Bayer, and Besins. Co-authors disclosed relationships with AbbVie, NIH, Aditum, OPKO Health, Endocrine Society, Otsuka, Lilly, Weight Watchers, Novartis, National Health, Medical Research Council Australia, and other organizations.

Primary Source

The Lancet Healthy Longevity

Source Reference: *Hudson J, et al "Adverse cardiovascular events and mortality in men during testosterone treatment: an individual patient and aggregate data meta-analysis" Lancet Healthy Longev 2022; DOI: 10.1016/S2666-7568(22)00096-4.*

Secondary Source

The Endocrine Society

Source Reference: *Jayasena C, et al "Adverse cardiovascular events and cause mortality in men during testosterone treatment: individual patient and aggregate data meta-analyses" ENDO 2022; Abstract OR25.*

1 Comment

Recommended For You

AIBD

Telehealth Pathway for IBD Surgery Expanded Access to Care in Small Study

Video

Quads, Frailty, and the Future: Evolving Frontline Strategies in Multiple Myeloma

Video

Health of Myeloma Patient's Marriage Tied to Recovery After Transplant

Video

Optimizing Sequencing of BCMA-Directed Therapies in Myeloma

AIBD

For IBD, No Cardiovascular Risk Difference Between JAK, TNF Inhibitors

Video

Mosunetuzumab in Follicular Lymphoma: Durable Responses and Manageable Safety

Medical News From Around the Web

CBS NEWS

When a teen's medication stopped working, he decided to try a surgery that could stop his episodes for good

USA TODAY

The popular weight-loss drug Zepbound can now be used to treat sleep apnea

CNN

FDA approves weight-loss drug Zepbound for obstructive sleep apnea | CNN

NPR

FDA approves weight loss drug Zepbound to treat obstructive sleep apnea

CIRCULATION

Activation of Imprinted Gene PW1 Promotes Cardiac Fibrosis After Ischemic Injury.

JOURNAL OF CLINICAL ONCOLOGY

Long-Term Follow-Up and Overall Survival in NRG258, a Randomized Phase III Trial of Chemoradiation Versus Chemotherapy for Locally Advanced Endometrial Carcinoma.