ENDOCRINE SOCIETY
Hormone Science to Health

The Risk of Cardiovascular Events in Men Receiving Testosterone Therapy

An Endocrine Society Statement

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A recent study by Finkle et al[1], published online in PLOS ONE, suggests that the risk of myocardial infarction is increased in men who are receiving testosterone therapy and who have pre-existing heart disease. This report follows on the heels of another study from the Veterans Health Care System[2], which also found a higher frequency of death and cardiovascular events in men who had documented coronary artery disease and who were administered testosterone therapy. In 2010, a randomized placebo-controlled trial of testosterone in older men with mobility limitation, funded by the National Institute on Aging (NIA), was stopped early by the trial's data and safety monitoring board, due to the higher frequency of cardiovascular-related events in men assigned to the testosterone arm of the trial than in those assigned to the placebo arm[3]. These studies have heightened concern about the safety of testosterone therapy in older men with pre-existing heart disease.

Finkle and colleagues[1] examined the health care records of 55,593 men who had been prescribed testosterone therapy. They found a twofold increase in the relative risk of myocardial infarctions in the 90 days after starting testosterone therapy in men who had heart disease compared to the year before. The increase in myocardial infarctions was even greater in men over the age of 65 than in men under the age of 65.

Another retrospective analysis and a small prospective randomized trial had reported lower cardiovascular events in men who were receiving testosterone than in those who were not receiving testosterone[5-6]. Retrospective database analyses are limited by their inherent inability to verify the indication for treatment, diagnoses, or other relevant quantitative information that is often not ascertainable from an administrative database. Nonrandomized retrospective analyses are also susceptible to unmeasured confounding due to a variety of other factors. These factors are particularly important because many patients in the

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United States are being prescribed testosterone for the treatment of age-related symptoms or age-related decline in testosterone levels, for which testosterone therapy has not been approved by the Food and Drug Administration.

Large scale, prospective, randomized controlled trials are needed to determine the risks and benefits of testosterone therapy in older men with age-related decline in testosterone levels. The NIA-funded T Trials, an ongoing randomized trial of testosterone in older men with unequivocally low testosterone levels and symptoms – sexual dysfunction, physical dysfunction or low vitality – will determine whether testosterone therapy improves these symptoms, and whether it is safe.

Until evidence from large randomized trials becomes available, the Endocrine Society believes that patients should be made aware of the potential risk of cardiovascular events in middle-aged and older men who are taking or considering testosterone therapy for age-related decline in testosterone levels and symptoms. Physicians and patients should have a conversation about the risks and benefits of using testosterone, especially in patients who have pre-existing heart disease. The Endocrine Society recommends that physicians prescribe testosterone in accordance with the Society's clinical practice guidelines on testosterone therapy in men with hypogonadism. Testosterone therapy should be accompanied by a standardized monitoring plan to optimize the dose and minimize the risk of adverse effects. The Endocrine Society encourages patients with concerns about this report or about their testosterone therapy to contact their health care providers. Patients with hypogonadism who have been on stable testosterone therapy should not stop their medication without consulting their health care provider.

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