

Preoperative Testosterone Replacement Therapy Is Associated With Increased Complication Risk After Total Knee Arthroplasty: A Propensity-Matched Analysis of 13,250 Patients

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INTRODUCTION: Testosterone replacement therapy (TRT) is prescribed with increasing frequency in both men and women for hypogonadism, mood, fatigue, and metabolic support. While testosterone promotes musculoskeletal strength, it may also influence thrombosis, immune function, and bone metabolism in ways that complicate surgical recovery. Prior research on TRT in arthroplasty has focused on short-term outcomes and small cohorts. This study investigated whether preoperative TRT is associated with increased medical and periprosthetic complications following total knee arthroplasty (TKA) using a national database with long-term follow-up.

METHODS: A retrospective cohort analysis was performed using TriNetX, a national electronic health record database. Adult patients undergoing primary TKA before February 2020 with five years of follow-up were identified. Patients with a history of septic arthritis, osteonecrosis, or pathologic fractures were excluded. Individuals were stratified by TRT use in the year preceding surgery. Propensity score matching (1:1) was used to balance demographic and clinical variables, including age, sex, race, obesity, smoking, cardiovascular disease, diabetes, chronic kidney disease, and hypogonadism. A total of 6,625 patients remained in each cohort after matching. Outcomes included medical complications (readmission, PE, DVT, AKI, cardiac events, pneumonia, sepsis) at 90 days and 1 year, and periprosthetic complications (PJI, PPF, loosening, instability, revision) at 1 and 5 years. Statistical analyses included odds ratios and chi-square testing, with significance set at $P < 0.05$.

RESULTS: At 90 days, TRT users had higher rates of PE (1.6% vs. 1.2%, $P = 0.041$), pneumonia (3.3% vs. 1.9%, $P < 0.001$), AKI (4.2% vs. 2.9%, $P < 0.001$), and sepsis (1.9% vs. 1.1%, $P < 0.001$). At 1 year, TRT was associated with increased rates of PE (2.6% vs. 2.0%, $P < 0.015$), DVT (4.5% vs. 3.3%, $P < 0.001$), cardiac events (3.0% vs. 2.4%, $P = 0.018$), pneumonia (6.0% vs. 4.0%, $P < 0.001$), AKI (7.9% vs. 5.2%, $P < 0.001$), and sepsis (2.4% vs. 0.9%, $P < 0.001$). Periprosthetic complications at 1 year were also significantly elevated in TRT users, including PJI (2.4% vs. 0.9%, $P < 0.001$), periprosthetic fracture (0.7% vs. 0.2%, $P < 0.001$), aseptic loosening (1.0% vs. 0.5%, $P = 0.001$), instability (0.6% vs. 0.3%, $P = 0.020$), and revision surgery (1.6% vs. 1.0%, $P = 0.002$). These complications remained elevated at 5 years, with TRT patients experiencing higher rates of PJI (4.3% vs. 1.9%, $P < 0.001$), periprosthetic fracture (1.6% vs. 0.6%, $P < 0.001$), loosening (2.7% vs. 1.3%, $P < 0.001$), instability (1.7% vs. 0.8%, $P < 0.001$), and revision (4.1% vs. 2.7%, $P < 0.001$).

DISCUSSION AND CONCLUSION: This large-scale, propensity-matched study indicates that TRT use prior to TKA is associated with increased risk of medical complications (VTE, AKI, pneumonia, sepsis) and periprosthetic complications (infection, fracture, loosening, revision) both in the short and long term. These findings support the hypothesis that exogenous testosterone may promote thrombotic and immunosuppressive effects, impair osseointegration, and negatively influence long-term implant stability. A notable portion of TRT users were female, consistent with emerging off-label trends in postmenopausal women. As TKA volume rises and TRT prescribing expands, preoperative screening and risk stratification for TRT users should be considered. Further studies are needed to investigate optimal management strategies and causality behind these associations.

Outcome	TRT	Control	OR	95%CI	P
Readmission	17	11	1.6	0.8, 3.1	0.15
PE	11	7	1.6	0.7, 3.5	0.26
DVT	10	7	1.5	0.7, 3.0	0.28
AKI	10	7	1.5	0.7, 3.0	0.28
Cardiac Event	10	7	1.5	0.7, 3.0	0.28
Pneumonia	10	7	1.5	0.7, 3.0	0.28
Sepsis	10	7	1.5	0.7, 3.0	0.28

Outcome	TRT	Control	OR	95%CI	P
PJI	10	7	1.5	0.7, 3.0	0.28
PPF	10	7	1.5	0.7, 3.0	0.28
Loosening	10	7	1.5	0.7, 3.0	0.28
Instability	10	7	1.5	0.7, 3.0	0.28
Revision	10	7	1.5	0.7, 3.0	0.28

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