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General News

# Testosterone Replacement Therapy Does Not Raise CV Risks

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Men who take testosterone replacement therapy (TRT) are not more likely to experience **cardiovascular events** or thromboembolism, but they are at higher risk of obstructive sleep apnea (OSA), according to a new study.

In fact, the study of 6844 male US military service members, retirees, and their dependents found that TRT was associated with a small but significant decrease in **cardiovascular** (CV) event risk, mainly due to a lower incidence of coronary artery disease (CAD), Alexander P. Cole, MD, of Brigham and Women's Hospital in Boston, and colleagues reported in a paper published online ahead of print in *BJU International*.

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Middle-aged men who use TRT are not at elevated risk of cardiovascular events.

The 2-year absolute risk of cardiovascular events was 8.2% for TRT users compared with 10.5% among controls (men not using TRT and who had no history of prostate cancer, cardiovascular disease, thromboembolism, or OSA). When the investigators looked at congestive heart failure, stroke, and CAD separately, CAD was the only end point with significantly lower risk among TRT users.

The 2-year absolute risk of thromboembolic events was 2% in the TRT group and 1.4% among controls, a non-significant difference between groups.

The 2-year absolute risk of OSA was significantly greater among TRT than controls (16.5% vs 12.7%). “While previously demonstrated in small prospective studies, this association has not previously been shown in a large national study such as this,” Dr Cole's team noted.

Possible explanations for the association include morphologic and neuromuscular changes to the airways, changes in metabolic requirements, and changes to the physiologic response to hypoxemia and hypercapnia, the investigators noted.

For the study, Dr Cole and his colleagues relied on data extracted from the Military Health System Data Repository, which includes inpatient and outpatient coding and pharmacy information for patients covered by the TRICARE benefit.

The study population consisted of 3422 TRT users and 3422 controls matched by birth year, race, marital status, military rank, comorbid conditions, and residence region. Men in both groups had a median age of 51 years.

With regard to study limitations, the authors pointed out that their study population, although geographically diverse, may differ from the civilian population, thus limiting the generalizability of their findings. Another limitation may be the possibility of unmeasured confounders. These include patient characteristics not captured by diagnostic codes, such as the specific etiology of low testosterone levels. In addition, they explained that because the data source consisted of International Classification of Diseases diagnostic and procedure codes obtained from the TRICARE insurance program, they lacked granular information on how OSA was diagnosed. They also were unable to analyze TRT doses. “This latter point is certainly a limitation, given some evidence for a dose-dependent effect of TRT.”

In the past few years, TRT use has increased dramatically in relatively healthy men without definitive testicular or pituitary disease, but with testosterone levels below reference ranges for young men, Dr Cole told *Renal & Urology News*. “This has led to a lot of controversy, especially given that many of the symptoms of hypogonadism such as fatigue, decreased libido, and adiposity are sometimes considered part of the ‘natural’ aging process, and also given some recent high-profile studies suggesting associations between testosterone replacement and medical side effects like heart disease.”

A problem with some of these studies, Dr Cole noted, is that they were disproportionately in older men, in some instances individuals with mobility impairments and other health problems.

“In terms of changing practice, I think that our results are probably consistent with a growing awareness that the cardiovascular and thrombotic risks of TRT may be less than once feared in younger, relatively healthy men,” Dr Cole said. “Regarding the modest increase in sleep apnea, this is important. The Endocrine Society Guidelines do include pre-existing OSA as a relative contraindication for TRT. Given our findings, I think that

this may be an increasingly important topic for men considering TRT.”

A collaboration between the Center for Surgery and Public Health at Brigham and Women's Hospital and the Uniformed Services University of the Health Sciences in Bethesda, Maryland, the study was funded by the Henry M. Jackson Foundation for the Advancement of Military Medicine.

## Reference

Cole AP, Hanske J, Jiang W, et al. [Impact of testosterone replacement therapy on thromboembolism, heart disease and obstructive sleep apnoea in men.](#) *BJU Int.* 2018; published online ahead of print.

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