Angiotensin Receptor Blockers Are Associated with Lower Risk of Postoperative Complications Following Total Knee Arthroplasty Compared to ACE Inhibitors

Alireza Mirahmadi, Jad Jack Lawand, Kaveh Momenzadeh, Mohamad Javad Shariati, Ara Nazarian

INTRODUCTION:

Total knee arthroplasty (TKA) is a highly successful intervention for end-stage knee arthritis, yet postoperative complications—including infections, thromboembolic events, and prosthesis-related failures—remain major sources of patient morbidity and healthcare burden. Identifying modifiable risk factors to mitigate these outcomes is a growing clinical priority.

The renin-angiotensin-aldosterone system (RAAS) plays a central role in inflammation, vascular remodeling, and fibrosis. Angiotensin-converting enzyme inhibitors (ACEis) and angiotensin II receptor blockers (ARBs), widely used in cardiovascular and renal disease management, exhibit divergent downstream effects and may differentially influence postoperative healing and immune response. While both drug classes are routinely prescribed in TKA populations, their impact on surgical outcomes remains poorly defined.

This study aimed to evaluate whether perioperative use of ACEis or ARBs was associated with differences in postoperative complication rates following TKA. In addition to thromboembolic events, we assessed a wide spectrum of short- and long-term surgical outcomes and directly compared the impact of ACEis versus ARBs to identify potential class-specific effects.

METHODS:

We conducted a retrospective cohort study using the TriNetX Research Network, a federated database of deidentified electronic health records from U.S. healthcare systems. Adult patients undergoing primary TKA between 2005 and 2025 were identified via ICD-10 and CPT codes. Perioperative ACEi/ARB exposure was defined as an active prescription within 3 months before or after surgery.

Four matched comparisons were constructed: (1) ACEi/ARB vs. no ACEi/ARB, (2) ACEi vs. no ACEi, (3) ARB vs. no ARB, and (4) ACEi vs. ARB. Propensity score matching (1:1) was performed for each comparison, adjusting for age, sex, race, BMI, comorbidities (e.g., diabetes, hypertension), and concurrent medications.

Short-term (90-day) complications included: sepsis, DVT, PE, composite VTE, transfusion, emergency department (ED) visits, readmission, and surgical site infection (SSI). Long-term (2-year) complications included: periprosthetic fracture (PPFx), prosthetic joint infection (PJI), mechanical loosening, revision TKA, osteolysis, and articular wear.

Chi-square and t-tests were used to compare groups, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A two-sided P-value < 0.01 was considered statistically significant.

RESULTS:

Following matching, the study included 105,072 patients for short-term and 75,277 for long-term follow-up. Cohorts were well-balanced across all comparisons (mean age 66.6–67.0 years, 59% female, BMI ~33; $P > 0.05$).

Regarding short-term outcomes:, ARB use was associated with significantly lower rates of DVT (1.2% vs. 1.4%; OR 0.89, 95% CI 0.82–0.98; $P = 0.01$) and transfusion (1.6% vs. 1.8%; $P = 0.006$). ACEis showed no significant protective effects for these outcomes; in fact, a higher transfusion rate was observed in the ACEi group compared to controls (2.0% vs. 1.5%; OR 1.20, 95% CI 1.10–1.30; $P < 0.001$).

Regarding infections, ARB use was not associated with differences in rates of sepsis, postoperative infection, or surgical site infection (SSI) ($P > 0.05$). However, ACEi use was associated with a significantly higher rate of postoperative infection (1.1% vs. 0.8%; $P < 0.001$).

When compared directly, ARBs significantly outperformed ACEis in reducing the rates of DVT (OR 0.86; $P < 0.001$), transfusion (OR 0.79; $P < 0.001$), and postoperative infection (OR 0.83; $P < 0.001$) at 90 days.

Regarding long-term outcomes, ARB use was not associated with significant differences in rates of prosthetic joint infection (PJI), mechanical loosening, or revision TKA at 2-year follow-up. In contrast, ACEi users showed higher rates of PJI ($P = 0.02$) and revision TKA ($P < 0.001$) compared to controls.

Direct comparison between ARBs and ACEis revealed a lower risk of revision surgery in the ARB group (OR 0.91; $P = 0.02$), suggesting a possible long-term protective effect.

DISCUSSION AND CONCLUSION:

This large, matched cohort study reveals that perioperative use of ARBs is associated with a lower incidence of key postoperative complications following total knee arthroplasty, including reduced rates of DVT, transfusion, infection, and revision surgery. In contrast, ACE inhibitor use was linked to higher short- and long-term complication rates, particularly postoperative infection and prosthesis failure.

These findings suggest a class-specific protective effect of ARBs that may stem from their anti-inflammatory and endothelial-stabilizing properties, which are not shared to the same extent by ACE inhibitors. In clinical practice,

preferential use of ARBs in the perioperative period may benefit TKA patients who require RAAS blockade, particularly those at elevated thromboembolic or infectious risk.

Further prospective studies and mechanistic investigations are warranted to validate these results and to explore whether targeted RAAS modulation could be integrated into perioperative optimization strategies to improve surgical outcomes in orthopedic patients.