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Meta-analysis: Testosterone Is Not a Risk for Prostate Cancer, But...

Nick Mulcahy | May 19, 2015

NEW ORLEANS — Testosterone, whether occurring naturally or taken as replacement therapy, does not cause prostate cancer or spur increases in prostate-specific antigen (PSA) levels in men, according to a new meta-analysis.

The results are "encouraging," but longer-term data from randomized trials are needed to strengthen the finding, said lead author Peter Boyle, PhD, DSc, who is president of the International Prevention Research Institute in Lyon, France

"You need 15 to 20 years of follow-up to see true prostate cancer risk," he told *Medscape Medical News* here at the American Urological Association 2015 Annual Meeting.

The average follow-up in the studies included in the meta-analysis is "much less" than what is needed, he said.

There are reasons to be concerned about the deleterious effects of testosterone on prostate cancer, Dr Boyle pointed out. "We know that high doses of testosterone induce prostate cancer in animals," he told reporters at a meeting press briefing.

Further, "androgens are important modifiers of the progression and metastasis of prostate cancer in humans," he said. "And most prostate cancers respond to androgen-deprivation therapy until they establish an androgen-independent growth mechanism."

"It looks as though androgens are important for prostate cancer," he summarized.

Nevertheless, "the available data suggest no association between exogenous or endogenous sources of testosterone and prostate cancer," he explained.

This appears to be good news, especially for Americans, where testosterone replacement therapy is commonly prescribed and is a $3 billion market, Dr Boyle said. It is not widely used in Europe, he noted.

Dr Boyle and his colleagues included two types of studies in their big summary study.

First, they assessed prospective cohort studies that reported data on the association between endogenous testosterone and prostate cancer.

They found 20 estimates derived from 18 epidemiologic studies that involved 5091 patients with prostate cancer and 11,930 control subjects. When these data were rolled into the meta-analysis, summary relative risk (SRR) for prostate cancer in the highest quantile of serum testosterone, compared with the lowest, was 0.98 (95% confidence interval [CI], 0.88 - 1.09). In other words, "there was no association between endogenous testosterone levels and the risk of prostate cancer," Dr Boyle summarized.

Second, the investigators assessed 24 randomized placebo-controlled trials of testosterone replacement therapy for symptomatic hypogonadism that reported data on PSA and prostate cancer cases.

The overall difference in PSA levels after the initiation of testosterone replacement therapy was 0.11 ng/mL (95% CI, –0.23 to 0.46), which was not statistically significant

When the analysis was restricted to a subgroup of 11 studies that used transdermal testosterone replacement therapy, the overall difference in PSA levels was 0.23 ng/mL (95% CI, –0.53 to 0.99), which, again, was not statistically significant.

The SRR for prostate cancer as an adverse effect of testosterone replacement therapy was 0.94 (95% CI, 0.37 - 2.40) and, thus, was not statistically significant.

"Testosterone replacement therapy for symptomatic hypogonadism does not appear to increase PSA levels nor the risk of prostate cancer development," write Dr Boyle and his coauthors in their study abstract.

Everything appears to be quite calm.

"Everything appears to be quite calm," said Dr Boyle about the overall findings.

Dr Boyle pointed out there have been other meta-analyses on this topics, but his team used the "best methodology" to date.

The confusion about the association between testosterone and prostate cancer stems, in part, from the fact that "if you take away testosterone from men with metastatic prostate cancer, their cancer will get better for a while," said Tobias Köhler, MD, MPH, from the Southern Illinois University School of Medicine in Carbondale, who moderated the press briefing. However, androgen deprivation does not improve survival, he also pointed out.

The old construct was that "prostate cancer was fire and testosterone was gasoline," said Dr Köhler. But a better analogy is that prostate cancer is a tree and testosterone is water, he said. "You need a certain amount of testosterone for prostate cancer to develop, but if you keep piling on more and more testosterone [water], the tree doesn't develop into a sequoia." This is known as the "saturation model," he explained.

Some primary care physicians and various specialists continue to be hesitant about prescribing testosterone to men because of the longstanding perceived risk for prostate cancer, he noted.

Partial funding for this study was provided by Repros Therapeutics. Dr Boyle has disclosed no relevant financial relationships. Dr Köhler reports financial ties to Abbott, AbbVie, American Medical Systems, Auxilium, and Coloplast.

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