

## Testosterone Use in Older Men Does Not Speed Up Atherosclerosis

Marlene Busko | August 14, 2015

Older men with low or low-normal testosterone who received testosterone gel daily for 3 years did not have a faster progression of subclinical atherosclerosis compared with their peers who received placebo gel, in a new study. However, the testosterone-treated men also did not report any improved sexual function or health-related quality of life.

These findings from Testosterone's Effects on Atherosclerosis Progression in Aging Men (TEAAM) trial in 308 men age 60 and older, by Dr Shehzad Basaria, from Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, and colleagues, are reported in the August 11 issue of the *Journal of the American Medical Association*.

"It doesn't necessarily mean that testosterone has no effects on cardiovascular events [such as myocardial infarction or stroke], it just means that if [it] has an effect on the cardiovascular-event rate, then it's not due to atherosclerosis progression," senior author Dr Shalender Bhasin, from Brigham and Women's Hospital and Harvard Medical School, explained to *Medscape Medical News*.

Normal testosterone is typically defined as a level of 300 to 1000 ng/dL, he explained, and in this study low testosterone was 100 to <300 ng/dL and low-normal testosterone was 300 to 400 ng/dL. "Many older men getting testosterone [therapy] have normal or only slightly low testosterone, and our study showed that these men do not benefit," he noted.

This population differs from men with overt androgen deficiency, where testosterone can improve sexual function, said Dr Bhasin, who was lead author of Endocrine Society guidelines on this topic (*J Clin Endocrinol Metab*. 2010;95: 2536-2559).

"The important lesson is that testosterone should not be used indiscriminately," he stressed.

Invited to comment, Dr Adrian Sandra Dobs, from the Johns Hopkins University School of Medicine, in Baltimore, Maryland, agreed. In these older men with low or low-normal testosterone, it was "interesting and perhaps disturbing that there was no improvement in overall sense of health or sexual function," she said. "Thus, one has to ask — where is the benefit?"

On the other hand, there also was no sign of worsening atherosclerosis. Since this study did not look at cardiovascular events, "there still might be a problem with blood clots, but there doesn't seem to be a problem with atherosclerosis," Dr Dobs summarized. "Overall, [the study] could suggest that testosterone therapy is likely safe, at least for atherosclerosis."

### Spiraling Sales of Testosterone, but Is It Warranted or Safe?

"Testosterone sales have increased substantially, particularly among older men, during the past decade. However, the benefits and risks of long-term testosterone administration to older men with age-related decline in testosterone levels remain poorly understood," Dr Basaria and colleagues write.

TEAAM aimed to study older men with low or low-normal testosterone levels to see whether raising testosterone to the mid-normal range for young men (500 to 900 ng/dL) would affect the progression of subclinical atherosclerosis.

From 2004 to 2009, the researchers enrolled 308 healthy men aged 60 and older with low or low-normal testosterone who were living in the community at three US sites (Los Angeles, Boston, and Phoenix).

The participants were randomized to receive 7.5 g of 1% testosterone gel or a placebo gel daily for 3 years. Two weeks after randomization, total testosterone levels were measured 2 to 12 hours after the gel was applied, and if the concentration was below 500 ng/dL, the dose was increased to 10 g daily; if the concentration was above 900 ng/dL, the dose was reduced to 5 g daily. Placebo doses were similarly adjusted, to maintain blinding.

The two co-primary outcomes were the rate of change in the distal right common carotid artery intima-media thickness (measured at baseline and every 6 months for 3 years) and the change in coronary artery calcium (measured at baseline and 18 and 36 months).

Secondary outcomes included self-reported sexual function, based on the International Index of Erectile Function questionnaire, and health-related quality of life based on the SF-36 questionnaire.

The two groups had similar baseline characteristics. They had a mean age of 67 and a mean body mass index of 28.1. A total of 42% had hypertension, 15% had diabetes, 15% had cardiovascular disease, 27% were obese, and 43% were receiving a statin.

There was no significant difference in the rate of change in carotid artery intima-media thickness in the placebo group and the testosterone-treated group: 0.010 mm/year vs 0.012 mm/year, respectively. The mean difference, adjusted for age and trial site, was 0.0002 mm/year ( $P = .89$ ).

There was also no significant difference in the rate of change in the coronary artery calcium score in the placebo group vs the testosterone-treated group: 41.4 Agatston units/year vs 31.4 Agatston units/year, respectively. The adjusted mean difference was -10.8 Agatston units/year ( $P = .54$ ).

And changes in these measures of atherosclerosis progression were not associated with changes in testosterone levels among men who received testosterone.

There were no significant between-group differences in reported sexual desire, erectile function, overall sexual-function scores, partner intimacy, and health-related quality of life, over the 3 years.

"In older men, there are many reasons for poor sexual function, such as diabetes and poor vascular flow," Dr Dobs noted. "Thus, testosterone may have very little influence, [whereas] maybe in younger men it does make more of a difference," she suggested.

Although this past March the US Food and Drug Administration issued an advisory warning of a possible heightened risk of cardiovascular events in men taking testosterone supplements, the advisory board noted that the evidence for this is incomplete and inconclusive, Dr Bhasin said.

Thus, "Larger randomized trials to look at testosterone effects on major cardiovascular events are much needed to clarify this issue," he concluded.

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