Low Testosterone in Diabetic Men Tied to Vascular Risk

Marlene Busko | October 22, 2014

In a cross-sectional study of men around 60 years old with type 2 diabetes, those with low total plasma testosterone levels had a sixfold higher risk for increased carotid artery intima media thickness (CIMT) and decreased endothelial function, compared with their peers with normal testosterone.

The study was published online October 16 in the *Journal of Clinical Endocrinology & Metabolism*.

The research identified that 31% of these middle-aged, overweight, diabetic men had low testosterone levels, and the latter was linked with a heightened level of atherosclerotic-disease risk markers, lead author Dr Javier Mauricio Farias (Hospital Universitario Sanatorio Guemes, Buenos Aires, Argentina) told *Medscape Medical News*.

"Several cross-sectional studies have reported that about one-third of adult patients with obesity and type 2 diabetes have low serum testosterone," coauthor Dr Guillermo E Umpierrez (Emory University, Atlanta, Georgia) observed.

"Our study indicates a strong association between cardiovascular disease and low testosterone but does not prove causation," he stressed.

Serum testosterone should be measured in patients with diabetes with symptoms and physical signs of hypogonadism, Dr Umpierrez added, and the Endocrine Society and American College of Endocrinology have published guidelines specifying who should receive testosterone-replacement therapy.

However, "prospective randomized studies are needed to assess the clinical significance of our findings and the clinical impact of testosterone replacement on cardiovascular risk factors in diabetic patients with low total testosterone," the researchers note in their paper.

In the meantime, "the decision to offer testosterone-replacement therapy needs to be individualized," Dr Farias said.

Low Testosterone, Narrow Arteries?

Few studies have examined the relationship between atherosclerotic disease markers and low total testosterone levels in patients with type 2 diabetes, the authors explain.

They conducted a prospective study in 115 middle-aged men, younger than 70, who had type 2 diabetes and no cardiovascular disease and who were seen in a single center in Buenos Aires between 2010 and 2012.

A total of 79 men had normal total testosterone ($\geq$ 12.1 nmol/L, or $\geq$ 3.5 ng/mL), and 36 men had low total testosterone (< 12.1 nmol/L, or < 3.5 ng/mL) — based on International Society of Andrology cutoffs.

The patients had a mean age of 59 and had had diabetes, on average, for 6 to 8 years. Mean body mass index (BMI) was 30, and HbA_{1c} was 7%.

The patients had blood tests to determine C-reactive protein (CRP) and testosterone levels. Three markers of atherosclerotic disease were determined: CIMT and atherosclerotic plaque (both assessed by ultrasound) and endothelial function (assessed by brachial-artery flow-mediated dilation).

Increased carotid IMT and the presence of carotid plaques are important risk factors for acute myocardial infarction and cardiovascular mortality in patients with and without type 2 diabetes.

More patients with low vs normal testosterone levels had a CIMT of 0.1 cm or greater (80% vs 39%), atherosclerotic plaques (68.5% vs 44.8%), and endothelial dysfunction (80.5% vs 42.3%). Low testosterone levels were also associated with higher CRP levels.

Odds of Abnormal Atherosclerotic Risk Marker, Low vs Normal Testosterone Levels

Risk Marker	Odds Ratio (95% CI)	*P*
Carotid IMT ≥ 0.1 cm	6.41 (2.5 – 16.4)	< .0001
Atherosclerotic plaques	2.60 (1.12 – 6.03)	< .0001
Endothelial dysfunction	5.77 (2.77 – 14.77)	< .003

More Than Half With Low Testosterone Had Higher Vascular Risk

When the presence of these three major atherosclerotic markers were analyzed together for each individual patient (IMT ≥ 0.1 cm, plaque presence, and endothelial dysfunction), 54% of the patients with low total testosterone and 10% of subjects with normal testosterone evidenced a higher risk for vascular disease.

However, after multivariable adjustment, having a low testosterone level was no longer linked with a greater likelihood of having atherosclerotic plaques, possibly because the presence of plaques was influenced by other risk factors such as smoking and hypertension, Dr Farias hypothesized.

"We still need to determine whether testosterone is directly involved in the development of atherosclerosis or if it is merely an indicator of advanced disease," he said. "This study is a stepping stone to better understanding the risks of cardiovascular events in men who have both low testosterone and type 2 diabetes."

Dr Umpierrez stressed that this study did not examine the role of testosterone therapy,

"In elderly patients with evidence of atherosclerosis, testosterone replacement has not been shown to be of benefit and may even increase the risk of cardiovascular events," he said.

Nor is there any evidence that testosterone-replacement therapy reduces the risk for cardiovascular disease in younger middle-aged patients, he added, noting that future studies are needed to determine the efficacy and benefit/risk of testosterone in different patient populations.

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