J Sex Med. 2017 Nov;14(11):1307-1317. doi: 10.1016/j.jsxm.2017.09.010.

## Testosterone Therapy and Risk of Acute Myocardial Infarction in Hypogonadal Men: An Administrative Health Care Claims Study.

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## Abstract

BACKGROUND: There are some ongoing debates on the potential link between testosterone therapy (TT) and risk of acute myocardial infarction (MI).

AIM: To investigate the association between acute MI and TT use compared with non-use in men having documented hypogonadism (diagnostic International Classification of Diseases, Ninth Revision codes 257.2, 257.8, 257.9, 758.7) in patient claims records.

METHODS: This retrospective cohort study used a real-world US-based administrative health care claims database (MarketScan 2004-2013; Truven Health Analytics, Ann Arbor, MI, USA) to compare MI rates between TT-treated men and a cohort of untreated hypogonadal men matched by a calendar time-specific propensity score. Subgroup analyses were performed by route of administration, age, and prior cardiovascular disease (CVD).

OUTCOMES: Incidence rates of MI (per 1,000 person-years) and hazard ratio.

RESULTS: After 1:1 calendar time-specific propensity score matching, 207,176 TT-treated men and 207,176 untreated hypogonadal men were included in the analysis (mean age = 51.8 years). Incidence rates of MI were 4.20 (95% CI = 3.87-4.52) in the TT-treated cohort and 4.67 (95% CI = 4.43-4.90) in the untreated hypogonadal cohort. Cox regression model showed no significant association between TT use and MI when comparing TT-treated with untreated hypogonadal men overall (hazard ratio = 0.99, 95% CI = 0.89-1.09), by age, or by prior CVD. A significant association was observed when comparing a subgroup of injectable (short- and long-acting combined) TT users with untreated hypogonadal men (hazard ratio = 1.55, 95% CI = 1.24-1.93).

CLINICAL IMPLICATION: In this study, there was no association between TT (overall) and risk of acute MI.

STRENGTHS AND LIMITATIONS: Strengths included the use of a comprehensive real-world database, sophisticated matching based on calendar blocks of 6 months to decrease potential bias in this observational study, carefully chosen index dates for the untreated cohort to avoid immortal time bias, and implemented sensitivity analysis to further investigate the findings (stratification by administration route, age, and prior CVD). Key limitations included no information about adherence, hypogonadism condition based solely on diagnosis (no information on clinical symptoms or testosterone levels), lack of information on disease severity, inability to capture diagnoses, medical procedures, and medicine dispensing if corresponding billing codes were not generated and findings could contain biases or fail to generalize well to other populations.

CONCLUSION: This large, retrospective, real-world observational study showed no significant association between TT use and acute MI when comparing TT-treated with untreated hypogonadal men overall, by age, or by prior CVD; the suggested association between injectable TT and acute MI deserves further investigation. Li H, Mitchell L, Zhang X, et al. Testosterone Therapy and Risk of Acute Myocardial Infarction in Hypogonadal Men: An Administrative Health Care Claims Study. J Sex Med 2017;14:1307-1317.

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KEYWORDS: Hypogonadism; Myocardial Infarction; Testosterone Therapy